DocCode – SEQ.TXT

# SCORE Placeholder Sheet for IFW Content

Application Number: 15398479 Document Date: 01/04/2017

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

- Sequence Listing

At the time of document entry (noted above):

- USPTO employees may access SCORE content via eDAN using the Supplemental Content tab, or via the SCORE web page.
- External customers may access SCORE content via PAIR using the Supplemental Content tab.

Form Revision Date: August 26, 2013

FISH.
FISH & RICHARDSON

Street Address
Fish & Richardson P.C.
One Marina Park Drive
Boston, MA 02210-1878

Mail Address
P.O. Box 1022
Minneapolis, MN 55440-1022

617 542 5070 main
877 769 7945 fax

January 4, 2017

Attorney Docket No.: 38767-0015002

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Presented for filing is a new continuation patent application for prioritized examination of:

Inventor(s): RACHEL FRASER, PATRICK O'REILLY BROWN, JESSICA KARR, CELESTE HOLZ-SCHIETINGER AND ELYSIA COHN

Title: METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES

Enclosed are the following papers, including those required to receive a filing date under 37 C.F.R. § 1.53(b):

| | Pages |
|---|---|
| Specification | 66 |
| Claims | 4 |
| Abstract | 1 |
| Declaration | 5 |
| Drawing(s) | 5 |

Enclosures:

- Application Data Sheet, 10 pages.
- New disclosure information, including:
- Information disclosure statement, 1 page.
- PTO-1449, 18 pages.
- Nucleotide and/or amino acid sequence listing (.txt format)
- Power of Attorney, 2 pages.
- Certification and Request for Prioritized Examination (Track I), 2 pages
- Preliminary Amendment, 8 pages

FISH.
FISH & RICHARDSON

Commissioner for Patents
January 4, 2017

| | | | |
|---|---|---|---|
| Basic Filing Fee | | | $280 |
| Search Fee | | | $600 |
| Examination Fee | | | $720 |
| Publication fee | | | $0 |
| Track I processing fee | | | $140 |
| Track I prioritized examination fee | | | $4000 |
| Total Claims 30 | over 20 | **10 x $80** | $800 |
| Independent Claims 2 | over 3 | **0 x $420** | $0 |
| Fee for Multiple Dependent claims | | | $0 |
| Application size fee for each 50 pages over 100<br>Total Sheets: 78x .75 - 100/50 = 0x | | | $0 |
| **Total Filing fee** | | | **$6540** |

The filing fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply all charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 38767-0015002.

I hereby authorize the USPTO to communicate in response to email communications from the undersigned and practitioners under Customer No. 26191 in accordance with 37 CFR 1.33 and 37 CFR 1.34 concerning any subject matter of this application via email. I understand that a copy of these communications will be made of record in the application file. (MPEP 502.03).

FISH.
FISH & RICHARDSON

Commissioner for Patents
January 4, 2017

If this application is found to be incomplete, or if a telephone conference would otherwise be helpful, please call the undersigned at (617) 956-5972.

Please direct all correspondence to the following:

26191
PTO Customer Number

Respectfully submitted,

/Ian J.S. Lodovice, Reg. No. 59,749/

Ian J. Lodovice

Reg. No. 59,749
Enclosures
IJL/jxw
61421054.doc

Attorney Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | | Examiner | : | Unknown |
| Filed | : | | | | |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Please consider the references listed on the enclosed PTO-1449 Form.

Under 35 USC §120, this application relies on the earlier filing date of application serial number 14/797,006, filed on July 10, 2015. All references listed on the PTO-1449 were submitted to and/or cited by the Office in the prior application, and so copies of those references are not provided in this application.

This statement is being filed with the application. Apply any necessary charges or credits to deposit account 06-1050, referencing the above attorney docket number.

Please contact the undersigned if there are any questions regarding this statement.

Respectfully submitted,

Date: January 4, 2017_____ /Ian J.S. Lodovice, Reg. No. 59,749/_____

Ian J. Lodovice
Reg. No. 59,749

Customer Number 26191
Fish & Richardson P.C.
Telephone: (612) 335-5070
Facsimile: (877) 769-7945

61420931.doc

Attorney's Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | | Examiner | : | Unknown |
| Filed | : | | | | |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as indicated on the following pages.

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. – 30. (Canceled)

31. (New) A food flavor additive composition comprising:

a) an isolated heme-containing protein;

b) a sugar, sugar alcohol, sugar acid, or sugar derivative selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose, and mixtures of two or more thereof; and

c) a compound selected from cysteine, cystine, selenocysteine, thiamine, methionine, and mixtures of two or more thereof;

wherein the flavor additive composition contains no animal tissue derived components; and

wherein the flavor additive composition is packaged and is in the form of a liquid, a gel, an emulsion, a powder, or a bouillon cube.

32. (New) The food flavor additive composition of claim 31, wherein the heme-containing protein is present in an amount between about 0.01% and about 5% by weight.

33. (New) The food flavor additive composition of claim 31, wherein the heme-containing protein is selected from the group consisting of a androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a leghemoglobin, an erythrocruorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histoglobin,

a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.

34. (New) The food flavor additive composition of claim 31, wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.

35. (New) The food flavor additive composition of claim 31, wherein the food flavor additive composition is a powder, a liquid, an emulsion or a gel composition.

36. (New) The food flavor additive composition of claim 31, wherein the heme-containing protein is a plant, a mammalian, a yeast or filamentous fungi, or bacterial heme-containing protein.

37. (New) The food flavor additive composition of claim 31, further comprising one or more of an extract or hydrolysate selected from a vegetable protein hydrolysate, a soy protein hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate.

38. (New) The food flavor additive composition of claim 31, further comprising one or more of a compound selected from alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, maltodextrin, thiamine, IMP, GMP, lactic acid, and creatine.

39. (New) The food flavor additive composition of claim 31, further comprising one or more of an oil selected from coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.

40. (New) The food flavor additive composition of claim 31, further comprising one or more of albumin or a globulin.

41. (New) A food flavor additive composition prepared by a process of:

a) combining an isolated heme-containing protein; a sugar, sugar alcohol, sugar acid, or sugar derivative selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, and galactose, and mixtures of two or more thereof; and a compound selected from cysteine, cystine, selenocysteine, thiamine, methionine, and mixtures of two or more thereof, to form a heme flavor reaction mixture, and

b) heating the heme flavor reaction mixture to result in the food flavor additive composition;

wherein the food flavoring additive composition contains products no animal tissue derived components.

42. (New) The food flavor additive composition of claim 41, wherein the process further comprises heating the heme flavor reaction mixture to at least 150°C for at least 1 minute.

43. (New) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture has a meaty flavor and/or meaty aroma during the heating of step b) and/or the food flavoring additive composition has a meaty flavor and/or meaty aroma after the heating of step b).

44. (New) The food flavor additive composition of claim 42, wherein the food flavoring additive composition further comprises a compound selected from the group consisting of 2-methyl-furan, bis(2-methyl-3-furyl)disulfide, 2-pentyl-furan, 3,3'-dithiobis-2-methyl-furan, 2,5-dimethyl-pyrazine, 2-methyl-3-furanthiol, bis(2-methyl-4,5-dihydro-3-furyl) disulfide, dihydro-3-(2H)-thiophenone, 5-methyl-2-thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, 2-methyl-thiazole, dimethyl sulfide, decanal, 5-ethyldihydro-2(3H)-furanone, dihydro-5-pentyl-2(3H)-furanone, 2-octanone, 3,5-octadien-2-one, p-Cresol, and hexanoic acid.

45. (New) The food flavor additive composition of claim 44, wherein the compound is detectable in the headspace above the heme flavor reaction mixture during the heating of step b) or in the headspace above the food flavoring additive composition after the heating of step b).

46. (New) The food flavor additive composition of claim 41, where the process further comprises removing the heme-containing protein from the food flavoring additive composition after the heating in step b) of the heme flavor reaction mixture.

47. (New) The food flavor additive composition of claim 41, wherein the process further comprises altering the pH of the heme flavor reaction mixture prior to the heating of step b).

48. (New) The food flavor additive composition of claim 41, wherein the process further comprises dehydrating the heme flavor reaction mixture to a powder form after the heating of step b).

49. (New) The food flavor additive composition of claim 41, wherein the heme-containing protein is present in an amount between about 0.01% and about 5% by weight in the heme flavor reaction mixture.

50. (New) The food flavor additive composition of claim 41, wherein the heme-containing protein is selected from the group consisting of an androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a leghemoglobin, an erythrocruorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histoglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.

51. (New) The food flavor additive composition of claim 41, wherein the heme-containing protein comprises an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.

52. (New) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture further comprises one or more oils selected from coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.

53. (New) The food flavor additive composition of claim 41, further comprising an ingredient selected from an emulsifier and a gelling agent.

54. (New) The food flavor additive composition of claim 41, the process further comprising adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b).

55. (New) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture is an aqueous solution.

56. (New) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture is an oil-based mixture.

57. (New) The food flavor additive composition of claim 41, further comprising removing the heme-containing protein from the food flavor additive composition.

58. (New) The food flavor additive composition of claim 41, further comprising one or more of an extract or hydrolysate selected from a vegetable protein hydrolysate, a soy protein hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate, and or an albumin or a globulin.

59. (New) A process for imparting a meaty flavor and/or meaty aroma to a consumable food product, comprising:

adding to the consumable food product a food flavor additive composition of claim 31.

60. (New) The process of claim 59, further comprising heating the consumable food product.

## REMARKS

Claims 1-30 have been canceled without prejudice, and new claims 31-60 have been added. Written description support for these amendments is found throughout the original specification. No new matter has been added.

Applicant asks that all claims be examined in view of the amendment to the claims.

The fees for excess claims will be paid on the Electronic Filing System. In addition, please apply any other necessary charges or credits to Deposit Account 06-1050, referencing the above attorney docket number.

Respectfully submitted,

Date: January 4, 2017

/Ian J.S. Lodovice, Reg. No. 59,749/

Ian J. Lodovice
Reg. No. 59,749

Customer Number 26191
Fish & Richardson P.C.
Telephone: (617) 956-5972
Facsimile: (877) 769-7945

61421070.doc

# Electronic Patent Application Fee Transmittal

| | |
|---|---|
| **Application Number:** | |
| **Filing Date:** | |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Filer:** | Ian J.S. Lodovice/Judith Witzel |
| **Attorney Docket Number:** | 38767-0015002 |

Filed as Large Entity

**Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)**

| Description | Fee Code | Quantity | Amount | Sub-Total in USD($) |
|---|---|---|---|---|
| **Basic Filing:** | | | | |
| UTILITY APPLICATION FILING | 1011 | 1 | 280 | 280 |
| UTILITY SEARCH FEE | 1111 | 1 | 600 | 600 |
| UTILITY EXAMINATION FEE | 1311 | 1 | 720 | 720 |
| REQUEST FOR PRIORITIZED EXAMINATION | 1817 | 1 | 4000 | 4000 |
| **Pages:** | | | | |
| **Claims:** | | | | |
| CLAIMS IN EXCESS OF 20 | 1202 | 10 | 80 | 800 |
| **Miscellaneous-Filing:** | | | | |

| Description | Fee Code | Quantity | Amount | Sub-Total in USD($) |
|---|---|---|---|---|
| PROCESSING FEE, EXCEPT PROV. APPLS. | 1830 | 1 | 140 | 140 |
| **Petition:** | | | | |
| **Patent-Appeals-and-Interference:** | | | | |
| **Post-Allowance-and-Post-Issuance:** | | | | |
| **Extension-of-Time:** | | | | |
| **Miscellaneous:** | | | | |
| | | | **Total in USD ($)** | **6540** |

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 27969227 |
| **Application Number:** | 15398479 |
| **International Application Number:** | |
| **Confirmation Number:** | 2358 |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Customer Number:** | 26191 |
| **Filer:** | Ian J.S. Lodovice/Susan Williams |
| **Filer Authorized By:** | Ian J.S. Lodovice |
| **Attorney Docket Number:** | 38767-0015002 |
| **Receipt Date:** | 04-JAN-2017 |
| **Filing Date:** | |
| **Time Stamp:** | 17:39:01 |
| **Application Type:** | Utility under 35 USC 111(a) |

## Payment information:

| | |
|---|---|
| Submitted with Payment | yes |
| Payment Type | DA |
| Payment was successfully received in RAM | $6540 |
| RAM confirmation Number | 010517INTEFSW00004363061050 |
| Deposit Account | |
| Authorized User | |
| The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: | |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | TrackOne Request | CertReqTrack1.pdf | 177091<br>c56721963b17899d5c84f3c174277a09c0442e64 | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 2 | Application Data Sheet | ADS.pdf | 1823571<br>b99eb5f95b790a0ca4ad21e97b733d5f66a60b8f | no | 10 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 3 | | Application.pdf | 419944<br>d973e83a8d5dd641b4cddee089224b0c2a0b6517 | yes | 71 |

**Multipart Description/PDF files in .zip description**

| Document Description | Start | End |
|---|---|---|
| Specification | 1 | 66 |
| Claims | 67 | 70 |
| Abstract | 71 | 71 |

| | | | | | |
|---|---|---|---|---|---|
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 4 | Drawings-only black and white line drawings | Drawings.pdf | 628225<br>83a39d892c98f774c96c4736c62d6bc1bfc6cf1e | no | 5 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 5 | Sequence Listing (Text File) | SEQ.TXT | 47599 | no | - |

| | | | | | |
|---|---|---|---|---|---|
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 6 | Information Disclosure Statement (IDS) Form (SB08) | IDS1449.pdf | 269300<br>6df8face7aa689f08c7f8cdf3cef3be96fd408a4 | no | 18 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 7 | Oath or Declaration filed | Declaration.pdf | 2771256<br>870b7bdd48e52a3cff94f9073da077ac760a9d6f | no | 5 |
| **Warnings:** | | | | | |
| The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing | | | | | |
| **Information:** | | | | | |
| 8 | Power of Attorney | TransPOA.pdf | 846013<br>eb5b8f1a054da5638609fabff64fcfd8f721ce2e | no | 3 |
| **Warnings:** | | | | | |
| The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing | | | | | |
| **Information:** | | | | | |
| 9 | Transmittal of New Application | TransLtr.pdf | 134598<br>3172f034d467a4ef091d0632188e0b61c7935962 | no | 3 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 10 | Transmittal Letter | ids.pdf | 50364<br>ae4ea9a9a34b056bccb8061fa30994080e475e52 | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 11 | | PreliminAmend.pdf | 81894<br>58179ca2198b4548b17577934f080916613e4f04 | yes | 8 |
| | **Multipart Description/PDF files in .zip description** | | | | |
| | **Document Description** | | **Start** | **End** | |

| | | | | | |
|---|---|---|---|---|---|
| | Preliminary Amendment | | 1 | 1 | |
| | Claims | | 2 | 7 | |
| | Applicant Arguments/Remarks Made in an Amendment | | 8 | 8 | |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 12 | Fee Worksheet (SB06) | fee-info.pdf | 40337<br>331f0a544fea40a862041fcd6ca66d80b203c946 | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | **Total Files Size (in bytes):** | 7290192 | | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**<u>New Applications Under 35 U.S.C. 111</u>**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**<u>National Stage of an International Application under 35 U.S.C. 371</u>**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**<u>New International Application Filed with the USPTO as a Receiving Office</u>**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

**Doc Code: TRACK1.REQ**
**Document Description: TrackOne Request**

PTO/AIA/424 (03-14)

## CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e) (Page 1 of 1)

| | | | |
|---|---|---|---|
| First Named Inventor: | Rachel Fraser | Non provisional Application Number (if known): | |
| Title of Invention: | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | |

**APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.**

1. The processing fee set forth in 37 CFR 1.17(i)(1), the prioritized examination fee set forth in 37 CFR 1.17(c), and if not already paid, the publication fee set forth in 37 CFR 1.18(d) have been filed with the request. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.

2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims.

3. The applicable box is checked below:

**I. ☒ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)**

i. (a) The application is an original non provisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.

---OR---

(b) The application is an original non provisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.

ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, **or** the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.

**II. ☐ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)**

i. A request for continued examination has been filed with, or prior to, this form.
ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
iii. The application is an original non provisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

| | |
|---|---|
| Signature /Ian J.S. Lodovice, Reg. No. 59,749/ | Date 1/4/2017 |
| Name (Print/Typed) Ian J. Lodovice | Practitioner Registration Number 59,749 |

***Note:*** *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.**

☐ *Total of _____ forms are submitted.

61421053.doc

American LegalNet, Inc.
www.FormsWorkFlow.com

# Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant *(i.e.,* GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.



American LegalNet, Inc.
www.FormsWorkFlow.com

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| **Application Data Sheet 37 CFR 1.76** | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

## Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

## Inventor Information:

**Inventor 1** Remove

**Legal Name**

| Prefix | Given Name | Middle Name | Family Name | Suffix |
|---|---|---|---|---|
| | Rachel | | Fraser | |

**Residence Information (Select One)** ● US Residency Non US Residency Active US Military Service

| City | San Francisco | State/Province | CA | Country of Residence i | US |
|---|---|---|---|---|---|

**Mailing Address of Inventor:**

| | | | |
|---|---|---|---|
| Address 1 | 123 Connecticut Street | | |
| Address 2 | | | |
| City | San Francisco | State/Province | CA |
| Postal Code | 94107 | Country i | US |

**Inventor 2** Remove

**Legal Name**

| Prefix | Given Name | Middle Name | Family Name | Suffix |
|---|---|---|---|---|
| | Patrick | O'Reilly | Brown | |

**Residence Information (Select One)** ◉ US Residency Non US Residency Active US Military Service

| City | Stanford | State/Province | CA | Country of Residence i | US |
|---|---|---|---|---|---|

**Mailing Address of Inventor:**

| | | | |
|---|---|---|---|
| Address 1 | 76 Peter Coutts Circle | | |
| Address 2 | | | |
| City | Stanford | State/Province | CA |
| Postal Code | 94305 | Country i | US |

**Inventor 3** Remove

**Legal Name**

| Prefix | Given Name | Middle Name | Family Name | Suffix |
|---|---|---|---|---|
| | Jessica | | Karr | |

**Residence Information (Select One)** ◉ US Residency Non US Residency Active US Military Service

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| Application Data Sheet 37 CFR 1.76 | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

| City | San Francisco | State/Province | CA | Country of Residence i | US |
|---|---|---|---|---|---|

**Mailing Address of Inventor:**

| | | | |
|---|---|---|---|
| Address 1 | 456 Kansas Street | | |
| Address 2 | | | |
| City | San Francisco | State/Province | CA |
| Postal Code | 94107 | Country i | US |

**Inventor 4** Remove

**Legal Name**

| Prefix | Given Name | Middle Name | Family Name | Suffix |
|---|---|---|---|---|
| | Celeste | | Holz-Schietinger | |

**Residence Information (Select One)** ◉ US Residency Non US Residency Active US Military Service

| City | East Palo Alto | State/Province | CA | Country of Residence i | US |
|---|---|---|---|---|---|

**Mailing Address of Inventor:**

| | | | |
|---|---|---|---|
| Address 1 | 1159 Sage Street | | |
| Address 2 | | | |
| City | East Palo Alto | State/Province | CA |
| Postal Code | 94303 | Country i | US |

**Inventor 5** Remove

**Legal Name**

| Prefix | Given Name | Middle Name | Family Name | Suffix |
|---|---|---|---|---|
| | Elysia | | Cohn | |

**Residence Information (Select One)** ◉ US Residency Non US Residency Active US Military Service

| City | Sunnyvale | State/Province | CA | Country of Residence i | US |
|---|---|---|---|---|---|

**Mailing Address of Inventor:**

| | | | |
|---|---|---|---|
| Address 1 | 1351 Navarro Drive | | |
| Address 2 | | | |
| City | Sunnyvale | State/Province | CA |
| Postal Code | 94087 | Country i | US |

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

## Correspondence Information:

**Enter either Customer Number or complete the Correspondence Information section below.**
**For further information see 37 CFR 1.33(a).**

☐ **An Address is being provided for the correspondence Information of this application.**

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| **Application Data Sheet 37 CFR 1.76** | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

| | | | |
|---|---|---|---|
| **Customer Number** | 26191 | | |
| **Email Address** | apsi@fr.com | Add Email | Remove Email |

## Application Information:

| | | | |
|---|---|---|---|
| **Title of the Invention** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | |
| **Attorney Docket Number** | 38767-0015002 | **Small Entity Status Claimed** | ☐ |
| **Application Type** | Nonprovisional | | |
| **Subject Matter** | Utility | | |
| **Total Number of Drawing Sheets (if any)** | 5 | **Suggested Figure for Publication (if any)** | |

## Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

| Application number of the previously filed application | Filing date (YYYY-MM-DD) | Intellectual Property Authority or Country |
|---|---|---|
| | | |

## Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

## Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

| | | | |
|---|---|---|---|
| Please Select One: | ● Customer Number | US Patent Practitioner | ◯ Limited Recognition (37 CFR 11.9) |
| Customer Number | 26191 | | |

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| Application Data Sheet 37 CFR 1.76 | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

## Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

| | | | |
|---|---|---|---|
| Prior Application Status | Pending | | Remove |
| Application Number | Continuity Type | Prior Application Number | Filing or 371(c) Date (YYYY-MM-DD) |
| | Continuation of | 14797006 | 2015-07-10 |
| Prior Application Status | Pending | | Remove |
| Application Number | Continuity Type | Prior Application Number | Filing or 371(c) Date (YYYY-MM-DD) |
| 14797006 | Continuation of | PCTUS2014011347 | 2014-01-13 |
| Prior Application Status | Expired | | Remove |
| Application Number | Continuity Type | Prior Application Number | Filing or 371(c) Date (YYYY-MM-DD) |
| PCTUS2014011347 | Continuation of | 13941211 | 2013-07-12 |
| Prior Application Status | Expired | | Remove |
| Application Number | Continuity Type | Prior Application Number | Filing or 371(c) Date (YYYY-MM-DD) |
| PCTUS2014011347 | Claims benefit of provisional | 61908634 | 2013-11-25 |
| Prior Application Status | Expired | | Remove |
| Application Number | Continuity Type | Prior Application Number | Filing or 371(c) Date (YYYY-MM-DD) |
| PCTUS2014011347 | Claims benefit of provisional | 61751816 | 2013-01-11 |

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

## Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| **Application Data Sheet 37 CFR 1.76** | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

Remove

| Application Number | Country[i] | Filing Date (YYYY-MM-DD) | Access Code[i] (if applicable) |
|---|---|---|---|
| | | | |

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

## Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| Application Data Sheet 37 CFR 1.76 | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

## Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

**NOTE**: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

**1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)**

**A. Priority Document Exchange (PDX)** - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

**B. Search Results from U.S. Application to EPO** - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

**2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)**

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

**NOTE:** Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| Application Data Sheet 37 CFR 1.76 | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

## Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

**Applicant** 1 Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

| ● Assignee | Legal Representative under 35 U.S.C. 117 | Joint Inventor |
|---|---|---|
| Person to whom the inventor is obligated to assign. | Person who shows sufficient proprietary interest | |

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

| Organization Name | Impossible Foods Inc. | | |
|---|---|---|---|
| **Mailing Address Information For Applicant:** | | | |
| **Address 1** | 525 Chesapeake Drive | | |
| Address 2 | | | |
| **City** | Redwood City | **State/Province** | CA |
| **Country** | US | Postal Code | 94063 |
| Phone Number | | Fax Number | |
| Email Address | | | |

Additional Applicant Data may be generated within this form by selecting the Add button. Add

## Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| **Application Data Sheet 37 CFR 1.76** | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

**Assignee 1**

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

| Prefix | **Given Name** | Middle Name | **Family Name** | Suffix |
|---|---|---|---|---|
| | | | | |

**Mailing Address Information For Assignee including Non-Applicant Assignee:**

| | | | |
|---|---|---|---|
| **Address 1** | | | |
| Address 2 | | | |
| **City** | | **State/Province** | |
| **Country** i | | Postal Code | |
| Phone Number | | Fax Number | |
| Email Address | | | |

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add

## Signature:

Remove

**NOTE:** This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

| **Signature** | /Ian J.S. Lodovice, Reg. No. 59,749/ | | | Date (YYYY-MM-DD) | 2017-01-04 |
|---|---|---|---|---|---|
| First Name | Ian | Last Name | Lodovice | Registration Number | 59749 |

Additional Signature may be generated within this form by selecting the Add button. Add

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| **Application Data Sheet 37 CFR 1.76** | Attorney Docket Number | 38767-0015002 |
|---|---|---|
| | Application Number | |
| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | |

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

# Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1 The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3 A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent CooperationTreaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

# METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES

## CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. Application No. 14/797,006 filed on July 10, 2105 which is a continuation of and claims priority to PCT/US2014/011347 which claims priority to U.S. Application Serial No. 13/941,211, filed July 12, 2013, U.S. Application Serial No. 61/908,634, filed November 25, 2013, and to U.S. Application Serial No. 61/751,816, filed January 11, 2013, and is related to the following co-pending patent applications: Application Serial No. PCT/US12/46560; Application Serial No PCT/US12/46552; Application Serial No. 61,876,676, filed September 11, 2013; and Application Serial No. 61/751,818, filed January 11, 2013, all of which are incorporated herein by reference.

## TECHNICAL FIELD

This invention relates to food products and more particularly, to food products that include a highly conjugated heterocyclic ring complexed to iron such as a heme-cofactor and one or more flavor precursor molecules.

## BACKGROUND

Food is any substance that is either eaten or drunk by any animal, including humans, for nutrition or pleasure. It is usually of plant or animal origin, and can contain essential nutrients, such as carbohydrates, fats, proteins, vitamins, or minerals. The substance is ingested by an organism and assimilated by the organism's cells in an effort to produce energy, maintain life, or stimulate growth.

Food typically has its origin in a photosynthetic organism, such as a plant. Some food is obtained directly from plants, but even animals that are used as food sources are raised by feeding them food which is typically derived from plants.

In most cases, the plant or animal food source is fractionated into a variety of different portions, depending upon the purpose of the food. Often, certain portions of the

plant, such as the seeds or fruits, are more highly prized by humans than others and these are selected for human consumption, while other less desirable portions, such as the stalks of grasses, are typically used for feeding animals.

Current plant-based meat substitutes have largely failed to cause a shift to a vegetarian diet. Meat substitute compositions are typically extruded soy/grain mixtures which largely fail to replicate the experience of cooking and eating meat. Common limitations of plant-based meat substitute products are a texture and mouth-feel that are more homogenous than that of equivalent meat products. Furthermore, as these products must largely be sold pre-cooked, with artificial flavors and aromas pre-incorporated, they fail to replicate the aromas, flavors, and other key features, such as texture and mouth-feel, associated with cooking or cooked meat. As a result, these products appeal largely to a limited consumer base that is already committed to vegetarianism/veganism, but have failed to appeal to the larger consumer segment accustomed to eating meat. It would be useful to have improved plant-based meat substitutes which better replicate the aromas and flavors of meat, particularly during and/or after cooking.

## SUMMARY

Provided herein are methods and compositions for modulating the flavor and/or aroma profile of consumable food products, including animal- or non-animal (e.g., plant) based food products, or mixtures of animal- and non-animal-based food products. In some embodiments, the methods and compositions are useful for modulating the flavor and/or aroma profile of a consumable food product during and/or after the cooking process. In some embodiments, the methods and compositions are used to generate one or more chemical compounds that modulate the flavor and/or aroma profile of the consumable food product during and/or after the cooking process.

As provided herein, and without being bound by theory, certain characteristic meaty flavors and/or aromas (e.g., beefy, bacony, umami, savory, bloody, brothy, gravy, metallic, bouillon-like; see Tables 2, 7, and 11), including one or more specific chemical compounds associated with the same (see Tables 3, 8, 9, 12, 14, 16, or 17), are believed to be produced during the cooking process of a consumable food product by chemical

reaction of one or more flavor precursor molecules or compositions catalyzed by the presence of a highly conjugated heterocyclic ring complexed to an iron ion (e.g., a heme moiety; or a porphyrin; a porphyrinogen; a corrin; a corrinoid; a chlorin; a bacteriochorophyll; a corphin; a chlorophyllin; a bacteriochlorin; or an isobacteriochlorin moiety complexed to an iron ion). Such highly conjugated heterocycylic moieties include heterocyclic aromatic rings composed of one or more (2, 3, or 4 more ) pyrrole, pyrrole-like, and/or pyrroline subunits. The highly conjugated heterocyclic ring complexed to an iron ion is referred to herein as an iron complex. In some embodiments, the heme moiety can be a heme cofactor such as a heme moiety bound to a protein; a heme moiety bound to a non-proteinaceous polymer; a heme moiety bound to a solid support; or a heme moiety encapsulated in a liposome. In some embodiments, the flavors and/or aromas are not generated in the absence of the iron complex (e.g., in the absence of a ferrous chlorin) or are not generated in the absence of a heme-cofactor (e.g., in the absence of a heme-containing protein). Accordingly, as described herein, the iron complexes such as isolated chlorin-iron complexes or heme-cofactors (e.g., heme-containing proteins) can be used to generate meaty flavors and/or aromas in a variety of food products, such as during the cooking process.

Combining one or more iron complexes such as a heme-cofactor (e.g., a heme-containing protein, including, for example a plant-derived heme protein such as a plant leghemoglobin (legH)), with one or more flavor precursor molecules or compositions (see, e.g., Table 1 or Table 13) can generate or provide a range of savory and meaty aromas and tastes (see, e.g., Tables 2, 7, and/or 11) in a cooked consumable food product. Flavor precursor molecules or compositions can be added to the uncooked food product in purified form and/or can be derived from ingredients in the uncooked consumable food product that contain and/or are enriched with one or more of the particular flavor precursors or compositions, including, for example, yeast extract, vegetable oil, corn oil, soybean oil, palm fruit oil, palm kernel oil, safflower oil, flaxseed oil, rice bran oil, cottonseed oil, olive oil, canola oil, sunflower oil, coconut oil, mango oil, or an algal oil. The resultant flavor and/or aroma profile can be modulated by the type and concentration of the flavor precursors, the pH of the reaction, the length of cooking, the type and

amount of iron complex (e.g., a heme cofactor such as a heme-containing protein), the temperature of the reaction, and the amount of water activity in the product, among other factors.

One or more flavor precursor molecules or compositions can be added along with a iron complex (e.g., ferrous chlorophyllin or a heme cofactor such as a heme-containing protein), to an uncooked food product, before and/or during the cooking process, to give the cooked consumable food product a particular meaty taste and smell, for example, the taste and smell of beef, bacon, pork, lamb, or chicken. Consumable food products can be animal or non-animal based (e.g., plant) food products, or combinations of an animal and non-animal based food product. For example, a plant based veggie burger or an animal-based burger, such as a chicken burger, can be modified with the compositions and methods of the present disclosure to result in a burger having a cooked flavor and/or aroma profile that is more meat like, e.g., beef-like, lamb-like, pork-like, turkey-like, duck-like, deer-like, yak-like, bison-like or other desirable meat flavor.

Food products for use in the present disclosure include those that have an iron-complex (e.g., a heme cofactor such as a heme-containing protein), and one or more flavor precursor molecules included therein. The iron-complex such as a heme cofactor (e.g., a heme-containing protein) and the one or more flavor precursor molecules can be homogenously or heterogeneously included in the food products. A heme protein can be isolated and purified prior to inclusion in the food product. Non-limiting examples of consumable food products which can include an iron complex such as a heme-cofactor (e.g., a heme-containing protein) and one or more flavor precursor molecules include animal-based or non-animal (e.g., plant-based), or combinations of animal-based and non-animal-based, food products in the form of hot dogs, burgers, ground meat, sausages, steaks, filets, roasts, breasts, thighs, wings, meatballs, meatloaf, bacon, strips, fingers, nuggets, cutlets, or cubes.

Consumable food products for use in the present disclosure can be flavor additive compositions, e.g., for addition to another consumable food product before, during, or after its cooking process. A flavor additive composition can include an iron complex

such as a heme-cofactor (e.g., a heme-containing protein), and one or more flavor precursors.

A flavor additive composition can include a heme protein, e.g., an isolated and purified heme protein; such a flavor additive composition can be used to modulate the flavor and/or aroma profile of a consumable food product that comprises one or more flavor precursor molecules or compositions. A flavor additive composition can include one or more flavor precursor molecules or compositions; such a flavor additive composition can be used to modulate the flavor and/or aroma profile of a consumable food product that comprises the heme protein, e.g., an isolated and purified heme protein.

A flavor additive composition can be in the form, of but not limited to, soup or stew bases, bouillon, e.g., powder or cubes, flavor packets, or seasoning packets or shakers. Such flavor additive compositions can be used to modulate the flavor and/or aroma profile for a variety of consumable food products, and can be added to a consumable food product before, during, or after cooking of the consumable food product.

In some embodiments, a flavor additive composition such as one including an iron complex (e.g., ferrous chlorin or a heme protein) and one or more flavor precursors can be reacted (e.g., *in vitro*) with heating to generate a particular flavor and/or aroma profile of interest and the resultant product mixture can be added to the consumable food product of interest, which can then be eaten as-is or can be additionally modified, e.g., by additional cooking. In some embodiments, the iron complex can be removed from the resultant product mixture before adding the product mixture to the consumable food product of interest. For example, the iron complex can be removed from the product mixture using chromatographic techniques such as column chromatography, e.g., a column containing heme or iron-chlorin.

In some embodiments, the iron complex such as a heme-cofactor, e.g., a heme-protein, and the one or more flavor precursor flavor additive compositions can be soy-free, wheat-free, yeast-free, MSG-free, and free of protein hydrolysis products, and can taste meaty, highly savory, and without off odors or flavors.

In one aspect, this document features a food product that includes an iron complex such as a heme moiety, or a porphyrin, a porphyrinogen, a corrin, a corrinoid, a chlorin, a bacteriochorophyll, a corphin, a chlorophyllin, a bacteriochlorin, or an isobacteriochlorin moiety complexed to an iron ion and one or more flavor precursor molecules selected from the group consisting of glucose, fructose, ribose, arabinose, glucose-6-phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, inosine monophosphate (IMP), guanosine monophosphate (GMP), pyrazine, adenosine monophosphate (AMP), lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, vegetable oil, algal oil, corn oil, soybean oil, palm fruit oil, palm kernel oil, safflower oil, flaxseed oil, rice bran oil, cottonseed oil, sunflower oil, canola oil, olive oil, a free fatty acid, cysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, tyrosine, glutathione, an amino acid derivative, a protein hydrolysate, a malt extract, a yeast extract, and a peptone. The heme moiety can be a heme-containing protein, a heme moiety bound to a non-peptidic polymer; or a heme moiety bound to a solid support. The heme-containing protein can be a plant, mammalian, a yeast or filamentous fungi, or bacterial heme-containing protein. The food product can include two to one hundred, two to fifty flavor precursors, two to forty flavor precursors, two to thirty-five flavor precursors, two to ten flavor precursors, or two to six flavor precursors. In some embodiments, the one or more flavor precursor molecules are selected from the group consisting of glucose, ribose, cysteine, a cysteine derivative, thiamine, alanine, methionine, lysine, a lysine derivative, glutamic acid, a glutamic acid derivative, IMP, GMP, lactic acid, maltodextrin, creatine, alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, linoleic acid, and mixtures thereof. The heme-containing protein can be a non-symbiotic hemoglobin or a leghemoglobin (e.g., a plant leghemoglobin such as one from soybean, alfalfa, lupin, pea, cow pea, or lupin). The heme-containing protein can include an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs:1-26.

The heme-containing protein can be isolated and purified. The food product further can include a food-grade oil, a seasoning agent, a flavoring agent, a protein, a protein concentrate, an emulsifier, a gelling agent, or a fiber. The food product can be a meat substitute, a soup base, stew base, snack food, bouillon powder, bouillon cube, a flavor packet, or a frozen food product. Any of the food products can be free of animal products. The food product can be sealed within a packet or shaker.

This document also features a method for producing a flavor compound. The method can include combining an iron complex (e.g., a heme moiety, a porphyrin, a porphyrinogen, a corrin, a corrinoid, a chlorin, a bacteriochorophyll, a corphin, a chlorophyllin, a bacteriochlorin, or an isobacteriochlorin complexed to an iron) and one or more flavor precursor molecules to form a mixture, the one or more flavor precursor molecules selected from the group consisting of glucose, fructose, arabinose, ribose glucose-6-phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, inosine monophosphate (IMP), guanosine monophosphate (GMP), pyrazine, adenosine monophosphate (AMP), lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, vegetable oil, algal oil, corn oil, soybean oil, palm fruit oil, palm kernel oil, safflower oil, flaxseed oil, rice bran oil, cottonseed oil, canola oil, olive oil, sunflower oil, flaxseed oil, coconut oil, mango oil, a free fatty acid, cysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, tyrosine, glutathione, an amino acid derivative, a protein hydrolysate, a malt extract, a yeast extract, and a peptone; and heating the mixture to form one or more flavor compounds selected from the group consisting of phenylacetaldehyde, 1-octen-3-one, 2-n-heptylfuran, 2-thiophenecarboxaldehyde, 3-thiophenecarboxaldehyde, butyrolactone, 2-undecenal, pyrazine, methyl-, furfural, 2-decanone, pyrrole, 1-octen-3-ol, 2-acetylthiazole, (E)-2-octenal, decanal, benzaldehyde, (E)-2-nonenal, pyrazine, 1-hexanol, 1-heptanol, dimethyl trisulfide, 2-nonanone, 2-pentanone, 2-heptanone, 2,3-butanedione, heptanal, nonanal, 2-octanone, 1-octanol, 3-ethylcyclopentanone, 3-octen-2-one, (E,E)-2,4-heptadienal, (Z)-2-heptenal, 2-heptanone, 6-methyl-, (Z)-4-heptenal,

(E,Z)-2,6-nonadienal, 3-methyl-2-butenal, 2-pentyl-furan, thiazole, (E, E)-2,4-decadienal,, hexanoic acid, 1-ethyl-5-methylcyclopentene, (E,E)-2,4-nonadienal, (Z)-2-decenal, dihydro-5-pentyl-2(3H)-furanone, trans-3-nonen-2-one, (E,E)-3,5-octadien-2-one, (Z)-2-octen-1-ol, 5-ethyldihydro-2(3H)-furanone, 2-butenal, 1-penten-3-ol, (E)-2-hexenal, formic acid, heptyl ester, 2-pentyl-thiophene, (Z)-2-nonenal, 2-hexyl-thiophene, (E)-2-decenal, 2-ethyl-5-methyl-pyrazine, 3-ethyl-2,5-dimethyl-pyrazine, 2-ethyl-1-hexanol, thiophene, 2-methyl-furan, pyridine, butanal, 2-ethyl-furan, 3-methyl-butanal, trichloromethane, 2-methyl-butanal, methacrolein, 2-methyl-propanal, propanal, acetaldehyde, 2-propyl-furan, dihydro-5-propyl-2(3H)- furanone, 1,3-hexadiene, 4-decyne, pentanal, 1-propanol, heptanoic acid, trimethyl-ethanethiol, , 1-butanol, 1-penten-3-one, dimethyl sulfide, 2-ethyl furan, 2-pentyl-thiophene, 2-propenal, 2-tridecen-1-ol, 4-octene, 2-methyl thiazole,, methyl-pyrazine, 2-butanone, 2-pentyl-furan, 2-methyl-propanal, butyrolactone,, 3-methyl-butanal, methyl-thiirane, 2-hexyl-furan, butanal,, 2-methyl-butanal, 2-methyl-furan, furan, octanal, 2-heptenal, 1-octene, formic acid heptyl ester, 3-pentyl-furan, and 4-penten-2-one. The heme moiety can be a heme-containing protein, a heme moiety bound to a non-peptidic polymer; or a heme moiety bound to a solid support. The method can include combining cysteine, ribose, lactic acid, lysine, and/or thiamine with the heme-containing protein.

In another aspect, this document features a method for producing a flavor compound. The method includes combining an iron complex, such as a heme-containing protein, and one or more flavor precursor molecules to form a mixture, the one or more flavor precursor molecules selected from the group consisting of glucose, fructose, ribose, arabinose, glucose-6-phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, IMP, GMP, pyrazine, AMP, lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, vegetable oil, algal oil, corn oil, soybean oil, palm fruit oil, palm kernel oil, safflower oil, flaxseed oil, rice bran oil, cottonseed oil, olive oil, sunflower oil, canola oil, flaxseed oil, coconut oil, mango oil, a free fatty acid, methionine, cysteine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine,

proline, serine, tyrosine, glutathione, an amino acid derivative, a protein hydrolysate, a malt extract, a yeast extract, and a peptone; and heating the mixture to form one or more flavor compounds set forth in Tables 3, 8, or 9. For example, the flavor precursors can include cysteine, a sugar, and one or more other precursors.

This document also features a method for imparting a meat like flavor (e.g., beef-like, chicken like, pork-like, lamb-like, turkey-like, duck-like, deer-like, or bison-like) to a food product. The method includes contacting the food product with a flavoring composition, the flavoring composition comprising i) an iron complex, such as a heme moiety (e.g., a heme-containing protein); and ii) one or more flavor precursor molecules selected from the group consisting of glucose, fructose, ribose, arabinose, glucose-6-phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, IMP, GMP, pyrazine, AMP, lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, vegetable oil, algal oil, corn oil, soybean oil, palm fruit oil, palm kernel oil, safflower oil, flaxseed oil, rice bran oil, cottonseed oil, olive oil, sunflower oil, canola oil, flaxseed oil, coconut oil, mango oil, a free fatty acid, cysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, tyrosine, glutathione, an amino acid derivative, a protein hydrolysate, a malt extract, a yeast extract, and a peptone; wherein after heating the food product and the flavoring composition together, a meat like flavor (e.g., beef-like, chicken like, pork-like, lamb-like, turkey-like, duck-like, deer-like, or bison-like) is imparted to the food product. In some embodiments, the iron complex is removed from the food product. The flavoring composition further can include a seasoning agent, a flavoring agent, a protein, a protein concentrate, or an emulsifier. The flavoring composition can be sealed within a packet or shaker.

In another aspect, this document features a method of making a food product. The method includes combining an isolated heme-containing protein and one or more flavor precursor molecules to form a mixture, the one or more flavor precursor molecules selected from the group consisting of glucose, fructose, ribose, arabinose, glucose-6-

phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, IMP, GMP, pyrazine, AMP, lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, sunflower oil, coconut oil, canola oil, flaxseed oil, mango oil, a free fatty acid, cysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, tyrosine, glutathione, an amino acid derivative, a protein hydrolysate, a malt extract, a yeast extract, and a peptone; and heating the mixture.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and materials similar or equivalent to those described herein can be used to practice the invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims. The word “comprising” in the claims may be replaced by “consisting essentially of” or with “consisting of,” according to standard practice in patent law.

## DESCRIPTION OF THE DRAWINGS

FIG. 1 contains amino acid sequences of exemplary heme-containing proteins.

FIG. 2 is a bar graph of the beefiness rating of the meat replica with or without the Magic Mix, both samples in triplicate with 1% w/v LegH protein. Tasters rated beefiness on a scale from 1-7, with 1 being not beefy at all and 7 being exactly like ground beef.

## DETAILED DESCRIPTION

This document is based on methods and materials for modulating the taste and/or aroma profile of food products. As described herein, compositions containing one or more flavor precursors and one or more highly conjugated heterocyclic rings complexed to an iron (referred to herein as an iron complex) can be used to modulate the taste and/or aroma profile of food products. Such iron complexes include heme moieties or other highly conjugated heterocylic rings complexed to an iron ion (referred to as an iron complex). "Heme" refers to a prosthetic group bound to iron ($Fe^{2+}$ or $Fe^{3+}$) in the center of a porphyrin ring. Thus, an iron complex can be a heme moiety, or a porphyrin, porphyrinogen, corrin, corrinoid, chlorin, bacteriochorophyll, corphin, chlorophyllin, bacteriochlorin, or isobacteriochlorin moiety complexed to iron ion. The heme moiety that can be used to modulate the taste and/or aroma profile of food products can be a heme cofactor such as a heme-containing protein; a heme moiety bound to a non-peptidic polymer or other macromolecule such as a liposome, a polyethylene glycol, a carbohydrate, a polysaccharide, a cyclodextrin, a polyethylenimine, a polyacrylate, or derivatives thereof; a siderophore (i.e., an iron chelating compound); or a heme moiety bound to a solid support (e.g., beads) composed of a chromatography resin, cellulose, graphite, charcoal, or diatomaceous earth.

In some embodiments, the iron complexes catalyze some reactions and produce flavor precursors without heating or cooking. In some embodiments, the iron complex destabilizes upon heating or cooking and releases the iron, e.g., the protein is denatured, so flavor precursors can be generated.

Suitable flavor precursors include sugars, sugar alcohols, sugar derivatives, oils (e.g., vegetable oils), free fatty acids, alpha-hydroxy acids, dicarboxylic acids, amino acids and derivatives thereof, nucleosides, nucleotides, vitamins, peptides, protein hydrolysates, extracts, phospholipids, lecithin, and organic molecules. Non-limiting examples of such flavor precursors are provided in Table 1.

**TABLE 1**

**Flavor Precursor Molecules**

| |
|---|
| Sugars, sugar alcohols, sugar acids, and sugar derivatives: glucose, fructose, ribose, sucrose, arabinose, glucose-6-phosphate,fructose-6-phosphate, fructose 1,6-diphosphate, inositol, maltose, molasses, maltodextrin, glycogen, galactose, lactose, ribitol, gluconic acid and glucuronic acid, amylose, amylopectin, or xylose |
| Oils: coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, oil from bacteria or fungi |
| Free fatty acids: caprylic acid, capric acid, lauric acid, myristic acid, palmititic acid, palmitoleic acid, stearic, oleic acid, linoleic acid, alpha linolenic acid, gamma linolenic acid, arachidic acid, arachidonic acid, behenic acid, or erucic acid |
| Amino acids and derivatives thereof: cysteine, cystine, a cysteine sulfoxide, allicin, selenocysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, 5-hydroxytryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, or tyrosine |
| Nucleosides and Nucleotides: inosine , inosine monophosphate (IMP), guanosine, guanoside monophosphate (GMP), adenosine, adenosine monophosophate (AMP) |
| Vitamins: thiamine, vitamin C, Vitamin D, Vitamin B6, or Vitamin E |
| Misc: phospholipid, lecithin, pyrazine, creatine, pyrophosphate |
| Acids: acetic acid, alpha hydroxy acids such as lactic acid or glycolic acid, tricarboxylic acids such as citric acid, dicarboxylic acids such as succinic acid or tartaric acid |
| Peptides and protein hydrolysates: glutathione, vegetable protein hydrolysates, soy protein hydrolysates, yeast protein hydrolysates, algal protein hydrolysatess, |

| meat protein hydrolysates |
| --- |
| Extracts: a malt extract, a yeast extract, and a peptone |

In some embodiments, one flavor precursor or combinations of two to one hundred flavor precursors, two to ninety, two to eighty, two to seventy, two to sixty, or two to fifty flavor precursors are used. For example, combinations of two to forty flavor precursors, two to thirty-five flavor precursors, two to ten flavor precursors, or two to six flavor precursors can be used with the one or more iron complexes (e.g., heme co-factors such as a heme-containing proteins). For example, the one or more flavor precursors can be glucose, ribose, cysteine, a cysteine derivative, thiamine, lysine, a lysine derivative, glutamic acid, a glutamic acid derivative, alanine, methionine, IMP, GMP, lactic acid, and mixtures thereof (e.g., glucose and cysteine; cysteine and ribose; cysteine, glucose or ribose, and thiamine; cysteine, glucose or ribose, IMP, and GMP; cysteine, glucose or ribose, and lactic acid). For example, the one or more flavor precursors can be alanine, arginine, asparagine, aspartate, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, glucose, ribose, maltodextrin, thiamine, IMP, GMP, lactic acid, and creatine.

As used herein, the term “heme containing protein” can be used interchangeably with “heme containing polypeptide” or “heme protein” or “heme polypeptide” and includes any polypeptide that can covalently or noncovalently bind a heme moiety. In some embodiments, the heme-containing polypeptide is a globin and can include a globin fold, which comprises a series of seven to nine alpha helices. Globin type proteins can be of any class (e.g., class I, class II, or class III), and in some embodiments, can transport or store oxygen. For example, a heme-containing protein can be a non-symbiotic type of hemoglobin or a leghemoglobin. A heme-containing polypeptide can be a monomer, i.e., a single polypeptide chain, or can be a dimer, a trimer, tetramer, and/or higher order oligomers. The life-time of the oxygenated $Fe2^{+}$ state of a heme-containing protein can be similar to that of myoglobin or can exceed it by 10%, 20%, 30% 50%, 100% or more under conditions in which the heme-protein-containing consumable is manufactured,

stored, handled or prepared for consumption. The life-time of the unoxygenated $Fe^{2+}$ state of a heme-containing protein can be similar to that of myoglobin or can exceed it by 10%, 20%, 30% 50%, 100% or more under conditions in which the heme-protein-containing consumable is manufactured, stored, handled or prepared for consumption

Non-limiting examples of heme-containing polypeptides can include an androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, an erythrocruorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histoglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin (e.g., HbN or HbO), a truncated 2/2 globin, a hemoglobin 3 (e.g., Glb3), a cytochrome, or a peroxidase.

Heme-containing proteins that can be used in the compositions and food products described herein can be from mammals (e.g., farms animals such as cows, goats, sheep, pigs, ox, or rabbits), birds, plants, algae, fungi (e.g., yeast or filamentous fungi), ciliates, or bacteria. For example, a heme-containing protein can be from a mammal such as a farm animal (e.g., a cow, goat, sheep, pig, ox, or rabbit) or a bird such as a turkey or chicken. Heme-containing proteins can be from a plant such as *Nicotiana tabacum* or *Nicotiana sylvestris* (tobacco); *Zea mays* (corn), *Arabidopsis thaliana*, a legume such as *Glycine max* (soybean), *Cicer arietinum* (garbanzo or chick pea), *Pisum sativum* (pea) varieties such as garden peas or sugar snap peas, *Phaseolus vulgaris* varieties of common beans such as green beans, black beans, navy beans, northern beans, or pinto beans, *Vigna unguiculata* varieties (cow peas), *Vigna radiata* (Mung beans), *Lupinus albus* (lupin), or *Medicago sativa* (alfalfa); *Brassica napus* (canola); *Triticum sps.* (wheat, including wheat berries, and spelt); *Gossypium hirsutum* (cotton); *Oryza sativa* (rice); *Zizania sps*. (wild rice); *Helianthus annuus* (sunflower); *Beta vulgaris* (sugarbeet); *Pennisetum glaucum* (pearl millet); *Chenopodium sp.* (quinoa); *Sesamum sp.* (sesame); *Linum usitatissimum* (flax); or *Hordeum vulgare* (barley). Heme-containing proteins can be isolated from fungi such as *Saccharomyces cerevisiae*, *Pichia pastoris*, *Magnaporthe oryzae*, *Fusarium graminearum*, *Aspergillus oryzae*, *Trichoderma reesei*, *Myceliopthera thermophile*, *Kluyvera lactis*, or *Fusarium oxysporum*. Heme-containing proteins can be isolated from bacteria such as *Escherichia coli*, *Bacillus subtilis, Bacillus licheniformis,*

*Bacillus megaterium, Synechocistis sp., Aquifex aeolicus, Methylacidiphilum infernorum*, or thermophilic bacteria such as *Thermophilus*. The sequences and structure of numerous heme-containing proteins are known. See for example, Reedy, *et al.*, *Nucleic Acids Research*, 2008, Vol. 36, Database issue D307–D313 and the Heme Protein Database available on the world wide web at http://hemeprotein.info/heme.php.

For example, a non-symbiotic hemoglobin can be from a plant selected from the group consisting of soybean, sprouted soybean, alfalfa, golden flax, black bean, black eyed pea, northern, garbanzo, moong bean, cowpeas, pinto beans, pod peas, quinoa, sesame, sunflower, wheat berries, spelt, barley, wild rice, or rice.

Any of the heme-containing proteins described herein that can be used for producing food products can have at least 70% (e.g., at least 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99%, or 100%) sequence identity to the amino acid sequence of the corresponding wild-type heme-containing protein or fragments thereof that contain a heme-binding motif. For example, a heme-containing protein can have at least 70% sequence identity to an amino acid sequence set forth in FIG. 1, including a non-symbiotic hemoglobin such as that from *Vigna radiata* (SEQ ID NO:1), *Hordeum vulgare* (SEQ ID NO:5), *Zea mays* (SEQ ID NO:13), *Oryza sativa subsp. japonica (rice)* (SEQ ID NO:14), or *Arabidopsis thaliana* (SEQ ID NO:15), a Hell's gate globin I such as that from *Methylacidiphilum infernorum* (SEQ ID NO:2), a flavohemoprotein such as that from *Aquifex aeolicus* (SEQ ID NO:3), a leghemoglobin such as that from *Glycine max* (SEQ ID NO:4), *Pisum sativum* (SEQ ID NO:16), or *Vigna unguiculata* (SEQ ID NO:17), a heme-dependent peroxidase such as from *Magnaporthe oryzae*, (SEQ ID NO:6) or *Fusarium oxysporum* (SEQ ID NO:7), a cytochrome c peroxidase from *Fusarium graminearum* (SEQ ID NO:8), a truncated hemoglobin from *Chlamydomonas moewusii* (SEQ ID NO:9), *Tetrahymena pyriformis* (SEQ ID NO:10, group I truncated), *Paramecium caudatum* (SEQ ID NO:11, group I truncated), a hemoglobin from *Aspergillus niger* (SEQ ID NO:12), or a mammalian myoglobin protein such as the *Bos taurus* (SEQ ID NO:18) myoglobin, *Sus scrofa* (SEQ ID NO:19) myoglobin, *Equus caballus* (SEQ ID NO:20) myoglobin, a heme-protein from *Nicotiana benthamiana* (SEQ ID NO:21), *Bacillus subtilis* (SEQ ID NO:22), *Corynebacterium glutamicum* (SEQ ID

NO:23), Synechocystis PCC6803 (SEQ ID NO:24), Synechococcus sp. PCC 7335 (SEQ ID NO:25), or *Nostoc commune* (SEQ ID NO:26).

The percent identity between two amino acid sequences can be determined as follows. First, the amino acid sequences are aligned using the BLAST 2 Sequences (Bl2seq) program from the stand-alone version of BLASTZ containing BLASTP version 2.0.14. This stand-alone version of BLASTZ can be obtained from Fish & Richardson's web site (e.g., www.fr.com/blast/) or the U.S. government's National Center for Biotechnology Information web site (www.ncbi.nlm.nih.gov). Instructions explaining how to use the Bl2seq program can be found in the readme file accompanying BLASTZ. Bl2seq performs a comparison between two amino acid sequences using the BLASTP algorithm. To compare two amino acid sequences, the options of Bl2seq are set as follows: -i is set to a file containing the first amino acid sequence to be compared (e.g., C:\seq1.txt); -j is set to a file containing the second amino acid sequence to be compared (e.g., C:\seq2.txt); -p is set to blastp; -o is set to any desired file name (e.g., C:\output.txt); and all other options are left at their default setting. For example, the following command can be used to generate an output file containing a comparison between two amino acid sequences: C:\Bl2seq –i c:\seq1.txt –j c:\seq2.txt –p blastp –o c:\output.txt. If the two compared sequences share homology, then the designated output file will present those regions of homology as aligned sequences. If the two compared sequences do not share homology, then the designated output file will not present aligned sequences. Similar procedures can be following for nucleic acid sequences except that blastn is used.

Once aligned, the number of matches is determined by counting the number of positions where an identical amino acid residue is presented in both sequences. The percent identity is determined by dividing the number of matches by the length of the full-length polypeptide amino acid sequence followed by multiplying the resulting value by 100. It is noted that the percent identity value is rounded to the nearest tenth. For example, 78.11, 78.12, 78.13, and 78.14 is rounded down to 78.1, while 78.15, 78.16, 78.17, 78.18, and 78.19 is rounded up to 78.2. It also is noted that the length value will always be an integer.

It will be appreciated that a number of nucleic acids can encode a polypeptide having a particular amino acid sequence. The degeneracy of the genetic code is well known to the art; i.e., for many amino acids, there is more than one nucleotide triplet that serves as the codon for the amino acid. For example, codons in the coding sequence for a given enzyme can be modified such that optimal expression in a particular species (e.g., bacteria or fungus) is obtained, using appropriate codon bias tables for that species.

Heme-containing proteins can be extracted from the source material (e.g., extracted from animal tissue, or plant, fungal, algal, or bacterial biomass, or from the culture supernatant for secreted proteins) or from a combination of source materials (e.g., multiple plant species). Leghemoglobin is readily available as an unused by-product of commodity legume crops (e.g., soybean, alfalfa, or pea). The amount of leghemoglobin in the roots of these crops in the United States exceeds the myoglobin content of all the red meat consumed in the United States.

In some embodiments, extracts of heme-containing proteins include one or more non-heme-containing proteins from the source material (e.g., other animal, plant, fungal, algal, or bacterial proteins) or from a combination of source materials (e.g., different animal, plant, fungi, algae, or bacteria).

In some embodiments, heme-containing proteins are isolated and purified from other components of the source material (e.g., other animal, plant, fungal, algal, or bacterial proteins). As used herein, the term “isolated and purified” indicates that the preparation of heme-containing protein is at least 60% pure, e.g., greater than 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% pure. Without being bound by theory, isolating and purifying proteins can allow the food products to be made with greater consistency and greater control over the properties of the food product as unwanted material is eliminated. Proteins can be separated on the basis of their molecular weight, for example, by size exclusion chromatography, ultrafiltration through membranes, or density centrifugation. In some embodiments, the proteins can be separated based on their surface charge, for example, by isoelectric precipitation, anion exchange chromatography, or cation exchange chromatography. Proteins also can be separated on the basis of their solubility, for example, by ammonium sulfate precipitation, isoelectric precipitation, surfactants,

detergents or solvent extraction. Proteins also can be separated by their affinity to another molecule, using, for example, hydrophobic interaction chromatography, reactive dyes, or hydroxyapatite. Affinity chromatography also can include using antibodies having specific binding affinity for the heme-containing protein, nickel NTA for His-tagged recombinant proteins, lectins to bind to sugar moieties on a glycoprotein, or other molecules which specifically binds the protein.

Heme-containing proteins also can be recombinantly produced using polypeptide expression techniques (e.g., heterologous expression techniques using bacterial cells, insect cells, fungal cells such as yeast, plant cells such as tobacco, soybean, or *Arabidopsis*, or mammalian cells). In some cases, standard polypeptide synthesis techniques (e.g., liquid-phase polypeptide synthesis techniques or solid-phase polypeptide synthesis techniques) can be used to produce heme-containing proteins synthetically. In some cases, *in vitro* transcription-translation techniques can be used to produce heme-containing proteins.

The protein used in the consumable may be soluble in a solution. In some embodiments, the isolated and purified proteins are soluble in solution at greater than 5, 10, 15, 20, 25, 50, 100, 150, 200, or 250g/L.

In some embodiments, the isolated and purified protein is substantially in its native fold and water soluble. In some embodiments, the isolated and purified protein is more than 50, 60, 70, 80, or 90% in its native fold. In some embodiments, the isolated and purified protein is more than 50, 60, 70, 80, or 90% water soluble.

*Modulating Flavor and/or Aroma Profiles*

As described herein, different combinations of flavor precursors can be used with one or more iron complexes (e.g., a ferrous chlorin, a chlorin-iron complex, or a heme-cofactor such as a heme-containing protein or heme bound to a non-peptidic polymer such as polyethylene glycol or to a solid support) to produce different flavor and aroma profiles when the flavor precursors and iron complexes are heated together (e.g., during cooking). The resultant flavor and/or aroma profile can be modulated by the type and concentration of the flavor precursors, the pH of the reaction, the length of cooking, the

type and amount of iron complex (e.g., a heme-cofactor such as heme-containing protein, heme bound to non-peptidic polymer or macromolecule, or heme bound to a solid support), the temperature of the reaction, and the amount of water activity in the product, among other factors. In embodiments in which a heme moiety is bound to a solid support such as cellulose or a chromatography resin, graphite, charcoal, or diatomaceous earth, the solid support (e.g., beads) can be incubated with sugars and/or one or more other flavor precursors to generate flavors, and then the solid support with attached heme moiety can be re-used, i.e., incubated again with sugars and/or one or more other flavor precursors to generate flavors.

Table 2 provides non-limiting examples of flavor types that can be generated by combining one or more flavor precursors and one or more heme co-factors (e.g., heme-containing proteins). See also Tables 7 and/or 11.

**TABLE 2**

| **Flavor Types** | |
|---|---|
| beef | beef broth |
| beef dripping | cheesy |
| cold-cut deli meat | squash |
| bacon | sharp |
| meaty | fruity |
| brothy | floral |
| ramen | musty |
| egg | fried food |
| malty | caramel |
| bready | barbeque |
| sulfur | chocolate |
| fried chicken | sweet |
| browned | potato |
| pretzel | french toast |

| | |
|---|---|
| grassy | breadcrust |
| bloody | mushroom |
| broccoli | chicken |
| brothy | cumin |
| buttery | umami |
| metallic | raisin |
| yeasty | goaty |
| vegetable broth | |

Flavor and aroma profiles are created by different chemical compounds formed by chemical reactions between the heme co-factor (e.g., heme-containing protein) and flavor precursors. Gas chromatography–mass spectrometry (GCMS) can be used to separate and identify the different chemical compounds within a test sample. For example, volatile chemicals can be isolated from the head space after heating a heme-containing protein and one or more flavor precursors.

Table 3 provides non-limiting examples of compounds that can be produced. See also Tables 8, 9, 12, and/or 14.

**TABLE 3**

**Compounds Produced**

| | | |
|---|---|---|
| phenylacetaldehyde | 2-butenal, 2-ethyl- | 1,3-hexadiene |
| 1-octen-3-one | acetonitrile | 4-decyne |
| 2-n-heptylfuran | | pentanal |
| 2-thiophenecarboxaldehyde | (E)-2-Hexenal | 1-propanol |
| 3-thiophenecarboxaldehyde | 4-ethyl-phenol, | heptanoic acid |
| 1-octene | 3-octanone | ethanethiol |
| butyrolactone | styrene | 2-methyl-1-heptene |
| 2-undecenal | furan, 3-pentyl- | (E)-4-octene |
| propyl-cyclopropane | formic acid, heptyl ester | 2-methyl-2-heptene |
| methyl-pyrazine | (E)-2-Heptenal | pentanoic acid |
| 1-hydroxy-propanone | 6-methyl-5-hepten-2-one | nonanoic acid |
| acetic acid | n-caproic acid vinyl ester | 1,3-dimethyl-benzene |
| furfural | 2-ethyl-2-hexenal | |
| 2-decanone | 1-hepten-3-ol | toluene |

| | | |
|---|---|---|
| pyrrole | 1-ethyl-1-methyl-cyclopentane | 1-butanol |
| 1-octen-3-ol | 3-ethyl-2-methyl-1,3-hexadiene | 2,3,3-trimethyl-pentane |
| 2-acetylthiazole | 2-pentyl-thiophene | isopropyl alcohol |
| (E)-2-octenal | (Z)-2-nonenal | 2,2,4,6,6-pentamethyl-heptane |
| decanal | 2-n-octylfuran | phenol |
| benzaldehyde | 2-hexyl-thiophene | 1-penten-3-one |
| (E)-2-Nonenal | 4-cyclopentene-1,3-dione | dimethyl sulfide |
| pyrazine | 1-nonanol | thiirane |
| 1-pentanol | (E)-2-decenal | (E)-2-octen-1-ol |
| trans-2-(2-pentenyl)furan | 4-ethyl-benzaldehyde | 2,4-dimethyl-1-heptene |
| 1-hexanol | 1,7-octadien-3-ol | 1,3-bis(1,1-dimethylethyl)-benzene |
| 1-heptanol | octanoic acid | heptane |
| dimethyl trisulfide | 2-ethyl-5-methyl-pyrazine | 4,7-dimethyl-undecane |
| 2-nonanone | 3-ethyl-2,5-dimethyl-pyrazine | acetophenone |
| 2-pentanone | 1,3,5-cycloheptatriene | tridecane |
| 2-heptanone | 2-ethyl-1-hexanol | thiophosphoramide, s-methyl ester |
| 2,3-butanedione | 4-methyl-octanoic acid | 2-methyl-thiazole |
| heptanal | m-aminophenylacetylene | 3-(1-methylethoxy)-propanenitrile, |
| nonanal | benzene | 2,4-bis(1,1-dimethylethyl)-phenol |
| 2-octanone | thiophene | 3-ethyl-2,2-dimethyl-pentane |
| 2-butanone | 2-methyl-furan | 3-ethyl-pentane |
| octanal | pyridine | 2,3,4-trimethyl-pentane |
| 1-octanol | furan | 2,4,6-trimethyl-octane |
| 3-ethylcyclopentanone | butanal | 2,6-dimethyl-nonane |
| 8-methyl-1-undecene | 2-ethyl-furan | 2-hexyl-furan |
| 3-octen-2-one | carbon disulfide | 4-methyl-5-thiazoleethanol |
| 2,4-Heptadienal, (E,E)- | Furan, 2-hexyl-:2 | 4-penten-2-one |
| (Z)-2-heptenal | 3-methyl-butanal | 4-methylthiazole |
| 6-methyl-2-heptanone | 2-methyl-butanal | 2-methyl-3-pentanone |
| (Z)-4-heptenal | methacrolein | 2,3-pentanedione |
| (E,Z)-2,6-nonadienal | octane | (E)-2-tridecen-1-ol |

| | | |
|---|---|---|
| 3-methyl-2-butenal | ethanol | 2-thiophenemethanamine |
| 2-pentyl-furan | 2-methyl-propanal | (Z)-2-nonenal, |
| thiazole | acetone | methyl thiolacetate |
| (E,E)-2,4-decadienal | propanal | methyl ethanoate |
| hexanoic acid | methyl-thiirane | isothiazole |
| 1-ethyl-5-methylcyclopentene | acetaldehyde | 3,3-dimethyl-hexane |
| (E,E)-2,4-nonadienal | 2-propenal | 4-methyl-heptane |
| (Z)-2-decenal | 2-propyl-furan | 2,4-dimethyl-heptane |
| dihydro-5-pentyl-2(3h)-furanone | dihydro-5-propyl-2(3H)-furanone | 2,3,4-trimethyl-heptane |
| trans-3-nonen-2-one | dihydro-3-(2H)-thiophenone | 2-methyl-heptane |
| (E,E)-3,5-octadien-2-one | 2,2,6-trimethyl-decane | 2-methyl-3-furanthiol |
| (Z)-2-octen-1-ol | 3,3'-dithiobis[2-methyl-furan | 4-amino-1,2,5-oxadiazole-3-carbonitrile |
| 5-ethyldihydro-2(3h)-furanone | 1-heptene | 1,2-benzisothiazol-3(2H)-one |
| 2-butenal | 1,3-octadiene | 2-acetyl-propen-2-ol, |
| 1-penten-3-ol | 1-nonene | 1-decen-3-one |
| 1-(ethylthio)-2-(methylthio)-buta-1,3-diene | | |

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein is heated in the presence of ground chicken, to increase specific volatile flavor and odorant components typically elevated in beef. For example, propanal, butanal, 2-ethyl-furan, heptanal, octanal, trans-2-(2-pentenyl)furan, (Z)-2-heptenal, (E)-2-octenal, pyrrole, 2,4-dodecadienal, 1-octanal, (Z)-2-decenal, or 2-undecenal can be increased in the presence of the heme-containing protein, which can impart a more beefy flavor to the chicken.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein is heated in the presence of cysteine and glucose or other combinations of flavor precursors to provide a different profile of volatile odorants than when any subset of the three components are used individually. Volatile flavor components that are increased under these conditions include but are not limited to furan, acetone, thiazole, furfural, benzaldehyde, 2-pyridinecarboxaldehyde, 5-

methyl-2-thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, 3-thiophenemethanol and decanol. See, e.g., Tables 8 and 9. Under these conditions, cysteine and glucose alone or in the presence of iron salts such as ferrous glucanate produced a sulfurous, odor, but addition of heme-containing proteins reduced the sulfurous odor and replaced it with flavors including but not limited to chicken broth, burnt mushroom, molasses, and bread.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein is heated in the presence of cysteine and ribose to provide a different profile of volatile odorants. Heating in the presence of ribose created some additional compounds as compared to when a heme-containing protein and glucose were heated together. See Tables 8 and 9.

In some embodiments, an iron complex (e.g., a ferrous chlorophillin or a heme-cofactor such as a heme-containing protein) described herein can be heated in the presence of thiamine and a sugar to affect the formation of 5-Thiazoleethanol, 4-methyl-furan, 3,3'-dithiobis[2-methyl-furan, and/or 4-Methylthiazole. These compounds are known to be present in meat and have beefy, meaty taste notes.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein can be heated in the presence of a nucleotide such as inosine monophosphate and/or guanosine monophosphate to control the formation of flavor compounds such as (E)-4-octene, 2-ethyl-furan, 2-pentanone, 2,3-butanedione, 2-methyl-thiazole, methyl-pyrazine, tridecane, (E)-2-octenal, 2-thiopenecarboxaldehyde, and/or 3-thiopenecarboxaldehyde. These compounds are known to be present in meat and have a beefy, meaty, buttery, and or savory flavor notes.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein can be heated in the presence of lysine, a sugar such as ribose, and cysteine to control the formation of flavor compounds such as dimethyl trisulfide, nonanal, 2-pentyl thiophene, 2-nonenal furfural, 1-octanol, 2-nonenal, thiazole, 2-acetylthiazole, phenylacetaldehyde, and/or 2-acetylthiazole. These compounds are known to be present in meat and some have a beefy, meaty, and or savory flavor.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein can be heated in the presence of lactic acid, a sugar such as ribose, and cysteine to control the formation of the flavor compounds nonanal, thiazole, 2-acetylthiazole, and/or 8-methyl 1-undecene. These compounds are known to be present in meat and have beefy, savory, browned, bready, and malty notes.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein can be heated in the presence of amino acids, sugars such as glucose, ribose, and maltodextrin, lactic acid, thiamine, IMP, GMP, creatine, and salts such as potassium chloride and sodium chloride, to control the formation of flavor compounds such as 1,3-bis(1,1-dimethylethyl)-benzene, 2-methyl 3-furanthiol, and/or bis(2-methyl-4,5-dihydro-3-furyl) disulfide. These compounds are known to be present in meat and have beefy notes. See also Table 14.

In some embodiments, a particular type of heme-containing protein is chosen to control the formation of flavor compounds. See, for example, the results of Table 9, which shows that the addition of different types of heme-proteins (LegH, Barley, *B. myoglobin*, or *A. aeolicus*) in flavor reaction mixtures containing one or more flavor precursor compounds results in many of the same key meat flavors, including but not limited to pentanone, 3-methyl butanal, 2-methyl butanal, 2-heptenal, 1-octene, nonanal, 2-propenal, 2-decenal, 2-nonanone, 2-octanone, 2-tridecen-1-ol, 2-octanone, 2-octenal, 4-methyl-2-heptanone, octanal, 2-undecenal, butyrolactone, 1-octen-3-one, 3-methylheptyl acetate, and 2-pentyl-thiophene. These differences in flavor compounds can change the overall taste profile.

In some embodiments, an iron complex (e.g., a ferrous chlorin or a heme-cofactor such as a heme-containing protein) described herein and one or more flavor precursors can be reacted (e.g., *in vitro*) with heating to generate a particular flavor and/or aroma profile of interest and the resultant flavor additive composition can be added to the consumable food product of interest, which can then be eaten as-is or can be additionally modified, e.g., by additional cooking.

In some embodiments, any undesirable flavors can be minimized by deodorizing with activated charcoal or by removing enzymes such as lipoxygenases (LOX), which can be present in trace amounts when using preparations of plant proteins, and which can convert unsaturated triacylglycerides (such as linoleic acid or linolenic acid) into smaller and more volatile molecules. LOX are naturally present in legumes such as peas, soybeans, and peanuts, as well as rice, potatoes, and olives. When legume flours are fractionated into separate protein fractions, LOX can act as undesirable "time-bombs" that can cause undesirable flavors on aging or storage. Compositions containing plant proteins (e.g., from ground plant seeds) can be subjected to purification to remove LOX using, for example, an affinity resin that binds to LOX and removes it from the protein sample. The affinity resin can be linoleic acid, linolenic acid, stearic acid, oleic acid, propyl gallate, or epigalloccatechin gallate attached to a solid support such as a bead or resin. See, e.g., WO2013138793. In addition, depending on the protein component of the food product, certain combinations of antioxidants and/or LOX inhibitors can be used as effective agents to minimize off-flavor or off-odor generation especially in the presence of fats and oils. Such compounds can include, for example, one or more of β-carotene, α-tocopherol, caffeic acid, propyl gallate, or epigallocatechin gallate.

In some embodiments, specific flavor compounds, such as those described in Tables 3, 8, 9, 12, 14, 16, or 17 can be isolated and purified from the flavor additive composition. These isolated and purified compounds can be used as an ingredient to create flavors useful to the food and fragrance industry.

A flavor additive composition can be in the form, of but not limited to, soup or stew bases, bouillon, e.g., powder or cubes, flavor packets, or seasoning packets or shakers. Such flavor additive compositions can be used to modulate the flavor and/or aroma profile for a variety of food products, and can be added to a consumable food product before, during, or after cooking of the food product.

*Food Products*

Food products containing one or more flavor precursors and one or more heme-containing proteins can be used as a base for formulating a variety of additional food

products, including meat substitutes, soup bases, stew bases, snack foods, bouillon powders, bouillon cubes, flavor packets, or frozen food products. Meat substitutes can be formulated, for example, as hot dogs, burgers, ground meat, sausages, steaks, filets, roasts, breasts, thighs, wings, meatballs, meatloaf, bacon, strips, fingers, nuggets, cutlets, or cubes.

In addition, food products described herein can be used to modulate the taste and/or aroma profile of other food products (e.g., meat replicas, meat substitutes, tofu, mock duck or other gluten based vegetable product, textured vegetable protein such as textured soy protein, pork, fish, lamb, or poultry products such as chicken or turkey products) and can be applied to the other food product before or during cooking. Using the food products described herein can provide a particular meaty taste and smell, for example, the taste and smell of beef or bacon, to a non-meat product or to a poultry product.

Food products described herein can be packaged in various ways, including being sealed within individual packets or shakers, such that the composition can be sprinkled or spread on top of a food product before or during cooking.

Food products described herein can include additional ingredients including food-grade oils such as canola, corn, sunflower, soybean, olive or coconut oil, seasoning agents such as edible salts (e.g., sodium or potassium chloride) or herbs (e.g., rosemary, thyme, basil, sage, or mint), flavoring agents, proteins (e.g., soy protein isolate, wheat glutin, pea vicilin, and/or pea legumin), protein concentrates (e.g., soy protein concentrate), emulsifiers (e.g., lecithin), gelling agents (e.g., k-carrageenan or gelatin), fibers (e.g., bamboo filer or inulin), or minerals (e.g., iodine, zinc, and/or calcium).

Food products described herein also can include a natural coloring agent such as turmeric or beet juice, or an artificial coloring agent such as azo dyes, triphenylmethanes, xanthenes, quinines, indigoids, titanium dioxide, red #3, red #40, blue #1, or yellow #5.

Food products described herein also can include meat shelf life extenders such as carbon monoxide, nitrites, sodium metabisulfite, Bombal, vitamin E, rosemary extract, green tea extract, catechins and other anti-oxidants.

Food products described herein can be free of animal products (e.g., animal heme-containing proteins or other animal products).

In some embodiments, the food products can be soy-free, wheat-free, yeast-free, MSG-free, and/or free of protein hydrolysis products, and can taste meaty, highly savory, and without off odors or flavors.

*Assessment of Food Products*

Food products described herein can be assessed using trained human panelists. The evaluations can involve eyeing, feeling, chewing, and tasting of the product to judge product appearance, color, integrity, texture, flavor, and mouth feel, etc. Panelists can be served samples under red or under white light. Samples can be assigned random three-digit numbers and rotated in ballot position to prevent bias. Sensory judgments can be scaled for "acceptance" or "likeability" or use special terminology. For example, letter scales (A for excellent, B for good, C for poor) or number scales may be used (1 = dislike, 2 = fair, 3 = good; 4 = very good; 5=excellent). A scale can be used to rate the overall acceptability or quality of the food product or specific quality attributes such beefiness, texture, and flavor. Panelists can be encouraged to rinse their mouths with water between samples, and given opportunity to comment on each sample.

In some embodiments, a food product described herein can be compared to another food product (e.g., meat or meat substitute) based upon olfactometer readings. In various embodiments, the olfactometer can be used to assess odor concentration and odor thresholds, odor suprathresholds with comparison to a reference gas, hedonic scale scores to determine the degree of appreciation, or relative intensity of odors.

In some embodiments, an olfactometer allows the training and automatic evaluation of expert panels. In some embodiments, a food product described herein causes similar or identical olfactometer readings. In some embodiments, the differences between flavors generated using the methods of the invention and meat are sufficiently small to be below the detection threshold of human perception.

In some embodiments, volatile chemicals identified using GCMS can be evaluated. For example, a human can rate the experience of smelling the chemical

responsible for a certain peak. This information could be used to further refine the profile of flavor and aroma compounds produced using a heme-containing protein and one or more flavor precursors.

Characteristic flavor and fragrance components are mostly produced during the cooking process by chemical reactions molecules including amino acids, fats and sugars which are found in plants as well as meat. Therefore, in some embodiments, a food product is tested for similarity to meat during or after cooking. In some embodiments human ratings, human evaluation, olfactometer readings, or GCMS measurements, or combinations thereof, are used to create an olfactory map of the food product. Similarly, an olfactory map of the food product, for example, a meat replica, can be created. These maps can be compared to assess how similar the cooked food product is to meat.

In some embodiments, the olfactory map of the food product during or after cooking is similar to or indistinguishable from that of cooked or cooking meat. In some embodiments the similarity is sufficient to be beyond the detection threshold of human perception. The food product can be created so its characteristics are similar to a food product after cooking, but the uncooked food product may have properties that are different from the predicate food product prior to cooking.

These results will demonstrate that the compositions of the invention are judged as acceptably equivalent to real meat products. Additionally, these results can demonstrate that compositions of the invention are preferred by panelist over other commercially available meat substitutes. So, in some embodiments the present invention provides for consumables that are significantly similar to traditional meats and are more meat like than previously known meat alternatives.

The invention will be further described in the following examples, which do not limit the scope of the invention described in the claims.

## EXAMPLES

### Example 1: Addition of heme-protein increases beefy qualities of replica burgers

Replica burgers containing the ingredients in Table 4 and the flavor precursors cysteine (10 mM), glutamic acid (10 mM), glucose (10 mM), and thiamine (1 mM) were prepared. Water was added to make up the balance. See, for example, U.S. Provisional Application No. 61/751,816, filed January 11, 2013. Control burgers were prepared as in Table 4 with precursors cysteine (10 mM), glutamic acid (10 mM), glucose (10 mM), and thiamine (1 mM) except LegH was omitted.

After cooking for 5 minutes at 150 C, the replica burgers were evaluated by a trained sensory panel. Panelists were served samples under red lights and each panelist individually evaluated the samples. Samples were assigned a random three-digit number and rotated in ballot position to prevent bias. Panelists were asked to evaluate cooked replica burger samples on multiple flavor, aroma, taste, texture and appearance attributes including but not limited to: beefiness, bloody quality, savory quality, and overall acceptability using a 7-point scale from 1=dislike extremely, to 7=like extremely. Panelists were encouraged to rinse their mouths with water between samples, and to fill out a survey to record their evaluation of each sample.

When replica burgers containing the LegH were compared to the control replica burgers without LegH, the samples containing LegH were rated significantly beefier, bloodier, more savory, and overall preferred compared to those that did not include LegH. See Table 5.

**TABLE 4**

**Replica Burger Ingredients**

| Replica burger | % precooked w/w |
|---|---|
| Pea vicilin | 3.86 |
| Soy protein concentrate (SPC) | 2.52 |
| Bamboo fiber | 0.34 |

| | |
|---|---|
| NaCl | 0.54 |
| Pea legumin | 2 |
| Soy Protein Isolate (SPI) (Solae, St. Louis, MO) | 4.68 |
| Wheat gluten | 4.68 |
| Coconut oil | 15 |
| Soy lecithin | 0.1 |
| k-carrageenan | 1 |
| LegH | 1 |

**TABLE 5**

**Sensory evaluation of replica burger with Heme**

| Attribute | Beef 20/80 | No Heme | 1% Heme |
|---|---|---|---|
| Beefyness | | | |
| mean | 5.33 | 1.30 | 3.20 |
| STDEV | 1.58 | 0.67 | 0.79 |
| Bloody | | | |
| mean | 4.00 | 1.10 | 2.78 |
| STDEV | 1.32 | 0.32 | 1.64 |
| Savory | | | |
| mean | 4.67 | 3.00 | 5.10 |
| STDEV | 1.22 | 1.63 | 0.57 |

**Example 2: Replica burgers with a flavor precursor mixture taste beefy and bloody**

Replica burgers containing a flavor precursor mixture of glucose, cysteine, thiamine, and glutamic acid and 1% LegH pre-cooked w/w (see Table 4) were prepared as described in Example 1, and evaluated by a trained sensory panel after the burgers were cooked for 5 minutes at 150 C. Control burgers included LegH and all other ingredients except for the flavor precursor mixture.

Panelists were asked to evaluate the samples overall improvement in taste and descriptively analyze each sample using a 5-point scale from 1=dislike extremely, to 5=like extremely. Panelists were encouraged to rinse their mouths with water between samples, and to fill out a survey to record their evaluation of each sample. The replicate burgers which included LegH and the flavor precursor mixture were described as having bouillon, gravy, meaty, bloody, savory, and beefy notes on taste, and were preferred to the same replica burger with LegH but no added flavor precursor mixture. See, Table 6

**TABLE 6**

**Improvement of overall taste with precursors added to LegH burgers**

| | with precursors | without precursors |
|---|---|---|
| Average | 3.5 | 1.8 |
| STDV | 0.6 | 0.5 |

**Example 3: Replica burgers with flavor precursor mixture resulting in a bacon taste**

Replica burgers (see Table 4) were cooked with different precursor mixes (see Table 7) and 1% LegH and evaluated by a trained sensory panel after the burgers were cooked for 5 minutes at 150 C. Control burgers contained LegH and all of the other ingredients except for the flavor precursors. Panelists were asked to evaluate each sample and descriptively analyze of each sample. 5-point scale from 1=dislike extremely, to 5=like extremely. Panelists were encouraged to rinse their mouths with water between samples, and to fill out a survey to record their evaluation of each sample. A replica burger with a precursor mixture of 10 mM glucose, 10 mM ribose, 10 mM cysteine, 1 mM thiamine, 1 mM glutamic acid, 1 mM GMP, and LegH was described as having a bacon aroma and taste, and overall meatiness, savory quality, a very umami quality, a brothy quality, and slight beefy notes. See Table 7 for a summary of the flavor description for the various combinations of flavor precursors and heme-containing protein.

**TABLE 7**

**Flavors generated by addition of precursors to LegH (1 %)**

| Precursor (concentration) | | | | | | Flavor Description |
|---|---|---|---|---|---|---|
| | ribose (10 mM) | cysteine (10 mM) | | | | some kind of cold-cut/sliced deli meat |
| | ribose (10 mM) | cysteine (10 mM) | | | IMP (2 mM) | bread crust with beef drippings, sweet, grassy, umami |
| | ribose (10 mM) | cysteine (10 mM) | | | lactic acid (1 mM) | bready, malty, browned, breadcrust |
| | ribose (10 mM) | cysteine (10 mM) | | | lysine (5 mM) | savory, beefy, little grassy, brothy, bread |
| | ribose (10 mM) | cysteine (10 mM) | | | alanine (5 mM) | savory, weak beefy, brothy, little metallic |
| | ribose (10 mM) | cysteine (10 mM) | | | I+G (2 mM) | savory, weak beefy, brothy, sweet |
| | ribose (10 mM) | cysteine (10 mM) | | | methionine | cooked potato |
| | ribose (10 mM) | cysteine (10 mM) | | glutamic acid (5 mM) | | little meaty, pretzel, brothy, savory, sweet, chocolate |
| glucose (10 mM) | ribose (10 mM) | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | | slight beefy, browned, grasssy, |
| glucose (10 mM) | ribose (10 mM) | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | IMP (2 mM) | bacon, very umami, savory, brothy, slight beef |
| glucose (10 mM) | | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | | beef jerky, bloody, meaty, brothy |
| glucose (10 mM) | | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | lactic acid (1 mM) | savory, beefy, bloody, meaty, savory, gravy |



Motif Exhibit 1002, Page 63 of 1290

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096

| | | | | | | |
|---|---|---|---|---|---|---|
| glucose (10 mM) | | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | lysine (5 mM) | roast beef |
| glucose (10 mM) | | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | alanine (5 mM) | boiled beef, sweet |
| glucose (10 mM) | | cysteine (10 mM) | thiamine (2 mM) | glutamic acid (5 mM) | I+G (2 mM) | beefy with a sulfury note |
| glucose (10 mM) | | cysteine (10 mM) | | | I+G (2 mM) | sweet, malty, umami, meaty |
| glucose (10 mM) | | | | | I+G (2 mM) | savory, roast beef, grassy |
| glucose (10 mM) | | | | glutamic acid (5 mM) | | umami, savory, meaty, sweaty, fermented |

**Example 4: Type of sugar modulates flavor compounds created in the presence of Hemeprotein**

The addition of different sugars to flavor reaction mixtures containing a hemeprotein and one or more flavor precursor compounds resulted in distinct differences in the flavor compounds generated and the overall flavor profile. LegH heme protein at 1% pre-cooked w/w/ was mixed with cysteine (10 mM) and glucose (20 mM) at pH 6 in phosphate buffer to form a flavor reaction mixture and heated to 150 C for 3 minutes; this reaction created flavor compounds known to be present in meat; *see* Table 8. Similarly, a flavor reaction mixture made when LegH heme protein at 1% was mixed with cysteine (10 mM) and ribose (20 mM) at pH 6 and heated to 150 C for 3 minutes created flavor compounds known to be in meat; *see* Table 8.

The characteristic flavor and fragrance components were mostly produced during the cooking process when the flavor precursor molecules reacted with the heme-protein. Gas chromatography–mass spectrometry (GCMS) is a method that combines the features of gas-liquid chromatography and mass spectrometry to separate and identify different substances within a test sample. Samples were evaluated by GCMS to identify the flavor compounds generated after heating and also evaluated for their sensory profiles. Volatile chemicals were isolated from the head space around the flavor reactions. The profile of the volatile chemicals in the headspace around the flavor reaction mixtures is shown in Table 8. In particular, the use of ribose created some additional compounds as compared to glucose, as shown in Table 8.

Notably, the control mixtures of cysteine with ribose or glucose heated in the absence of the LegH heme-protein did not generate the same set of flavor compounds. The flavor reaction mixtures containing LegH also were evaluated by a blinded trained sensory panel, which described the samples with ribose as having beefy, savory, brothy, and gravy-like notes, and the samples with glucose as savory, bloody, metallic, raw meat, and bouillon-like.

**TABLE 8**

**Flavor compounds generated with cysteine, LegH, and either glucose or ribose in the flavor reaction mixture.**

| LegH 1% | | |
|---|---|---|
| Compounds created | cysteine (10 mM), glucose (20 mM) | cysteine (10 mM), ribose (20 mM) |
| benzaldehyde | X | X |
| 2-butanone | X | X |
| dimethyl trisulfide | X | X |
| 2-pentyl-furan | X | X |
| 2-methyl-propanal | X | X |
| thiazole | X | X |
| butyrolactone | X | X |
| 2-acetylthiazole | X | X |
| pentanal | X | X |
| 3-methyl-butanal | X | X |
| methyl-thiirane | X | X |
| nonanal | X | X |
| heptanal | X | X |
| 2,3-butanedione | X | X |
| 1,3,5-cycloheptatriene | X | X |
| propyl-cyclopropane | X | X |
| 2-hexyl-furan | X | X |
| butanal | X | X |
| 2-methyl-butanal | X | X |
| 2-ethyl-furan | | X |
| 2-octanone | X | X |
| propanal | X | X |

| | | |
|---|---|---|
| trichloromethane | X | |
| 2-methyl-furan | X | X |
| furan | X | X |
| pyrazine | X | X |
| thiophene | X | X |
| 1,3-dimethyl-benzene | X | X |
| octane | | X |
| octanal | X | X |
| thiazole | X | X |
| 2-pentanone | | X |
| furfural | X | X |
| 2-nonanone | X | X |
| (Z)-2-heptenal | X | X |
| (E)-2-heptenal | X | X |
| 1-octene | X | X |
| formic acid, heptyl ester | X | X |
| 2-pentyl-thiophene | | X |
| 1-octen-3-one | X | X |
| 3-pentyl-furan | X | X |
| 2-propenal | | X |
| (E)-2-tridecen-1-ol | | X |
| benzene | | X |
| (E)-4-octene | | X |
| 1-penten-3-one | | X |
| 4-penten-2-one | X | X |
| 2-methyl-thiazole | | X |
| methyl-pyrazine | | X |
| trans-2-(2-pentenyl)furan | | X |
| 3-ethylcyclopentanone | | X |

| | | |
|---|---|---|
| pyrrole | X | X |
| 2-thiophenecarboxaldehyde | | X |
| 3-thiophenecarboxaldehyde | | X |

**Example 5: Heme-protein in the presence of thiamine affects the production of certain flavor compounds**

The addition of thiamine in a flavor reaction mixtures with a heme protein and other flavor precursors affected the formation of 5-Thiazoleethanol, 4-methyl-furan, 3,3'-dithiobis[2-methyl-thiazole, and 4-methylthiazole. These compounds are known to be present in meat and have beefy, meaty taste notes.

Flavor reaction mixtures at pH 6 containing LegH (1%), cysteine (10 mM), thiamine (1 mM), either glucose or ribose (20 mM), and with or without glutamic acid (10 mM) were prepared and subsequently heated to 150 C for 3 minutes. These flavor reaction samples then were evaluated by GCMS for the flavor compounds generated and evaluated by a trained panel for their sensory profiles. Volatile chemicals were isolated from the head space around the flavor reactions. GCMS showed 4-methyl-5-thiazoleethanol, 3,3'-dithiobis[2-methyl]-furan, and 4-methylthiazole compounds were created by a mixture of LegH with thiamine, a sugar (either glucose or ribose), and cysteine. The same flavor reaction mixtures without thiamine did not generate these compounds; additionally these compounds were not generated when heme-proteins were not present in the flavor reaction mixtures.

The flavor reaction samples also were evaluated by a blinded trained sensory panel, which described the samples with the addition of thiamine as more complex in taste and more beefy, meaty, and savory.

**Example 6: Heme-proteins with nucleotides controls particular flavor compound production.**

The addition of inosine monophosphate and guanosine monophosphate in mixes with heme protein and other precursors controlled the formation of flavor compounds (E)-4-octene, 2-ethyl-furan, 2-pentanone, 2,3-butanedione, 2-methyl-thiazole, , methyl-

pyrazine, tridecane, (E)-2-octenal, 2-thiophenecarboxaldehyde, and 3-thiophenecarboxaldehyde. These compounds are known to be present in meat and have a beefy, meaty, buttery, and or savory flavor notes.

Reactions containing heme protein at 1% (LegH) with cysteine (10 mM), and glucose (20 mM), 1 mM IMP and 1 mM GMP, at pH 6.0 were prepared and heated to 150C for 3 minutes. Characteristic flavor and fragrance components were mostly produced during the cooking process where precursors reacting heme-protein. These samples were evaluated by GCMS for the flavor compounds generated and evaluated for the sensory experience. Volatile chemicals were isolated from the head space around the flavor reaction and identified using GCMS, creating a profile of the volatile chemicals in the headspace around the flavor reaction mixture. GCMS showed 4-octene, 2-ethyl furan, 2-pentanone, 2,3-butanedione, 2-methyl-thiazole, methyl-pyrazine, tridecane, 2-octenal, 2-thiophenecarboxaldehyde, 3-thiophenecarboxaldehyde compounds were created by a mixture of hemeprotein LegH with IMP, GMP, glucose, and cysteine. The same samples without IMP and GMP did not generate these compounds, additionally these compounds were also not created when heme-proteins were not present, just precursor molecules. Sensory evaluation by blinded trained panelist found the samples with the addition of inosine and guanosine as described as having more complexity in taste and more beefy, meaty, brothy and savory. Figure 2 shows the abundance of the novel flavor compounds created with heme protein at 1% was mixed in a reaction at pH 6, with cysteine (10 mM), and glucose (20 mM), IMP (1 mM) and GMP (1 mM), and detected by solid phase microextraction (SPME) and then detected by GCMS.

**Example 7: Flavor generation with the addition of a particular organic acid**

The addition of lactic acid in mixes with heme protein, ribose, and cysteine controlled the formation of the flavor compounds nonanal, thiazole, 2-acetylthiazole, and 8-methyl-1-undecene. These compounds are known to be present in meat.

Reactions containing heme protein at 1%, cysteine (10 mM), and ribose (20 mM), and lactic acid (1mM), pH 6.0, were prepared and heated to 150C for 3 minutes. Characteristic flavor and fragrance components were mostly produced during the cooking

process where precursors reacting heme-protein. These samples were evaluated by GCMS for the flavor compounds generated and evaluated for the sensory experience. Volatile chemicals were isolated from the head space around the flavor reaction and identified using GCMS, creating a profile of the generated compounds. Nonanal, thiazole, 2-acetylthiazole, and 8-methyl-1-undecene compounds were created by a mixture of LegH with lactic acid, ribose, and cysteine. The same samples without lactic acid did not generate these compounds, additionally these compounds were not created in the absence of heme-proteins.

Sensory evaluation by blinded trained panelist found the samples with the addition of lactic acid as described as beefy, savory, browned, bready, and having malty notes. The sample with everything but lactic acid rated lower in browned, bready and malty notes.

**Example 8: Flavor generated with the addition of a particular amino acid.**

The addition of lysine in mixes with heme protein ribose, and cysteine controlled the formation of flavor compounds dimethyl trisulfide, nonanal, 2-pentyl-thiophene, furfural, 2-nonenal, 1-octanol, 2-nonenal, thiazole, 2-acetylthiazole, phenylacetaldehyde, 2-acetylthiazole. These compounds are known to be present in meat and some have a beefy, meaty, and or savory flavor.

Reactions containing heme protein at 1%, cysteine (10 mM), and ribose (20 mM), and lysine (1mM), at pH 6.0, were prepared and heated to 150C for 3 minutes. These samples were evaluated by GCMS for the flavor compounds generated and evaluated for the sensory experience. Characteristic flavor and fragrance components were mostly produced during the cooking process where precursors could react with the heme-protein. These samples were evaluated by GCMS for the flavor compounds generated and evaluated for the sensory experience. Volatile chemicals were isolated from the head space around the flavor reaction. Dimethyl trisulfide, nonanal, 2-pentyl-thiophene, furfural, 2-nonenal, 1-octanol, 2-nonenal, thiazole, 2-acetylthiazole, phenylacetaldehyde, 2-acetylthiazole compounds were created by a mixture of LegH with lactic acid, ribose, and cysteine. The same samples without lactic acid did not generate these compounds,

additionally these compounds were not created when heme-proteins were not present, just precursor molecules. Sensory evaluation by blinded trained panelist found the samples with the addition of lysine as described as roast beefy, savory, and browned. The addition of lysine increased the roasted browned notes.

**Example 9 - Flavor compound production by different Heme-proteins**

The addition of different types of heme-proteins (LegH, Barley, *B. myoglobin*, or *A. aeolicus*) in flavor reaction mixtures containing one or more flavor precursor compounds results in many of the same key meat flavors, including but not limited to 2-pentyl-furan, 2,3-Butanedione, Thiophene, 2-methyl-thiazole, Pyrazine, Furan, Pyrrole, 2-methyl-furan and distinct differences in the flavor compounds, including but not limited to 2-pentyl-thiophene, Nonanal, 2-Nonanone, and 1-Octen-3-one. These differences in flavor compounds can change the overall taste profile. The different types of heme-protein were LegH, Barley, *B. myoglobin*, or *A. aeolicus* used at 1% w/w in a reaction mixed with cysteine (10 mM) and ribose (10 mM) at pH 6. The pre- reaction mixture was heated to 150 C for 3 minutes; this reaction created flavor compounds known to be present in meat; see Table 9. The characteristic flavor and fragrance components are mostly produced during the cooking process where the flavor precursor molecules react with the heme-protein. Samples were evaluated by GCMS to identify the flavor compounds generated after heating and also evaluated for their sensory profiles. Volatile chemicals were isolated from the head space around the flavor reactions. Table 9 shows the similarity and differences in volatile flavor compounds created by the different types of heme-proteins.

**TABLE 9**

**Flavor compounds created by different heme-protein when heated with ribose and cysteine.**

| Name | LegH | Barley | *B. myoglobin* | *A. aeolicus* |
|---|---|---|---|---|
| Furan | x | x | x | x |
| Thiazole | x | x | x | x |
| benzaldehyde | x | x | x | x |
| 2-acetylthiazole | x | x | x | x |

| | | | | |
|---|---|---|---|---|
| 2-methyl-propanal | x | x | x | x |
| furfural | x | x | x | x |
| 2,3-butanedione | x | x | x | x |
| 2-pentyl-furan | x | x | x | x |
| 2-pentanone | x | x | | |
| pyrazine | x | x | x | x |
| dimethyl trisulfide | x | x | x | x |
| 3-methyl-butanal | x | x | | x |
| 2-methyl-thiazole | x | x | x | x |
| pentanal | x | x | x | x |
| 1,3,5-cycloheptatriene | x | x | x | x |
| methacrolein | x | x | x | x |
| heptanal | x | x | x | x |
| 2-methyl-butanal | x | x | | x |
| isothiazole | x | x | x | x |
| thiophene | x | x | x | x |
| propanal | x | x | x | x |
| 2-heptenal | x | | x | x |
| methyl-pyrazine | x | x | x | x |
| 1-octene | x | | x | x |
| butanal | x | x | x | x |
| 2-acetyl-propen-2-ol | x | x | x | x |
| pyrrole | x | x | x | x |
| 2-methyl-furan | x | x | x | x |
| nonanal | | x | x | x |
| 2-propenal | | x | x | x |
| 2-decenal | | x | x | x |
| 2-nonanone | | x | | x |
| 2-octanone | | x | x | x |
| 2-tridecen-1-ol, | | | x | x |
| 2-octanone | | | x | |
| 2-octenal | | | x | x |
| 4-methyl-2-heptanone | | | x | x |
| octanal | | | x | x |
| 2-undecenal | | | | x |
| butyrolactone | | | | x |
| 1-octen-3-one | | | | x |
| 3-methylheptyl acetate | | | | x |

| | | | | |
|---|---|---|---|---|
| 2-pentyl-thiophene | | | | x |

**Example 10 - Generation of Meat flavors from different lipids**

Several different samples including oils (canola oil or coconut oil), free fatty acids (FFA) (linoleic acid (C18:2), oleic acid (C18:1), stearic acid (C18:0), or myristic acid (C14:0)) and phospholipids (PL) (beef heart polar lipids extract, Biolipon95 (from Perimond), or NatCholinePC40 (from Perimond)) were tested for their ability to produce beefy flavor in the absence and in the presents of other precursors. Oils, FFAs, and PLs were added to 50 mM potassium phosphate buffer (PPB) pH 6.0 or a Maillard reaction mix (MRM) containing 50 mM potassium phosphate pH 6.0, 5 mM Cysteine, 10 mM Glucose, 0.1 mM Thiamine, and 0.1% (w/v) LegHemoglobin. Lipids in combination with MRM were designed to capture the cross reactions of lipid degradation and Maillard reaction productions while lipids in phosphate buffer functioned as a lipid control. The oils were added at 3% of the total 1 mL volume of solution while FFAs and PLs were added at 1% of the total 1 mL volumes. All samples were cooked at 150°C for 3 mins, cooled to 50°C and then analyzed using GCMS (SPME fiber sampling of headspace). After all samples were analyzed by GCMS the caps were removed and samples were smelled by a trained flavor scientist and aromas recorded.

**Table 10**

**Legend showing components of each sample**

| Sample Name | Solution | Additives |
|---|---|---|
| MRM None | Maillard Reaction Mix | None |
| MRM_Linoelic Acid | Maillard Reaction Mix | 1% linoleic acid |
| MRM_Oleic Acid | Maillard Reaction Mix | 1% oleic acid |
| MRM_C14 | Maillard Reaction Mix | 1% C14:0 free fatty acid |
| MRM_C18 | Maillard Reaction Mix | 1% C18:0 free fatty acid |
| MRM_Canola | Maillard Reaction Mix | 3% Canola Oil |
| MRM_Coconut | Maillard Reaction Mix | 3% Coconut Oil |
| MRM_BeefHeart | Maillard Reaction Mix | 1% Beef Heart Polar Lipids Extract |
| MRM_Biolipon95 | Maillard Reaction Mix | 1% Biolipon95 (emulsifier) |

| | | |
|---|---|---|
| MRM_NatCholinePC40 | Maillard Reaction Mix | 1% NatCholinePC40 (emulsifier) |
| KPhos6_Linoelic Acid | PPB, pH 6 | 1% linoelic acid |
| KPhos6_Oleic Acid | PPB, pH 6 | 1% oleic acid |
| KPhos6_C14 | PPB, pH 6 | 1% C14:0 free fatty acid |
| KPhos6_C18 | PPB, pH 6 | 1% C18:0 free fatty acid |
| KPhos6_Canola | PPB pH 6 | 3% Canola Oil |
| KPhos6_Coconut | PPB, pH 6 | 3% Coconut Oil |
| KPhos6_BeefHeart | PPB, pH 6 | 1% Beef Heart Polar Lipids Extract |
| KPhos6_Biolipon95 | PPB, pH 6 | 1% Biolipon95 (emulsifier) |
| KPhos6_NatCholinePC40 | PPB, pH 6 | 1% NatCholinePC40 (emulsifier) |

Table 11 contains the aroma descriptions and Table 12 contains the GCMS data from the most interesting samples analyzed. Many of the lipids introduced a "fatty" aroma to MRM that was otherwise absent. The combinations of Linoleic Acid or NatCholinePC40 in MRM produced the greatest abundance of fatty compounds suggesting that these lipids may improve the flavor perception of beef tallow. Linoleic Acid and NatCholinePC40 also showed high abundance of earthy-mushroom aromas. The addition of lipids to MRM significantly increased the abundance of "nutty & roasted" aromas. Less desirable "green" aroma compounds were most prominent in samples with unsaturated free fatty acids (linoleic acid or oleic acid) or phospholipids. In general, the addition of lipids significantly increased the number of target beef compounds made.

**TABLE 11**

**Aroma descriptions of each sample after it was cooked.**

| Sample Names | Aroma Descriptions |
|---|---|
| MRM_Only | brothy, malty, beef stew |
| KPhos6_BeefHeart | fatty, creamy, beef tallow, slight sweet, slight roasted nutty |
| MRM_BeefHeart | fatty, beef tallow, old meat, mushroom |
| KPhos6_Biolipon95 | fatty, fresh |
| MRM_Biolipon95 | fatty, brothy, hay, malty green |

| | |
|---|---|
| KPhos6_NatCholinePC40 | light fatty, fresh |
| MRM_NatCholinePC40 | fatty, beef tallow, brothy |
| K-Phos6_C14 | light/faint plastic/waxy |
| MRM_C14 | brothy, beefy, minty, fresh |
| K-Phos6_C18 | light/faint plastic/waxy |
| MRM_C18 | beefy with cucumber &/or pepper aroma |
| K-Phos6_Canola | fresh, cucumber |
| MRM_Canola | fatty, brothy, oil, roasted nuts |
| K-Phos6_Coconut | nothing |
| MRM_Coconut | brothy, beefy, slight fatty, crackers |
| K-Phos6_Oleic Acid | fresh, cucumber, camphorous/minty-like |
| MRM_Oleic Acid | herbal, plastic, slight cheesy, brothy |
| K-Phos6_Linoelic Acid | light plastic |
| MRM_Linoelic Acid | fatty, light waxy, brothy, herbal |

**Table 12**

**List of aromatic compounds found in Beef by GCMS and a chart showing which were detected in each lipid plus MRM sample.**

| Compounds in Beef | MRM only | MRM_BeefHeart | MRM_NatCholinePC40 | MRM_Linoleic acid |
|---|---|---|---|---|
| (s)-isopropyl lactate | N | N | N | N |
| 1-ethyl-5-methylcyclopentene | Y | Y | Y | Y |
| 1-heptanol | N | Y | N | N |
| 1-hepten-3-ol | N | Y | Y | Y |
| 1-heptene | N | Y | Y | Y |
| 2-methyl-1-heptene | N | N | N | N |
| 1-hexanol | N | Y | Y | Y |
| 2-ethyl-1-hexanol | N | N | N | N |
| 1-nonanol | N | N | Y | N |
| 1-nonene | N | Y | Y | N |
| 1-octanol | N | Y | Y | N |
| 1-octen-3-ol | N | Y | Y | Y |

| | | | | |
|---|---|---|---|---|
| 1-octen-3-one | Y | Y | Y | Y |
| 1-octene | N | N | N | N |
| 1-pentanol | N | Y | Y | Y |
| 1-penten-3-ol | N | Y | Y | N |
| 1-propanol | N | N | N | N |
| 8-methyl-1-undecene | N | Y | Y | Y |
| 1,3-hexadiene | N | N | N | Y |
| 3-ethyl-2-methyl-1,3-hexadiene | N | Y | Y | Y |
| 1,3-octadiene | Y | N | N | Y |
| 1,3,5-cycloheptatriene | N | N | N | N |
| 2,3-dihydro-5,6-dimethyl-1,4-dioxin | N | N | N | N |
| 1,7-octadien-3-ol | N | Y | N | N |
| 1h-pyrrole-2-carboxaldehyde | N | N | N | N |
| 2-methyl-1H-pyrrole | N | N | N | N |
| 2-acetyl-2-thiazoline | Y | N | N | N |
| 2-acetylthiazole | Y | Y | Y | Y |
| 2-butanone | N | Y | Y | Y |
| 2-butenal | N | Y | Y | Y |
| 2-ethyl-2-butenal | N | N | N | Y |
| 3-methyl-2-butenal | N | N | Y | Y |
| 3-methyl-2-cyclohexen-1-one | N | N | N | N |
| 2-decanone | Y | Y | Y | N |
| (E)-2-decenal | N | N | N | N |
| (Z)-2-decenal | Y | Y | Y | Y |
| 2-furanmethanol | N | N | N | N |
| 2-heptanone | Y | Y | Y | Y |
| 6-methyl-2-heptanone | N | N | Y | N |
| (E)-2-heptenal | N | Y | Y | Y |
| (Z)-2-heptenal | N | N | N | Y |
| (E)-2-hexenal | N | Y | Y | Y |
| 2-ethyl-2-hexenal | N | N | N | N |
| 2-methyl-2-heptene | Y | N | N | N |
| 2-n-heptylfuran | Y | N | N | N |
| 2-n-octylfuran | Y | Y | Y | N |

| | | | | |
|---|---|---|---|---|
| 2-nonanone | N | Y | Y | N |
| (E)-2-nonenal | Y | Y | Y | Y |
| (Z)-2-nonenal | N | N | N | Y |
| 2-octanone | Y | Y | Y | Y |
| (Z)-2-octen-1-ol | Y | Y | Y | Y |
| (E)-2-octenal | N | Y | Y | Y |
| 2-pentanone | N | Y | Y | N |
| 1-propoxy-2-propanol | N | N | N | N |
| 1-(acetyloxy)-2-propanone | Y | N | N | N |
| 1-hydroxy-2-propanone | Y | N | N | N |
| 2-propenal | N | N | N | Y |
| 2-thiophenecarboxaldehyde | Y | Y | Y | Y |
| 2-undecenal | N | Y | Y | Y |
| 2,3-butanedione | N | N | N | Y |
| 2,3-pentanedione | N | N | N | N |
| (E,E)-2,4-decadienal | N | Y | Y | Y |
| 2,4-decadienal | N | N | N | Y |
| (E,E)-2,4-heptadienal | N | Y | Y | Y |
| (E,E)-2,4-nonadienal | N | Y | Y | Y |
| 2,6-dimethylpyrazine | N | N | N | N |
| (E,Z)-2,6-nonadienal | N | N | Y | N |
| 5-ethyldihydro-2(3H)-furanone | N | Y | Y | Y |
| 5-methyl-2(3H)-furanone | N | N | N | N |
| dihydro-5-pentyl-2(3H)-furanone | N | N | Y | Y |
| dihydro-5-propyl-2(3H)-furanone | N | N | N | N |
| 2(5H)-furanone | N | N | N | N |
| tetrahydro-6-methyl-2H-pyran-2-one | N | N | N | N |
| 3-ethylcyclopentanone | N | Y | Y | Y |
| 3-hexanone | N | N | N | N |
| 3-methyl-2-thiophenecarboxaldehyde | N | N | N | N |
| 3-octanone | Y | Y | N | Y |
| 3-octen-2-one | N | Y | Y | Y |
| 3-thiophenecarboxaldehyde | N | Y | Y | Y |

| | | | | |
|---|---|---|---|---|
| (E,E)-3,5-octadien-2-one | N | N | Y | Y |
| dihydro-2-methyl-3(2H)-furanone | N | N | N | N |
| 4-cyanocyclohexene | N | N | N | N |
| 4-cyclopentene-1,3-dione | N | N | Y | N |
| 4-decyne | N | Y | N | N |
| (Z)-4-heptenal | N | Y | Y | Y |
| 4-methyloctanoic acid | N | N | N | N |
| (E)-4-octene | N | N | N | N |
| 2,3-dihydro-3,5-dihydroxy-6-methyl-4(H)-pyran-4-one | Y | N | N | N |
| 6-methyl-5-hepten-2-one | Y | N | N | N |
| acetaldehyde | N | N | N | Y |
| acetic acid | N | N | N | N |
| acetic acid ethenyl ester | Y | N | N | N |
| acetoin | Y | N | N | N |
| acetone | Y | N | N | Y |
| acetonitrile | N | N | N | Y |
| benzaldehyde | Y | Y | Y | Y |
| 4-ethyl-benzaldehyde | N | Y | Y | N |
| benzene | Y | N | N | N |
| benzoic acid, hydrazide | Y | N | N | N |
| butanal | Y | N | N | Y |
| 2-methyl-butanal | N | N | N | N |
| 3-methyl-butanal | Y | N | N | N |
| butanoic acid | N | N | N | N |
| butyrolactone | Y | Y | N | Y |
| caprolactam | N | N | N | N |
| carbon disulfide | N | N | N | Y |
| 1-ethyl-1-methyl-cyclopentane | Y | Y | Y | Y |
| propyl-cyclopropane | N | N | Y | Y |
| decanal | N | Y | Y | N |
| dihydro-3-(2H)-thiophenone | N | N | N | N |
| Dimethyl sulfide | Y | N | N | N |
| dimethyl sulfone | N | N | N | N |
| dimethyl trisulfide | Y | Y | N | N |
| ethanethiol | N | N | N | N |

| | | | | |
|---|---|---|---|---|
| ethanol | N | N | N | Y |
| 1-(1(H)-pyrrol-2-yl)-ethanone | N | N | N | N |
| 1-(2-furanyl)-ethanone | N | N | N | N |
| ethosuximide | Y | N | N | N |
| formic acid, heptyl ester | Y | Y | N | N |
| furan | Y | N | N | Y |
| 2-ethyl-furan | Y | N | N | N |
| 2-hexyl-furan | Y | N | N | Y |
| 2-methyl-furan | N | N | N | Y |
| 2-pentyl-furan | N | Y | Y | Y |
| 2-propyl-furan | N | N | Y | Y |
| 3-methyl-furan | Y | N | N | N |
| 3-pentyl-furan | Y | Y | Y | Y |
| furfural | N | Y | Y | Y |
| heptanal | N | Y | Y | Y |
| heptanoic acid | N | N | N | Y |
| 2-methyl-hex-2-yn-4-one | N | N | N | N |
| hexanoic acid | N | N | N | Y |
| hydrogen sulfide | N | N | N | N |
| m-aminophenylacetylene | N | N | N | N |
| maleic anhydride | N | N | N | N |
| methacrolein | N | N | N | N |
| methanethiol | N | N | N | N |
| methyl ethanoate | N | N | N | N |
| methyl isobutyl ketone | Y | N | N | N |
| n-caproic acid vinyl ester | N | Y | Y | N |
| nonanal | N | Y | Y | Y |
| 3-methyl-nonane | Y | N | N | N |
| nonanoic acid | Y | N | N | N |
| octanal | N | Y | Y | Y |
| octane | N | N | N | Y |
| octanoic acid | N | N | N | Y |
| oxalic acid, isobutyl pentyl ester | Y | N | N | N |
| p-cresol | N | N | N | N |
| pentanal | N | N | N | Y |
| pentanoic acid | Y | N | N | Y |

| | | | | |
|---|---|---|---|---|
| 4-ethyl-phenol | N | Y | Y | N |
| phenylacetaldehyde | Y | Y | Y | Y |
| (p-hydroxyphenyl)-phosphonic acid | Y | N | N | N |
| propanal | N | N | N | Y |
| 2-methyl-propanal | N | N | N | N |
| propanoic acid | N | N | N | N |
| 2-methyl-propanoic acid | Y | N | N | N |
| propanoic acid, ethenyl ester | N | N | N | N |
| pyrazine | N | Y | N | Y |
| 2-ethyl-5-methyl-pyrazine | N | N | N | N |
| 2-ethyl-6-methyl-pyrazine | N | N | N | N |
| 2,3-dimethyl-pyrazine | N | N | N | N |
| 2,5-dimethyl-pyrazine | N | N | N | N |
| 3-ethyl-2,5-dimethyl-pyrazine | Y | N | N | N |
| ethyl-pyrazine | N | N | N | N |
| methyl-pyrazine | N | N | N | N |
| trimethyl-pyrazine | Y | N | N | N |
| pyridine | Y | N | Y | N |
| pyrrole | Y | Y | Y | Y |
| styrene | Y | N | Y | N |
| thiazole | Y | Y | Y | Y |
| methyl-thiirane | N | N | N | N |
| thiophene | N | N | N | Y |
| 2-hexyl-thiophene | Y | N | Y | N |
| 2-pentyl-thiophene | N | Y | N | N |
| trans-2-(2-pentenyl)furan | N | Y | Y | N |
| trans-3-nonen-2-one | N | Y | Y | Y |
| undecanoic acid | N | N | N | N |
| Total # of Compounds Detected: | 54 | 63 | 66 | 76 |

In samples having fatty or creamy aromas, 2,4-decadienal, (E,E)-2,4-nonadienal, (E,E)-2,4-heptadienal, and/or (E,E)-2,4-decadienal were detected in the KPhos6_BeefHeart, MRM_BeefHeart, MRM_BioLipon95, MRM_NatCholinePC40,

Kphos6_Canola, MRM_Canola, KPhos6_Oleic Acid, KPhos6_Linoleic acid and MRM_Linoleic acid samples. For (E,E)-2,4-decadienal, the strongest signal intensity was in the MRM_NatCholinePC40 sample, followed by the MRM_Linoleic acid, KPhos6_Linoleic acid, MRM_BeefHeart, MRM_BioLipon95, KPhos6_BeefHeart, MRM_Oleic Acid, and KPhos6_Oleic Acid samples. For (E,E)-2,4-heptadienal, the strongest signal intensity was in the MRM_NatCholinePC40 sample followed by the MRM_Canola sample. (E,E)-2,4-heptadienal also was detected in the MRM_BioLipon95, MRM_BeefHeart, and MRM_Linoleic acid samples. For (E,E)-2,4-nonadienal, the strongest signal intensity was in the MRM_Canola and MRM_Linoleic acid samples. (E,E)-2,4-nonadienal also was detected in the Kphos6_Canola, MRM_NatCholinePC40, MRM_BioLipon95, MRM_BeefHeart, and KPhos6_Linoleic acid samples. For 2,4-decadienal, the strongest signal intensity was in the MRM_Linoleic acid sample. 2,4-decadienal also was detected in KPhos6_Linoleic acid, MRM_Canola, and KPhos6_Oleic Acid samples.

In samples having earthy or mushroom aromas, 3-octen-2-one, 1-octen-3-one, 3-octanone, and/or 1-octen-3-ol were detected in the KPhos6_BeefHeart, MRM_BeefHeart, Kphos_BioLipon95, MRM_BioLipon95, Kphos_NatCholinePC40, MRM_NatCholinePC40, MRM_Canola, KPhos6_Oleic Acid, MRM_Oleic Acid, KPhos6_Linoleic acid, and MRM_Linoleic acid samples. For 1-octen-3-ol, the strongest signal intensity was in the MRM_Linoleic acid sample, followed by MRM_NatCholinePC40, KPhos6_Linoleic acid, MRM_BeefHeart, KPhos6_BeefHeart, MRM_Canola, MRM_BioLipon95, KPhos6_Oleic Acid, and MRM_Oleic Acid samples. 3-octanone was detected in the MRM_Oleic Acid, KPhos6_Linoleic acid, and MRM_Linoleic acid samples. For 1-octen-3-one, the strongest signal intensity was in the MRM_Linoleic acid and MRM_BeefHeart samples, followed by KPhos6_Linoleic acid, MRM_NatCholinePC40, KPhos6_BeefHeart, MRM_BioLipon95, MRM_Oleic Acid, and KPhos6_Oleic Acid samples. For 3-octen-2-one, the strongest signal intensity was in the KPhos6_Linoleic acid sample, followed by MRM_Linoleic acid, MRM_NatCholinePC40, KPhos6_BeefHeart, KPhos6_Oleic Acid, MRM_Oleic Acid, MRM_BeefHeart, MRM_BioLipon95, MRM_Canola, Kphos_BioLipon95, and

Kphos_NatCholinePC40. Pyrazine was detected in the MRM_Coconut, MRM_C18, MRM_C14, and MRM_BioLipon95 samples.

In samples having a nutty and roasted aroma, thiazole and 2-acetylthiazole were the most abundant compounds detected, along with pyrazine, methyl pyrazine, trimethyl pyrazine, and 3-ethyl-2,5-dimethylpyrazine. 2-acetylthiazole was detected in all samples with MRM and most abundant in samples with MRM_Beefheat, MRM_biolipon95, MRM_Canola, and MRM_coconut. Thiazole was created in samples with MRM-Coconut, MRM_BeefHeat, MRM_Biolipon95, MRM_C14, MRM_C18, MRM_Canola, MRM_Oleic acid and MRM_Linoleic acid and MRM_NatCholinePC40. Pyrazine was present in the largest amount in samples with MRM-Coconut, followed by samples MRM_BeefHeat, MRM_Biolipon95, MRM_C14, MRM_C18, MRM_Canola having roughly equal amount, MRM_Oleic acid and MRM_Linoleic acid sample had even less. Methyl-pyrazine was present in MRM_Biolipon95 and MRM_Coconut. 3-ethyl-2,5-dimethyl- pyrazine and trimethyl- pyrazine, were present only without phospholipids in the MRM.

In samples having green, vegetable, or grass aromas, 1-heptanol, 1-hepten-3-ol, 1-hexanol, (E)-2-heptenal, (Z)-2-heptenal, (E)-2-hexenal, 2-pentyl-furan, and/or heptanal were detected in the KPhos6_BeefHeart, MRM_BeefHeart, Kphos_BioLipon95, MRM_BioLipon95, Kphos_NatCholinePC40, MRM_NatCholinePC40, Kphos_C14, MRM_C14, Kphos_C18, MRM_C18, MRM_Canola, MRM_Coconut, KPhos6_Oleic Acid, MRM_Oleic Acid, KPhos6_Linoleic acid, and MRM_Linoleic acid samples. For 2-pentyl-furan, the strongest signal intensity was in the KPhos6_BeefHeart sample, followed by the KPhos6_Linoleic acid, MRM_BioLipon95, MRM_Linoleic acid, MRM_BeefHeart, MRM_Oleic Acid, MRM_NatCholinePC40, MRM_Canola, KPhos6_Oleic Acid, and Kphos_NatCholinePC40 samples. For (E)-2-heptenal, the strongest signal intensity was in the MRM_BeefHeart, MRM_Canola, MRM_Oleic Acid, and KPhos6_Linoleic acid samples, followed by the KPhos6_Oleic Acid, MRM_BioLipon95, KPhos6_BeefHeart, MRM_Linoleic acid, MRM_NatCholinePC40, Kphos_BioLipon95, and Kphos_NatCholinePC40 samples. For (Z)-2-heptenal, the strongest signal intensity was in the MRM_Linoleic acid sample. MRM_Linoleic acid

also was detected in the KPhos6_Linoleic acid sample. For heptanal, the strongest signal intensity was in the MRM_Oleic Acid sample, followed by the KPhos6_Oleic Acid, MRM_C14, MRM_C18, MRM_Canola, MRM_BeefHeart, MRM_NatCholinePC40, MRM_Linoleic acid, and KPhos6_BeefHeart samples. For , (E)-2-hexenal, the strongest signal intensity was in the MRM_Linoleic acid sample, followed by the MRM_NatCholinePC40, KPhos6_Linoleic acid, and MRM_Oleic Acid samples.

**Example 11 - Creation of beefy flavors using complex precursor mixtures**

A formulation was prepared (the "magic mix," see Table 13 containing the estimated concentrations of amino acids, sugars, and other small molecules in beef based on their values reported in literature. The magic mix was tested for its ability to produce beefy flavors in the presence of LegHemoglobin (LegH). The magic mix and 1% w/v LegH were added to the meat replica, pH 6.0 (see Table 4) and baked in a convection oven for 7 minutes at 160°C. A control sample was prepared by adding 1% w/v LegH to the meat replica, pH 6.0 and baking in a convection oven for 7 minutes at 160°C.

The meat replica sample containing only LegH, was compared to the meat replica sample containing the magic mix and LegH by a sensory panel and GCMS analysis. Five tasters rated the flavored meat replicas for beefiness, bitterness, and levels of savory flavors, and off flavors. Each property was rated on a 7 point scale in which 7 was the highest amount of the specified property (e.g., a standard 80:20 ground beef would be rated 7 on the beefy scale). The Magic Mix flavor was rated one point higher in beefy character than the LegH only sample (FIG. 1).

To determine which chemical products were produced upon heating, a solution of Magic Mix was prepared with 1% w/v LegH at pH 6.0. The samples were cooked with shaking at 150°C for three minutes, then Solid Phase Micro Extraction (SPME) was performed for twelve minutes at 50°C to extract the volatile compounds above the headspace of the reaction. A search algorithm was used to analyze the retention time and mass fingerprint information of the volatile compounds and assign chemical names to peaks. Table 14 shows the compounds identified in both the Magic Mix + LegH (MM, average of two samples) and in the LegH alone in buffer (LegH, average of five samples)

samples. The compounds in Table 14 are listed in order of the retention time (R.T., in seconds), and are designated as having a zero peak area (0), or a small (S), medium (M), or large (L) average peak area. Hundreds of compounds were identified between the samples, many of which are characteristic of beefy aroma, including but not limited to 1,3-bis(1,1-dimethylethyl)-benzene, 2-methyl 3-furanthiol, and Bis(2-methyl-4,5-dihydro-3-furyl) disulfide, which increased in the samples containing the Magic Mix and LegH.

**Table 13**

**Chemical entities added to the Magic Mix**

| Chemical entity | mM |
|---|---|
| Alanine | 5.6 |
| Arginine | 0.6 |
| Asparagine | 0.8 |
| Aspartate | 0.8 |
| Cysteine | 0.8 |
| Glutamic acid | 3.4 |
| Glutamine | 0.7 |
| Glycine | 1.3 |
| Histidine | 0.6 |
| Isoleucine | 0.8 |
| Leucine | 0.8 |
| Lysine | 0.7 |
| Methionine | 0.7 |
| Phenylalanine | 0.6 |
| Proline | 0.9 |
| Threonine | 0.8 |
| Tryptophan | 0.5 |
| Tyrosine | 0.6 |

| | |
|---|---|
| Valine | 0.9 |
| glucose | 5.6 |
| Ribose | 6.7 |
| Maltodextrin | 5.0 |
| Thiamine | 0.5 |
| GMP | 0.24 |
| IMP | 0.6 |
| Lactic acid | 1.0 |
| creatine | 1.0 |
| NaCl | 10 |
| KCl | 10 |
| Kphos pH 6.0 | 10 |

**TABLE 14**

**Compounds identified with GC-MS analysis in samples with MM and LegH, or LegH alone (average of five samples)**

| R.T.(s) | Name | MM with LegH | LegH alone |
|---|---|---|---|
| 248 | acetaldehyde | L | S |
| 256.3 | carbon disulfide | L | S |
| 264.3 | dimethyl sulfide | S | 0 |
| 265 | oxalic acid, isobutyl pentyl ester | M | 0 |
| 268.1 | 2,3,4-trimethyl-pentane | M | 0 |
| 269.2 | methanethiol | S | 0 |
| 283.4 | propanal | M | 0 |
| 285.4 | octane | M | 0 |
| 287.1 | furan | M | 0 |
| 295.3 | 2-methyl-propanal | L | S |
| 297.6 | acetone | L | S |
| 319.3 | 2-propenal | M | S |
| 338.1 | 2-methyl-furan | M | S |
| 342.1 | butanal | L | S |

| | | | |
|---|---|---|---|
| 344.2 | 2,4-dimethyl-1-heptene | M | 0 |
| 346.3 | methacrolein | M | 0 |
| 357.4 | methyl-thiirane | L | 0 |
| 360.2 | 3-methyl-furan | S | 0 |
| 363.7 | butanone | L | S |
| 368.9 | 2,3-dihydro-5-methyl-furan | M | S |
| 376.4 | 2-methyl-butanal | L | M |
| 381.1 | 3-methyl-butanal | L | M |
| 390.6 | isopropyl alcohol | 0 | S |
| 399.6 | ethanol | L | M |
| 406.2 | 2-propenoic acid, methyl ester | M | 0 |
| 408.2 | benzene | S | 0 |
| 414.4 | methyl vinyl ketone | M | 0 |
| 416.4 | 2,2,4,6,6-pentamethyl-heptane | M | 0 |
| 422.6 | 2-ethyl-furan | S | 0 |
| 438.4 | 2-ethylacrolein | M | 0 |
| 449.9 | 2-pentanone | S | 0 |
| 453.2 | pentanal/2,3-butanedione | L | 0 |
| 453.8 | 2,3-butanedione | L | M |
| 472.8 | 4,7-dimethyl-undecane | M | S |
| 485.9 | 2-methyl-pentanal | M | 0 |
| 492.6 | 2-methyl-1-penten-1-one | S | 0 |
| 496.6 | (E)-3-penten-2-one | M | 0 |
| 508.6 | 1-penten-3-one | M | 0 |
| 510.6 | trichloromethane | M | M |
| 520.4 | p-dithiane-2,5-diol | M | 0 |
| 525.5 | 3-methyl-pentanal | M | 0 |
| 535.1 | (E)-5-decene | M | 0 |
| 536.5 | toluene | M | S |
| 537.9 | 2-butenal | M | S |
| 543.8 | 4-penten-2-one | M | 0 |
| 550.8 | methyl thiolacetate | M | 0 |
| 683.7 | p-xylene | S | 0 |
| 727.4 | dimethyl selenone | M | 0 |
| 738.3 | methyl isopropyl disulphide | M | 0 |
| 755 | 2-heptanone | M | 0 |
| 758.7 | heptanal | L | 0 |
| 781.9 | 1,3-diisopropoxy-1,3-dimethyl-1,3- | S | M |

| | | | |
|---|---|---|---|
| | disilacyclobutane | | |
| 789.4 | 3-methyl-2-butenal | M | 0 |
| 793.4 | 4-methyl-2-heptanone | M | 0 |
| 810.4 | pyrazine | M | 0 |
| 818.8 | isothiazole | S | 0 |
| 827.1 | acetyl valeryl | M | 0 |
| 831.8 | 2-pentyl-furan | L | 0 |
| 851 | 2-methyl-thiazole | S | 0 |
| 853.3 | isothiocyanato-methane | S | 0 |
| 870.9 | thiazole | L | 0 |
| 879.2 | styrene | M | 0 |
| 890.7 | 1-(methylthio)-propane | M | 0 |
| 895.6 | methyl-pyrazine | M | 0 |
| 910.5 | thiocyanic acid, methyl ester | S | 0 |
| 918.6 | 4-methylthiazole | M | 0 |
| 921.4 | 2-octanone | M | 0 |
| 923.9 | 2-methyl-cyclopentanone | M | 0 |
| 927.9 | octanal | L | S |
| 934.3 | tridecane | M | 0 |
| 948.8 | trans-2-(2-pentenyl)furan | S | 0 |
| 961.9 | 1-hydroxy-2-propanone | M | 0 |
| 974.5 | (E)-2-heptenal | M | 0 |
| 987.4 | 5-methyl-1-undecene | M | 0 |
| 993.8 | 2-hexyl-furan | M | 0 |
| 1007.8 | 7-methyl-(E)-5-undecene | M | 0 |
| 1024.1 | 2-methyl-5-(methylthio)-furan, | S | 0 |
| 1058.6 | 2-butyl-1-decene | M | 0 |
| 1079.3 | dimethyl trisulfide | L | S |
| 1085.3 | 2-nonanone | M | 0 |
| 1093.2 | nonanal | L | M |
| 1142.3 | 1,3-bis(1,1-dimethylethyl)-benzene | M | 0 |
| 1149.6 | (E)-2-octenal | M | 0 |
| 1164.5 | 1-heptanol | M | 0 |
| 1193.5 | methional | L | 0 |
| 1198.8 | acetic acid | M | S |
| 1207.2 | furfural | M | 0 |
| 1242.1 | 2-decanone | M | 0 |
| 1250.8 | decanal | M | 0 |

| | | | |
|---|---|---|---|
| 1265.2 | 1-decen-3-one | M | 0 |
| 1283.3 | pyrrole | M | 0 |
| 1292.6 | 5-ethenyl-4-methyl-thiazole | M | 0 |
| 1294.3 | benzaldehyde | L | M |
| 1303.7 | 2-n-octylfuran | M | 0 |
| 1305.6 | (E)-2-nonenal | M | 0 |
| 1341.4 | 1-octanol | M | 0 |
| 1361.1 | 2-methyl-1(H)-pyrrole | S | 0 |
| 1391.7 | 2-undecanone | M | 0 |
| 1401.2 | (E)-2-octen-1-ol | M | 0 |
| 1448 | butyrolactone | S | S |
| 1456.3 | (E)-2-decenal | M | 0 |
| 1462.4 | phenylacetaldehyde | L | S |
| 1466.3 | 2-acetylthiazole | L | 0 |
| 1471.3 | acetophenone | M | S |
| 1475.4 | 1-nonanol | M | 0 |
| 1487 | methyl (methylthio)methyl disulfide | M | 0 |
| 1497.1 | 5-(2-chloroethyl)-4-methylthiazole | L | 0 |
| 1497.5 | 1-(ethylthio)-2-(methylthio)-buta-1,3-diene | L | S |
| 1512 | 3-thiophenecarboxaldehyde | M | 0 |
| 1518.8 | 2-nonen-4-one | M | 0 |
| 1531.7 | 2-thiophenecarboxaldehyde | S | 0 |
| 1543.9 | dodecanal | M | 0 |
| 1551.6 | 4-ethyl-2-methyl-pyrrole | S | 0 |
| 1558.2 | 3-(methylthio)-propanenitrile | S | 0 |
| 1561.2 | 3-decen-2-one | M | 0 |
| 1613.1 | bis(2-methyl-4,5-dihydro-3-furyl) disulfide | M | 0 |
| 1615.6 | 1,10-undecadiene | M | 0 |
| 1619.5 | 2-undecenal | S | 0 |
| 1668.9 | 2-phenylpropenal | M | 0 |
| 1692.3 | (Z)-3-decen-1-ol, acetate | M | 0 |
| 1733.1 | 3-phenyl-furan | S | 0 |
| 1739.7 | 4-nitrophenyl 2-thiophenecarboxylic acid ester | S | 0 |
| 1741.2 | 5-formyl-4-methylthiazole | M | 0 |
| 1749.7 | pentanoic acid, 2,2,4-trimethyl-3-hydroxy-, isobutyl ester | M | 0 |
| 1765.5 | benzyl alcohol | S | 0 |

| | | | |
|---|---|---|---|
| 1774.2 | pentanoic acid, 2,2,4-trimethyl-3-hydroxy-, isobutyl ester | S | 0 |
| 1796.9 | dodecanal | M | 0 |
| 1806.1 | (1-ethyl-1-propenyl)-benzene | S | 0 |
| 1825.6 | 1-undecanol | M | S |
| 1827.9 | 2-methyl-3-furanthiol | M | 0 |
| 1828.3 | 2-methyl-3-(methylthio) furan | M | 0 |
| 1836.1 | 4-chloro-2,6-bis(1,1-dimethylethyl)-phenol | S | 0 |
| 1844.1 | phenol | S | S |
| 1845.3 | [(methylsulfonyl)methyl]-benzene | S | 0 |
| 1850.3 | (e)-2-tridecen-1-ol | M | 0 |
| 1859.9 | 1-heptyl-1,2,3,4-tetrahydro-4-methyl-naphthalene | S | 0 |
| 1863.2 | 2,4-decadienal | S | 0 |
| 1905.1 | 3,3'-dithiobis[2-methyl]-furan | M | 0 |
| 1906.9 | 3,5-di-tert-butylbenzoic acid | S | 0 |
| 1909.6 | 4-ethoxy-benzoic acid, ethyl ester | S | 0 |
| 1921.5 | 3-(phenylmethyl)-2,5-piperazinedione | S | 0 |
| 1944.5 | 9-octadecenal | M | 0 |
| 1959.7 | 3,5-bis(1,1-dimethylethyl)-phenol | M | S |
| 1968.4 | 4-methyl-5-thiazoleethanol | M | S |
| 2007.8 | 1,1'-(1,2-cyclobutanediyl)bis-cis-benzene | S | 0 |
| 2019.8 | benzoic acid | S | S |
| 2026.4 | 4-quinolinecarboxaldehyde | S | 0 |
| 2027.8 | m-aminophenylacetylene | M | 0 |

**Example 12 – Ferrous Chlorin Catalyzes Production of Meat-like flavor compounds**

Fresh green spinach (10 lb) was added to 500 mL water and finely ground in a Vitamix blender to yield 2 L of green suspension. Acetone (8L) was added with mixing and the material was allowed to extract for 1 hour. The material was filtered through Whatman filter paper and the acetone was removed on a rotary evaporator (Buchi). To the residual green suspension (500 mL) was added 2 mL of 10 M HCl, causing the suspension to turn brown. To this was added 1g of $FeCl_2.4H_2O$ in 10 mL $H_20$. The

solution was shaken then left at 4°C for 16 hours. This suspension was extracted with diethyl ether (3x50mL) to give a bright green organic phase, the combined organics were washed with saturated sodium chloride solution, dried over sodium sulfate, filtered and evaporated to leave a black paste (1.1g). The pellet was dissolved in chloroform for fractionation.

Chlorophyll and Ferrous chlorin crude fractions were stored at -20°C. Crude extracts were fractionated by reverse-phase high-pressure liquid chromatography (RP-HPLC). HPLC conditions are outlined in Table 15. Both chlorophyll and ferrous chlorophyll were eluted from the column with a peak retention time of 7.6 minutes. Eluted material was collected from 7.3 – 8.0 minutes. Collected fractions were pooled and stored on ice. Collected fractions were re-chromatographed and showed a single peak with retention time 7.6 minutes. The desired fractions were pooled, then 10% sunflower oil was added, methanol was removed on a rotary evaporator (Buchi).

**TABLE 15**

**HPLC conditions for purification of chlorophyll and ferrous chlorin from crude extract.**

| | |
|---|---|
| Sample: | Chlorophyll or Fe-chlorin (~2mg/mL in $CHCl_3$) |
| System: | Agilent 1100 with Chemstation |
| Column: | Zorbax Bonus-RP (4.6 x 250 mm, 5uM) |
| Mobile phase: | acetonitrile, methanol, ethyl acetate (60:20:20) isocratic flow |
| Temperature: | 30°C |
| Flow Rate: | 1.0 mL per minute |
| Injection volume: | 0.05 mL |

**Preparation of Flavor Reaction Containing Ferrous Chlorin or Leghemoglobin**

A solution of ferrous chlorophyll was mixed with the Magic Mix (Table 13) to a final concentration of 0.35% ferrous chlorin, 1% glycerol, 0.005% tween-20, 5% sunflower oil, 100 mM NaCl, 20 mM phosphate at pH 6. Leghemoglobin (0.35%) at pH 6 in phosphate buffer (20 mM), 100 mM NaCl, was mixed with the Magic Mix (Table

13), 1% glycerol, and 0.005% tween-20. The flavor reaction mixtures were heated to 150°C for 3 minutes; this reaction created flavor compounds known to be present in meat, created by hemoglobin and also created by ferrous chlorin; *see* Table 16.

The characteristic flavor and fragrance components were mostly produced during the cooking process when the flavor precursor molecules reacted with the heme-protein or the ferrous chlorophyll. Samples were evaluated by GCMS to identify the flavor compounds generated after heating. Volatile chemicals were isolated from the headspace around the flavor reactions. The profile of the volatile chemicals in the headspace around the flavor reaction mixtures that were similar between heme-protein and ferrous chlorin are shown in Table 16. Notabily, many of the compounds created by the ferrous chlorin are important in the flavor of meat.

**TABLE 16**

**Flavor Compounds created by both Ferrous Chlorin and LegH with Magic Mix.**

| | |
|---|---|
| 1-heptanol | acetone |
| 1-hexanol | acetonitrile |
| 1-octanol | benzaldehyde |
| 1-octen-3-ol | butanal |
| 1-octen-3-one | 2-methyl-butanal |
| 1-pentanol | dimethyl trisulfide |
| 2-acetylthiazole | ethyl acetate |
| 2-butenal | furan |
| 3-methyl-2-butenal, | 2-ethyl-furan |
| (Z)-2-decenal | 2-hexyl furan |
| 6-methyl-2-heptanone | 2-pentyl-furan |
| (E)-2-heptenal | furfural |
| (E)-2-hexenal | heptanal |
| 2-methyl-3-furanthiol | aminophenylacetylene |
| (E)-2-nonenal | methacrolein |
| (E)-2-octenal | methional |
| 2-pentanone | octanal |
| 1-hydroxy-2-propanone | octane |
| 2-thiophenecarboxaldehyde | oxalic acid, diallyl ester |
| 2-undecenal | 2,3-butanedione |

| | |
|---|---|
| 3-methyl-3-buten-2-one | 2-methyl-propanal |
| 3-thiophenecarboxaldehyde | pyrazine |
| (E)-4-octene, | 2,3-dimethyl-pyrazine |
| methyl-pyrazine | 2,5-dimethyl-pyrazine |
| thiazole | |

**Example 13 - Flavor creation by immobilized Hemin**

**Preparation of hemin linked CM Sepharose**.

200 mg of bovine hemin (Sigma Aldrich) was loaded into a scintillation vial. A small magnetic stir bar, 800 µL acetonitrile, 64 µL 4-methylmorpholine, and 71 mg of N-hydroxysuccinimide were added in that order. The vial was placed in an ice bath and chilled then 118 mg of N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide hydrochloride was added with stirring, followed by 845 µL of Jeffamine ED900. This was stirred while allowing the black mixture to warm to ambient temperature. Chloroform (10 mL) was added to the mixture followed by water (4 mL). A flashlight was used to distinguish between organic and aqueous layers since both were black and the organic layer was pipetted off and concentrated to a dark black oil. The oil was dissolved in a 4:1 mixture of acetonitrile and ethanol to make an approximately 10% strength solution that was inky black in color.

2 mL of water swelled and equilibrated CM Sepharose was equilibrated in a BioRad minicolumn with 3 volumes of acetonitrile. The resin was resuspended in 1 mL acetonitrile and pipetted into a scintillation vial. This was followed with 44 microliters 4-methylmorpholine, 23 mg N-hydroxysuccinimide, and 39 mg of solid N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide hydrochloride. The mixture was vortexed vigorously and then shaken for three hours. To this white solid was added 570 microliters of inky black 20% strength hemin coupled diamine. The black solid was vortexed and shaken for an hour. The slurry strongly resembled Turkish coffee. The mixture was poured into a BioRad minicolumn and filtered, washed with acetonitrile until what came out no longer resembled espresso, then switched to deionized water, and finally 20 mM pH 9 sodium carbonate buffer. The black solid was washed until the effluent ran clear and then resuspended in 2 mL of buffer for storage until use.

**Flavor reaction**

The flavor reaction was created with heme protein (equine myoglobin -Sigma) at 0.35% in a phosphate buffer (20 mM) at pH 6.0 with 100 mM NaCl , this was mixed with Magic Mix (Table 13). Another flavor reaction was created with Immobilized Hemin at 0.35% in a phosphate buffer (20 mM) at pH 6.0 with 100 mM NaCl, this was mixed with Magic Mix (Table 13). The flavor reaction mixtures were heated to 150°C for 3 minutes; this reaction created flavor compounds known to be present in meat.

The characteristic flavor and fragrance components were mostly produced during the cooking process when the flavor precursor molecules reacted with the Heme-protein or the immobilized Hemin. Samples were evaluated by GCMS to identify the flavor compounds generated after heating. Volatile chemicals were isolated from the headspace around the flavor reactions. As can be seen in Table 17, immobilized hemin catalyzed production of compounds similar to those whose production was catalyzed by myoglobin free in solution. Notably, the profiles of flavor compounds, measured by GCMS, produced by cooking mixtures containing the immobilized hemin and the heme-protein, respectively, were very similar.

**TABLE 17**

**Flavor compounds produced by cooking mixtures containing either myoglobin free in solution or hemin coupled to a solid support**

| Flavor compound | myoglobin | hemin-linker-resin |
|---|---|---|
| 2-methyl-5-(methylthio)-thiophene | Low | |
| dihydro-5-propyl-2(3H)-furanone | Low | |
| octane | Low | |
| pyrrole | Low | Low |
| methanethiol | Low | Low |
| 2-thiophenecarboxaldehyde | Low | Low |
| methyl-pyrazine | Low | Low |
| 1-hydroxy-2-propanone | Low | Low |
| propanal | Low | Low |

| | | |
|---|---|---|
| thiophene | Low | medium |
| pyridine | Low | Low |
| 2-methyl-furan | Low | medium |
| oxalic acid, butyl propyl ester | Low | Low |
| pyrazine | medium | Low |
| oxalic acid, diallyl ester | medium | medium |
| 2-butenal | medium | large |
| furfural | medium | medium |
| nonanal | medium | medium |
| 2-ethyl-furan | medium | Low |
| ethanol | medium | very large |
| tert-butanol | medium | |
| 3,3'-dithiobis[2-methyl]-furan | medium | medium |
| m-aminophenylacetylene | medium | medium |
| 2,5-dihydro-3,4-dimethyl-furan | medium | medium |
| 2-acetylthiazole | medium | medium |
| cyclohexane | medium | |
| ethyl tert-butyl ether | medium | |
| carbon disulfide | medium | medium |
| thiazole | medium | medium |
| acetonitrile | medium | large |
| 2-pentyl-furan | medium | Low |
| 3-thiophenecarboxaldehyde | medium | medium |
| 2-methyl-butanal | medium | medium |
| thiazole | medium | large |
| 2-methyl-3-furanthiol | larege | large |
| 2-propenal | large | large |
| 3-methyl-2-butenal | large | medium |
| 2-methyl-3-(methylthio) furan | large | large |
| ethyl acetate | large | medium |
| methacrolein | large | medium |
| methyl-thiirane | large | large |
| methional | large | large |
| methyl alcohol | large | medium |
| 2-butanone | large | Low |
| 2,3-butanedione | large | medium |
| acetone | large | large |
| furan | large | medium |

| | | |
|---|---|---|
| benzaldehyde | large | medium |
| methyl thiolacetate | large | medium |
| acetaldehyde | very large | very large |
| 2-methyl-propanal | very large | very large |
| dimethyl trisulfide | very large | very large |
| 3-methyl-butanal | very large | very large |
| propyl-cyclopropane | | medium |
| (E)-2-octenal | | medium |
| 2-n-propylaziridine | | medium |
| thiirane | | medium |
| ethyl formate | | medium |
| methyl vinyl ketone | | medium |
| 2-propenoic acid, ethyl ester | | medium |
| 1-nonanol | | large |
| 1-octene | | large |
| 1-heptanol | | large |
| 1-dodecene | | large |
| phorone | | very large |

**Example 14. The combination of precursors with Heme protein drives flavor reactions.**

Three samples were compared: precursor mix alone, 1% heme protein alone, and precursor mix with 1% heme. The precursor mix was made of glucose (20 mM), ribose (20 mM), cysteine (10 mM), thiamine (1 mM), and glutamic acid (1 mM). Reactions were all at pH 6.0, prepared and heated to 150°C for 3 minutes. These three samples were run in duplicate. These samples were evaluated by GCMS for the flavor compounds generated. Characteristic flavor and fragrance components were mostly produced during the cooking process where precursors could react with the heme-protein. These samples were evaluated by GCMS for the flavor compounds generated and evaluated for the sensory experience. Volatile chemicals were isolated from the head space around the flavor reaction. The flavor compounds created in each sample is indicated in Table 18. As shown most of the flavor molecules were created on when the precursors are combined with the heme protein.

**Table 18**

**Flavor molecules created by the combination of LegH and precursor mix.**

| Compound | Precursor mix | LegH | Precursor mix + Leg H |
|---|---|---|---|
| carbon disulfide | medium | medium | high |
| isopropyl alcohol | medium | medium | low |
| 2-methyl-furan | low | | low |
| butanal | low | | medium |
| thiophene | low | | low |
| 2,3-butanedione | low | low | high |
| furan | low | | medium |
| 2,4-dimethyl-1-heptene | | high | high |
| acetone | | high | high |
| dimethyl trisulfide | | medium | medium |
| 2-methyl-heptane | | medium | medium |
| 2-pentanone | | medium | |
| pentanal | | medium | medium |
| 2-pentyl-furan | | medium | medium |
| 2-methyl-propanal | | low | high |
| 2-acetatyl-1-propene | | low | low |
| 2-methyl-butanal | | low | medium |
| 1,3-dimethyl-benzene | | low | low |
| octane | | low | low |
| benzene | | low | low |
| benzaldehyde | | | very high |
| 2-butanone | | | very high |
| furfural | | | very high |
| thiazole | | | high |
| nonanal | | | high |
| thiazole | | | high |
| 2-acetylthiazole | | | medium |
| 3-methyl-butanal | | | medium |
| (Z)-2-heptenal | | | medium |
| heptanal | | | medium |
| methyl-thiirane | | | medium |
| 3-ethyl-pentane | | | medium |
| phenylacetaldehyde | | | medium |
| 2-hexyl-furan | | | medium |

| | | | |
|---|---|---|---|
| 2-nonanone | | | medium |
| propanal | | | medium |
| pyrazine | | | medium |
| (Z)-2-heptenal | | | medium |
| 2-methyl-1-heptene | | | medium |
| 2-ethyl-furan | | | medium |
| octanal | | | medium |
| (E)-4-octene | | | low |
| (E)-2-octenal | | | low |
| 2-methyl-thiazole | | | low |
| 2-propenal | | | low |
| 1-octen-3-one | | | low |
| 1-octene | | | low |
| 2-octanone | | | low |
| dimethyl sulfide | | | low |
| 3-pentyl-furan | | | low |
| 2-n-octylfuran | | | low |
| 2-pentyl-thiophene | | | low |

## OTHER EMBODIMENTS

It is to be understood that while the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.

**WHAT IS CLAIMED IS:**

1. A food product comprising:

a) an isolated and purified heme-containing protein or a highly conjugated heterocyclic ring complexed to iron ion; and

b) one or more flavor precursor molecules selected from the group consisting of glucose, fructose, ribose, arabinose, glucose-6-phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, inosine monophosphate (IMP), guanosine monophosphate (GMP), pyrazine, adenosine monophosphate (AMP), lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, vegetable oil, algal oil, sunflower oil, corn oil, soybean oil, palm fruit oil, palm kernel oil, safflower oil, flaxseed oil, rice bran oil, cottonseed oil, olive oil, sunflower oil, canola oil, flaxseed oil, coconut oil, mango oil, linoleic acid, a free fatty acid, cysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, tyrosine, glutathione, an amino acid derivative, a protein hydrolysate, a malt extract, a yeast extract, and a peptone.

2. The food product of claim 1, wherein the highly conjugated heterocyclic ring complexed to an iron ion is selected from the group consisting of porphyrin, porphyrinogen, corrin, corrinoid, chlorin, bacteriochorophyll, corphin, chlorophyllin, bacteriochlorin, and isobacteriochlorin moiety complexed to iron ion.

3. The food product of claim 2, wherein the highly conjugated heterocyclic ring complexed to iron is ferrous chlorin.

4. The food product of claim 1, wherein the heme-containing protein is a plant heme-containing protein, an animal heme-containing protein, a yeast or filamentous fungus heme-containing protein, or a bacterial or archeal heme-containing protein.

5. The food product of claim 1, wherein the heme-containing protein is a non-symbiotic hemoglobin.

6. The food product of claim 1, wherein the heme-containing protein is a leghemoglobin.

7. The food product of claim 6, wherein the leghemoglobin is from soybean, alfalfa, lupin, fava bean, pea, cow pea, or lupine.

8. The food product of claim 1, wherein the isolated and purified heme-containing protein is recombinantly produced, chemically synthesized, or translated *in vitro*.

9. The food product of claim 1, wherein the heme-containing protein comprises an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NO:1.

10. The food product of claim 1, wherein the heme-containing protein is selected from the group consisting of androglobin, cytoglobin, globin E, globin X, globin Y, hemoglobin, myoglobin, erythrocruorin, beta hemoglobin, alpha hemoglobin, protoglobin, cyanoglobin, cytoglobin, histoglobin, neuroglobins, chlorocruorin, a truncated hemoglobin, truncated 2/2 globin, hemoglobin 3, cytochrome, and peroxidase.

11. The food product of claim 1, wherein the food product comprises two to fifty flavor precursors.

12. The food product of claim 1, wherein the food product comprises two to thirty-five flavor precursors.

13. The food product of claim 1, wherein the food product comprises two to ten flavor precursors.

14. The food product of claim 1, wherein the food product comprises two to six flavor precursors.

15. The food product of claim 1, further comprising a food-grade oil, a seasoning agent, a flavoring agent, a protein, a protein concentrate, an emulsifier, a gelling agent, or a fiber.

16. The food product of claim 1, wherein the food product is a meat substitute.

17. The food product of claim 1, wherein the food product is a broth, soup base, stew base, snack food, bouillon powder, bouillon cube, or a flavor packet.

18. The food product of claim 1, wherein the food product is a frozen food product.

19. The food product of claim 1, wherein the food product is sealed within a packet or shaker.

20. The food product of claim 1, wherein the food product is free of animal products.

21. A method of making a food product, the method comprising combining an isolated and purified heme-containing protein or a highly conjugated heterocyclic ring complexed to iron ion with one or more flavor precursor molecules to form a mixture, the one or more flavor precursor molecules selected from the group consisting of glucose, fructose, ribose, arabinose, glucose-6-phosphate, fructose 6-phosphate, fructose 1,6-diphosphate, inositol, maltose, sucrose, maltodextrin, glycogen, nucleotide-bound sugars, molasses, a phospholipid, a lecithin, inosine, IMP, GMP, pyrazine, AMP, lactic acid, succinic acid, glycolic acid, thiamine, creatine, pyrophosphate, sunflower oil, canola oil, flaxseed oil, coconut oil, mango oil, a free fatty acid, cysteine, methionine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, valine, arginine, histidine, alanine, asparagine, aspartate, glutamate, glutamine, glycine, proline, serine, tyrosine, glutathione, an amino acid derivative, a hydrolyzed protein, a malt extract, a yeast extract, and a peptone; and heating the mixture.

22. The method of claim 21, wherein the highly conjugated heterocyclic ring complexed to an iron ion is selected from the group consisting of porphyrin, porphyrinogen, corrin, corrinoid, chlorin, bacteriochorophyll, corphin, chlorophyllin, bacteriochlorin, and isobacteriochlorin moiety complexed to iron ion.

23. The method of claim 21, wherein the highly conjugated heterocyclic ring complexed to iron is ferrous chlorin.

24. The method of claim 21, wherein the heme-containing protein is a plant heme-containing protein, an animal heme-containing protein, a yeast or filamentous fungus heme-containing protein, or a bacterial or archeal heme-containing protein.

25. The method of claim 21, wherein the heme-containing protein is a non-symbiotic hemoglobin.

26. The method of claim 21, wherein the heme-containing protein is a leghemoglobin.

27. The method of claim 26, wherein the leghemoglobin is from soybean, alfalfa, lupin, fava bean, pea, cow pea, or lupine.

28. The method of claim 21, wherein the heme-containing protein is recombinantly produced, chemically synthesized, or transcribed and translated *in vitro*.

29. The method of claim 21, wherein the heme-containing protein comprises an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NO:1.

30. The method of claim 21, wherein the heme-containing protein is selected from the group consisting of androglobin, cytoglobin, globin E, globin X, globin Y, hemoglobin, myoglobin, erythrocruorin, beta hemoglobin, alpha hemoglobin, protoglobin, cyanoglobin, cytoglobin, histoglobin, neuroglobins, chlorocruorin, a truncated hemoglobin, truncated 2/2 globin, hemoglobin 3, cytochrome, and peroxidase.

## ABSTRACT

This document relates to food products containing highly conjugated heterocyclic rings complexed to an iron ion and one or more flavor precursors, and using such food products to modulate the flavor and/or aroma profile of other foods. The food products described herein can be prepared in various ways and can be formulated to be free of animal products.

61185697.doc

**FIG. 1**

SEQ ID NO:1 *Vigna radiata*
MTTTLERGFTEEQEALVVKSWNVMKKNSGELGLKFFLKIFEIAPSAQKLFSFLRDSTVPLEQNPK
LKPHAVSVFVMTCDSAVQLRKAGKVTVRESNLKKLGATHFRTGVANEHFEVTKFALLETIKEAVP
EMWSPAMKNAWGEAYDQLVDAIKYEMKPPSS

SEQ ID NO:2 *Methylacidiphilum infernorum*
MIDQKEKELIKESWKRIEPNKNEIGLLFYANLFKEEPTVSVLFQNPISSQSRKLMQVLGILVQGI
DNLEGLIPTLQDLGRRHKQYGVVDSHYPLVGDCLLKSIQEYLGQGFTEEAKAAWTKVYGIAAQVM
TAE

SEQ ID NO:3 *Aquifex aeolicus*
MLSEETIRVIKSTVPLLKEHGTEITARMYELLFSKYPKTKELFAGASEEQPKKLANAIIAYATYI
DRLEELDNAISTIARSHVRRNVKPEHYPLVKECLLQAIEEVLNPGEEVLKAWEEAYDFLAKTLIT
LEKKLYSQP

SEQ ID NO:4 *Glycine max*
MGAFTEKQEALVSSSFEAFKANIPQYSVVFYTSILEKAPAAKDLFSFLSNGVDPSNPKLTGHAEK
LFGLVRDSAGQLKANGTVVADAALGSIHAQKAITDPQFVVVKEALLKTIKEAVGDKWSDELSSAW
EVAYDELAAAIKKAF

SEQ ID NO:5 *Hordeum vulgare*
MSAAEGAVVFSEEKEALVLKSWAIMKKDSANLGLRFFLKIFEIAPSARQMFPFLRDSDVPLETNP
KLKTHAVSVFVMTCEAAAQLRKAGKITVRETTLKRLGGTHLKYGVADGHFEVTRFALLETIKEAL
PADMWGPEMRNAWGEAYDQLVAAIKQEMKPAE

SEQ ID NO:6 *Magnaporthe oryzae*
MDGAVRLDWTGLDLTGHEIHDGVPIASRVQVMVSFPLFKDQHIIMSSKESPSRKSSTIGQSTRNG
SCQADTQKGQLPPVGEKPKPVKENPMKKLKEMSQRPLPTQHGDGTYPTEKKLTGIGEDLKHIRGY
DVKTLLAMVKSKLKGEKLKDDKTMLMERVMQLVARLPTESKKRAELTDSLINELWESLDHPPLNY
LGPEHSYRTPDGSYNHPFNPQLGAAGSRYARSVIPTVTPPGALPDPGLIFDSIMGRTPNSYRKHP
NNVSSILWYWATIIIHDIFWTDPRDINTNKSSSYLDLAPLYGNSQEMQDSIRTFKDGRMKPDCYA
DKRLAGMPPGVSVLLIMFNRFHNHVAENLALINEGGRFNKPSDLLEGEAREAAWKKYDNDLFQVA
RLVTSGLYINITLVDYVRNIVNLNRVDTTWTLDPRQDAGAHVGTADGAERGTGNAVSAEFNLCYR
WHSCISEKDSKFVEAQFQNIFGKPASEVRPDEMWKGFAKMEQNTPADPGQRTFGGFKRGPDGKFD
DDDLVRCISEAVEDVAGAFGARNVPQAMKVVETMGIIQGRKWNVAGLNEFRKHFHLKPYSTFEDI
NSDPGVAEALRRLYDHPDNVELYPGLVAEEDKQPMVPGVGIAPTYTISRVVLSDAVCLVRGDRFY
TTDFTPRNLTNWGYKEVDYDLSVNHGCVFYKLFIRAFPNHFKQNSVYAHYPMVVPSENKRILEAL
GRADLFDFEAPKYIPPRVNITSYGGAEYILETQEKYKVTWHEGLGFLMGEGGLKFMLSGDDPLHA
QQRKCMAAQLYKDGWTEAVKAFYAGMMEELLVSKSYFLGNNKHRHVDIIRDVGNMVHVHFASQVF
GLPLKTAKNPTGVFTEQEMYGILAAIFTTIFFDLDPSKSFPLRTKTREVCQKLAKLVEANVKLIN
KIPWSRGMFVGKPAKDEPLSIYGKTMIKGLKAHGLSDYDIAWSHVVPTSGAMVPNQAQVFAQAVD
YYLSPAGMHYIPEIHMVALQPSTPETDALLLGYAMEGIRLAGTFGSYREAAVDDVVKEDNGRQVP
VKAGDRVFVSFVDAARDPKHFPDPEVVNPRRPAKKYIHYGVGPHACLGRDASQIAITEMFRCLFR
RRNVRRVPGPQGELKKVPRPGGFYVYMREDWGGLFPFPVTMRVMWDDE

SEQ ID NO:7 *Fusarium oxysporum*
MKGSATLAFALVQFSAASQLVWPSKWDEVEDLLYMQGGFNKRGFADALRTCEFGSNVPGTQNTAE
WLRTAFHDAITHDAKAGTGGLDASIYWESSRPENPGKAFNNTFGFFSGFHNPRATASDLTALGTV
LAVGACNGPRIPFRAGRIDAYKAGPAGVPEPSTNLKDTFAAFTKAGFTKEEMTAMVACGHAIGGV

**FIG. 1-CONT.**

HSVDFPEIVGIKADPNNDTNVPFQKDVSSFHNGIVTEYLAGTSKNPLVASKNATFHSDKRIFDND
KATMKKLSTKAGFNSMCADILTRMIDTVPKSVQLTPVLEAYDVRPYITELSLNNKNKIHFTGSVR
VRITNNIRDNNDLAINLIYVGRDGKKVTVPTQQVTFQGGTSFGAGEVFANFEFDTTMDAKNGITK
FFIQEVKPSTKATVTHDNQKTGGYKVDDTVLYQLQQSCAVLEKLPNAPLVVTAMVRDARAKDALT
LRVAHKKPVKGSIVPRFQTAITNFKATGKKSSGYTGFQAKTMFEEQSTYFDIVLGGSPASGVQFL
TSQAMPSQCS

SEQ ID NO:8 *Fusarium graminearum*
MASATRQFARAATRATRNGFAIAPRQVIRQQGRRYYSSEPAQKSSSAWIWLTGAAVAGGAGYYFY
GNSASSATAKVFNPSKEDYQKVYNEIAARLEEKDDYDDGSYGPVLVRLAWHASGTYDKETGTGGS
NGATMRFAPESDHGANAGLAAARDFLQPVKEKFPWITYSDLWILAGVCAIQEMLGPAIPYRPGRS
DRDVSGCTPDGRLPDASKRQDHLRGIFGRMGFNDQEIVALSGAHALGRCHTDRSGYSGPWTFSPT
VLTNDYFRLLVEEKWQWKKWNGPAQYEDKSTKSLMMLPSDIALIEDKKFKPWVEKYAKDNDAFFK
DFSNVVLRLFELGVPFAQGTENQRWTFKPTHQE

SEQ ID NO: 9 *Chlamydomonas eugametos*
MSLFAKLGGREAVEAAVDKFYNKIVADPTVSTYFSNTDMKVQRSKQFAFLAYALGGASEWKGKDM
RTAHKDLVPHLSDVHFQAVARHLSDTLTELGVPPEDITDAMAVVASTRTEVLNMPQQ

SEQ ID NO:10 *Tetrahymena pyriformis*
MNKPQTIYEKLGGENAMKAAVPLFYKKVLADERVKHFFKNTDMDHQTKQQTDFLTMLLGGPNHYK
GKNMTEAHKGMNLQNLHFDAIIENLAATLKELGVTDAVINEAAKVIEHTRKDMLGK

SEQ ID NO:11 *Paramecium caudatum*
MSLFEQLGGQAAVQAVTAQFYANIQADATVATFFNGIDMPNQTNKTAAFLCAALGGPNAWTGRNL
KEVHANMGVSNAQFTTVIGHLRSALTGAGVAAALVEQTVAVAETVRGDVVTV

SEQ ID NO:12 *Aspergillus niger*
MPLTPEQIKIIKATVPVLQEYGTKITTAFYMNMSTVHPELNAVFNTANQVKGHQARALAGALFAY
ASHIDDLGALGPAVELICNKHASLYIQADEYKIVGKYLLEAMKEVLGDACTDDILDAWGAAYWAL
ADIMINREAALYKQSQG

SEQ ID NO:13 *Zea mays*
MALAEADDGAVVFGEEQEALVLKSWAVMKKDAANLGLRFFLKVFEIAPSAEQMFSFLRDSDVPLE
KNPKLKTHAMSVFVMTCEAAAQLRKAGKVTVRETTLKRLGATHLRYGVADGHFEVTGFALLETIK
EALPADMWSLEMKKAWAEAYSQLVAAIKREMKPDA

SEQ ID NO:14 *Oryza sativa subsp. japonica*
*MALVEGNNGVSGGAVSFSEEQEALVLKSWAIMKKDSANIGLRFFLKIFEVAPSASQMFSFLRNSD*
*VPLEKNPKLKTHAMSVFVMTCEAAAQLRKAGKVTVRDTTLKRLGATHFKYGVGDAHFEVTRFALL*
*ETIKEAVPVDMWSPAMKSAWSEAYNQLVAAIKQEMKPAE*

SEQ ID NO:15 *Arabidopsis thaliana*
MESEGKIVFTEEQEALVVKSWSVMKKNSAELGLKLFIKIFEIAPTTKKMFSFLRDSPIPAEQNPK
LKPHAMSVFVMCCESAVQLRKTGKVTVRETTLKRLGASHSKYGVVDEHFEVAKYALLETIKEAVP
EMWSPEMKVAWGQAYDHLVAAIKAEMNLSN

**FIG. 1-CONT.**

SEQ ID NO:16 *Pisum sativum*
MGFTDKQEALVNSSWESFKQNLSGNSILFYTIILEKAPAAKGLFSFLKDTAGVEDSPKLQAHAEQ
VFGLVRDSAAQLRTKGEVVLGNATLGAIHVQRGVTDPHFVVVKEALLQTIKKASGNNWSEELNTA
WEVAYDGLATAIKKAMT

SEQ ID NO:17 *Vigna unguiculata*
MVAFSDKQEALVNGAYEAFKANIPKYSVVFYTTILEKAPAAKNLFSFLANGVDATNPKLTGHAEK
LFGLVRDSAAQLRASGGVVADAALGAVHSQKAVNDAQFVVVKEALVKTLKEAVGDKWSDELGTAV
ELAYDELAAAIKKAY

SEQ ID NO:18 *Bos taurus*
MGLSDGEWQLVLNAWGKVEADVAGHGQEVLIRLFTGHPETLEKFDKFKHLKTEAEMKASEDLKKH
GNTVLTALGGILKKKGHHEAEVKHLAESHANKHKIPVKYLEFISDAIIHVLHAKHPSDFGADAQA
AMSKALELFRNDMAAQYKVLGFHG

SEQ ID NO:19 *Sus scrofa*
MGLSDGEWQLVLNVWGKVEADVAGHGQEVLIRLFKGHPETLEKFDKFKHLKSEDEMKASEDLKKH
GNTVLTALGGILKKKGHHEAELTPLAQSHATKHKIPVKYLEFISEAIIQVLQSKH
PGDFGADAQGAMSKALELFRNDMAAKYKELGFQG

SEQ ID NO:20 *Equus caballus*
MGLSDGEWQQVLNVWGKVEADIAGHGQEVLIRLFTGHPETLEKFDKFKHLKTEAEMKASEDLKKH
GTVVLTALGGILKKKGHHEAELKPLAQSHATKHKIPIKYLEFISDAIIHVLHSKH
PGDFGADAQGAMTKALELFRNDIAAKYKELGFQG

SEQ ID NO:21 *Nicotiana benthamiana*
MSSFTEEQEALVVKSWDSMKKNAGEWGLKLFLKIFEIAPSAKKLFSFLKDSNVPLEQNAKLKPHS
KSVFVMTCEAAVQLRKAGKVVVRDSTLKKLGATHFKYGVADEHFEVTKFALLETIKEAVPEMWSV
DMKNAWGEAFDQLVNAIKTEMK

SEQ ID NO:22 *Bacillus subtilis*
MGQSFNAPYEAIGEELLSQLVDTFYERVASHPLLKPIFPSDLTETARKQKQFLTQYLGGPPLYTE
EHGHPMLRARHLPFPITNERADAWLSCMKDAMDHVGLEGEIREFLFGRLELTARHMVNQTEAEDR
SS

SEQ ID NO:23 *Corynebacterium glutamicum*
MTTSENFYDSVGGEETFSLIVHRFYEQVPNDDILGPMYPPDDFEGAEQRLKMFLSQYWGGPKDYQ
EQRGHPRLRMRHVNYPIGVTAAERWLQLMSNALDGVDLTAEQREAIWEHMVRAADMLINSNPDPH
A

SEQ ID NO:24 *Synechocystis* PCC6803
MSTLYEKLGGTTAVDLAVDKFYERVLQDDRIKHFFADVDMAKQRAHQKAFLTYAFGGTDKYDGRY
MREAHKELVENHGLNGEHFDAVAEDLLATLKEMGVPEDLIAEVAAVAGAPAHKRDVLNQ

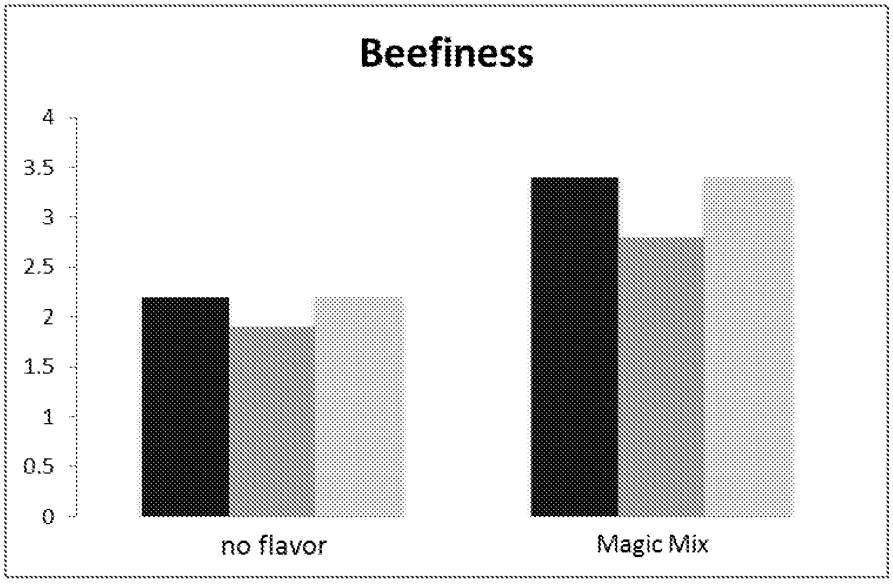
SEQ ID NO:25 *Synechococcus* sp. PCC 7335
MDVALLEKSFEQISPRAIEFSASFYQNLFHHHPELKPLFAETSQTIQEKKLIFSLAAIIENLRNP
DILQPALKSLGARHAEVGTIKSHYPLVGQALIETFAEYLAADWTEQLATAWVEAYDVIASTMIEG
ADNPAAYLEPELTFYEWLDLYGEESPKVRNAIATLTHFHYGEDPQDVQRDSRG

**FIG. 1-CONT.**

SEQ ID NO:26 *Nostoc commune*
MSTLYDNIGGQPAIEQVVDELHKRIATDSLLAPVFAGTDMVKQRNHLVAFLAQIFEGPKQYGGRP
MDKTHAGLNLQQPHFDAIAKHLGERMAVRGVSAENTKAALDRVTNMKGAILNK

SEQ ID NO:27 *Bacillus megaterium*
MREKIHSPYELLGGEHTISKLVDAFYTRVGQHPELAPIFPDNLTETARKQKQFLTQYLGGPSLYT
EEHGHPMLRARHLPFEITPSRAKAWLTCMHEAMDEINLEGPERDELYHRLILTAQHMINSPEQTD
EKGFSH

FIG. 2



Sheet 1 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## U.S. Patent Documents

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 1. | 2001/0024677 | 9/27/2001 | Bringe | | | |
| | 2. | 2001/0049132 | 12/6/2001 | Kringelum et al. | | | |
| | 3. | 2003/0198700 | 10/23/2003 | Gruber | | | |
| | 4. | 2003/0224476 | 12/4/2003 | Chou | | | |
| | 5. | 2004/0151778 | 8/5/2004 | Richard et al. | | | |
| | 6. | 2004/0161513 | 8/19/2004 | Akashe et al. | | | |
| | 7. | 2005/0037111 | 2/17/2005 | Berry | | | |
| | 8. | 2006/0035003 | 2/16/2006 | McMindes et al. | | | |
| | 9. | 2006/0035006 | 2/16/2006 | McMindes et al. | | | |
| | 10. | 2006/0233721 | 10/19/2006 | Tamarkin et al. | | | |
| | 11. | 2007/0269567 | 11/22/2007 | McMindes et al. | | | |
| | 12. | 2007/0269571 | 11/22/2007 | Akita et al. | | | |
| | 13. | 2007/0269583 | 11/22/2007 | McMindes et al. | | | |
| | 14. | 2008/0226810 | 9/18/2008 | Passe et al. | | | |
| | 15. | 2008/0254168 | 10/16/2008 | Mueller et al. | | | |
| | 16. | 2008/0268112 | 10/30/2008 | Rolan et al. | | | |
| | 17. | 2008/0292749 | 11/27/2008 | Goodwins et al. | | | |
| | 18. | 2008/0299254 | 12/4/2008 | Kim et al. | | | |
| | 19. | 2009/0264520 | 10/22/2009 | Bhagat et al. | | | |
| | 20. | 2009/0274817 | 11/5/2009 | Yamaguchi et al. | | | |
| | 21. | 2010/0074998 | 3/25/2010 | Vega et al. | | | |
| | 22. | 2010/0136201 | 6/3/2010 | Bigeard et al. | | | |
| | 23. | 2010/0233347 | 9/16/2010 | Uhrhan | | | |
| | 24. | 2010/0249560 | 9/30/2010 | Levinson et al. | | | |
| | 25. | 2010/0281765 | 11/11/2010 | Schwartz | | | |
| | 26. | 2010/0311950 | 12/9/2010 | Kugitani | | | |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 27. | 2011/0008502 | 1/13/2011 | Hosomi et al. | | | |
| | 28. | 2011/0064862 | 3/17/2011 | McCready et al | | | |
| | 29. | 2011/0065847 | 3/17/2011 | Miwa et al. | | | |
| | 30. | 2011/0081386 | 4/7/2011 | Guth et al. | | | |
| | 31. | 2011/0081435 | 4/7/2011 | Guth et al. | | | |
| | 32. | 2011/0117180 | 5/19/2011 | Yan et al. | | | |
| | 33. | 2011/0286992 | 11/24/2012 | Gruber et al. | | | |
| | 34. | 2011/0288389 | 11/24/2011 | Levinson et al. | | | |
| | 35. | 2012/0059150 | 3/8/2012 | Moloney et al. | | | |
| | 36. | 2012/0093994 | 4/19/2012 | Hsieh et al. | | | |
| | 37. | 2013/0004617 | 1/3/2013 | Zhang et al. | | | |
| | 38. | 2015/0366233 | 12/24/2015 | Brown et al. | | | |
| | 39. | 3,658,550 | 4/25/1972 | Hawley | | | |
| | 40. | 3,693,533 | 9/26/1972 | Liepa | | | |
| | 41. | 3,829,582 | 8/13/1974 | Guadagni et al. | | | |
| | 42. | 3,870,801 | 3/11/1975 | Tombs | | | |
| | 43. | 3,973,043 | 8/3/1976 | Lynn | | | |
| | 44. | 3,966,985 | 6/29/1976 | Jonas | | | |
| | 45. | 4,045,587 | 8/30/1977 | Katz et al. | | | |
| | 46. | 4,094,997 | 6/13/1978 | Aishima et al. | | | |
| | 47. | 4,218,487 | 8/19/1980 | Jaeggi | | | |
| | 48. | 4,435,438 | 3/6/1984 | Lehnhardt et al. | | | |
| | 49. | 4,604,290 | 8/5/1986 | Lee et al. | | | |
| | 50. | 4,678,676 | 7/7/1987 | Ishizuka et al. | | | |
| | 51. | 4,994,285 | 2/19/1991 | Hisano et al. | | | |
| | 52. | 5,055,310 | 10/18/1991 | Nonaka et al. | | | |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet _3_ of _18_

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## U.S. Patent Documents

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 53. | 5,264,239 | 11/23/1993 | Cornet et al. | | | |
| | 54. | 5,443,852 | 8/22/1995 | Shahidi et al. | | | |
| | 55. | 5,650,554 | 7/22/1997 | Moloney et al. | | | |
| | 56. | 5,753,295 | 5/19/1998 | Goldman | | | |
| | 57. | 5,807,601 | 9/15/1998 | Carpenter et al | | | |
| | 58. | 5,856,452 | 1/5/1999 | Moloney et al. | | | |
| | 59. | 5,922,392 | 7/13/1999 | Kelly et al. | | | |
| | 60. | 6,093,424 | 7/25/2000 | Han et al. | | | |
| | 61. | 6,146,645 | 11/14/2000 | Deckers et al. | | | |
| | 62. | 6,183,762 | 2/6/2001 | Deckers et al. | | | |
| | 63. | 6,210,742 | 4/3/2001 | Deckers et al. | | | |
| | 64. | 6,228,418 | 5/8/2001 | Gluck | | | |
| | 65. | 6,242,036 | 6/5/2001 | Han et al. | | | |
| | 66. | 6,287,620 | 9/11/2001 | Van Den Ouweland et al. | | | |
| | 67. | 6,372,234 | 4/16/2002 | Deckers et al. | | | |
| | 68. | 6,372,961 | 4/16/2002 | Tarczynski | | | |
| | 69. | 6,379,738 | 4/30/2002 | Dingman et al. | | | |
| | 70. | 6,383,531 | 5/7/2002 | Gottemoller | | | |
| | 71. | 6,399,135 | 6/4/2002 | Gottemoller | | | |
| | 72. | 6,413,569 | 7/2/2002 | Borders et al. | | | |
| | 73. | 6,416,797 | 7/9/2002 | Han et al. | | | |
| | 74. | 6,420,148 | 7/16/2002 | Yamaguchi | | | |
| | 75. | 6,495,184 | 12/17/2002 | Zheng et al. | | | |
| | 76. | 6,495,187 | 12/17/2002 | Borders et al. | | | |
| | 77. | 6,509,453 | 1/21/2003 | Moloney | | | |
| | 78. | 6,582,710 | 6/24/2003 | Deckers et al. | | | |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 4 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## U.S. Patent Documents

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 79. | 6,596,287 | 7/22/2003 | Deckers et al. | | | |
| | 80. | 6,599,513 | 7/29/2003 | Deckers et al. | | | |
| | 81. | 6,692,788 | 2/17/2004 | Mottram et al. | | | |
| | 82. | 6,761,914 | 7/13/2004 | Deckers et al. | | | |
| | 83. | 6,908,634 | 6/21/2005 | Hwang | | | |
| | 84. | 6,936,749 | 8/30/2005 | Guy et al. | | | |
| | 85. | 7,052,879 | 5/30/2006 | Shaw et al. | | | |
| | 86. | 7,332,587 | 2/19/2008 | Moloney | | | |
| | 87. | 7,407,786 | 8/5/2008 | Giver et al. | | | |
| | 88. | 7,479,472 | 1/20/2009 | Harbury et al. | | | |
| | 89. | 7,585,645 | 9/8/2009 | Deckers et al. | | | |
| | 90. | 7,622,290 | 11/24/2009 | Brunstedt et al. | | | |
| | 91. | 7,666,618 | 2/23/2010 | Miasnikov et al. | | | |
| | 92. | 7,666,628 | 2/23/2010 | Moloney | | | |
| | 93. | 7,674,953 | 3/9/2010 | Mulet Salort et al. | | | |
| | 94. | 7,709,044 | 5/4/2010 | Ishimoto | | | |
| | 95. | 7,807,870 | 10/5/2010 | Geigenberger et al. | | | |
| | 96. | 7,931,925 | 4/26/2011 | Nielsen | | | |
| | 97. | 8,012,732 | 9/6/2011 | Brunstedt et al. | | | |
| | 98. | 8,021,695 | 9/20/2011 | Gruber et al. | | | |
| | 99. | 8,188,415 | 5/29/2012 | Kats et al. | | | |
| | 100. | 8,304,522 | 11/6/2012 | Kungitani | | | |
| | 101. | 8,597,694 | 12/3/2013 | Guth et al. | | | |
| | 102. | 9,011,949 | 4/21/2015 | Brown et al. | | | |

## Foreign Patent Documents or Published Foreign Patent Applications

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|

| Examiner Signature | Date Considered |
|---|---|
| | |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | 103. | CN 101138405 | 3/12/2008 | CHINA | | | | |
| | 104. | CN 101541187A | 9/23/2009 | CHINA | | | | |
| | 105. | CN 101606574A | 12/23/2009 | CHINA | | | | |
| | 106. | CN 1252231A | 5/10/2000 | CHINA | | | | |
| | 107. | CN 1301811A | 7/4/2001 | CHINA | | | | |
| | 108. | CN 1407108A | 4/2/2003 | CHINA | | | | |
| | 109. | CN 1593223A | 3/16/2005 | CHINA | | | | |
| | 110. | CN 1634524A | 7/6/2005 | CHINA | | | | |
| | 111. | CN1466903 | 1/14/2004 | CHINA | | | | |
| | 112. | CN1557188 | 12/29/2004 | CHINA | | | | |
| | 113. | DE 102007061256 | 6/25/2009 | GERMANY | | | | |
| | 114. | DE 202011002097 | 3/24/2011 | GERMANY | | | | |
| | 115. | EP 0500132 | 8/26/1992 | EPO | | | | |
| | 116. | EP 0680751 | 11/24/2004 | EPO | | | | |
| | 117. | EP 0815736 | 1/7/1998 | EPO | | | | |
| | 118. | EP 1166653 | 1/2/2002 | EPO | | | | |
| | 119. | EP 1254601 | 11/6/2002 | EPO | | | | |
| | 120. | EP 1361264 | 4/18/2007 | EPO | | | | |
| | 121. | EP 1529444 | 5/11/2005 | EPO | | | | |
| | 122. | EP 1952695 | 8/6/2008 | EPO | | | | |
| | 123. | EP 2138052 | 12/30/2009 | EPO | | | | |
| | 124. | EP1759593 | 3/7/2007 | EPO | | | | |
| | 125. | GB 2016255 | 9/26/1979 | GB | | | | |
| | 126. | JP 2009171877 | 8/6/2009 | JAPAN | | | | |
| | 127. | JP 2011000073 | 1/6/2011 | JAPAN | | | | |
| | 128. | JP 52156962 | 12/27/1977 | JAPAN | | | | |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 6 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | 129. | JP S54122766 | 9/22/1979 | JAPAN | | | | |
| | 130. | JP S573338 | 01/21/1982 | JAPAN | | | | |
| | 131. | WO 1993/025697 | 12/23/1993 | WIPO | | | | |
| | 132. | WO 1994/017673 | 8/18/1994 | WIPO | | | | |
| | 133. | WO 1996/017981 | 6/13/1996 | WIPO | | | | |
| | 134. | WO 1997/01961 | 1/23/1997 | WIPO | | | | |
| | 135. | WO 1998/012913 | 4/2/1998 | WIPO | | | | |
| | 136. | WO 1998/053698 | 12/3/1998 | WIPO | | | | |
| | 137. | WO 2001/022829 | 4/5/2001 | WIPO | | | | |
| | 138. | WO 2001/022830 | 4/5/2001 | WIPO | | | | |
| | 139. | WO 2003/070172 | 8/28/2003 | WIPO | | | | |
| | 140. | WO 2004/113543 | 12/29/2004 | WIPO | | | | |
| | 141. | WO 2005/013713 | 2/17/2005 | WIPO | | | | |
| | 142. | WO 2005/097059 | 10/20/2005 | WIPO | | | | |
| | 143. | WO 2006/042608 | 4/27/2006 | WIPO | | | | |
| | 144. | WO 2007/060288 | 5/31/2007 | WIPO | | | | |
| | 145. | WO 2007/115899 | 10/18/2007 | WIPO | | | | |
| | 146. | WO 2007/118751 | 12/21/2007 | WIPO | | | | |
| | 147. | WO 2007/137125 | 11/29/2007 | WIPO | | | | |
| | 148. | WO 2008/017499 | 2/14/2008 | WIPO | | | | |
| | 149. | WO 2008/030089 | 3/13/2008 | WIPO | | | | |
| | 150. | WO 2008/083117 | 7/10/2008 | WIPO | | | | |
| | 151. | WO 2009/060678 | 5/14/2009 | WIPO | | | | |
| | 152. | WO 2010/101625 | 9/10/2010 | WIPO | | | | |
| | 153. | WO 2012/106751 | 8/16/2012 | WIPO | | | | |
| | 154. | WO 2012/110797 | 8/23/2012 | WIPO | | | | |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | 155. | WO 2012/116703 | 9/7/2012 | WIPO | | | | |
| | 156. | WO 2013/010037 | 1/17/2013 | WIPO | | | | |
| | 157. | WO 2013/010042 | 1/17/2013 | WIPO | | | | |
| | 158. | WO 2013/138793 | 9/19/2013 | WIPO | | | | |

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| | 159. | "Heterlolgous," Merriam-Webster Dictionary, retrieved on 9/10/2015, http://www.merriam-webster.com/dictionary/heterologous, 1 page |
| | 160. | "Rethink Meat," Presented at the 6th Annual Sustainable Innovation Forum, Paris, France, December 7-8, 2015, retrieved on 2/1/2016, https://amp.twimg.com/v/7c7f7084-b173-42cb-bc12-723f35994dff, 1 page (Video Submission) |
| | 161. | "Silicon Valley gets a taste for food," The Economist Technology Quarterly, March 7, 2015, http://cdn.static-economist.com/sites/default/files/sponsorships/accenture_tq_march2015/20150307_tq_mailout.pdf, pages 11-13 |
| | 162. | "Veggie burgers that look, taste, and bleed like real meat," CBS News, August 9, 2016, retrieved August 25, 2016 <http://www.cbsnews.com/news/food-trend-veggie-burgers-that-look-bleed-taste-like-real-meat/>, 4 pages |
| | 163. | "Watch Momofuku Cook Impossible Foods' Plant-Based Burger that 'Bleeds'," Vice, July 27, 2016, retrieved August 25, 2016, <https://munchies.vice.com/en/videos/watch-momofuku-cook-impossible-foods-plant-based-burger-that-bleeds>, 3 pages |
| | 164. | "Acidified Milk Products and Protein Stabilisation," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 15 pages |
| | 165. | "Ice Cream and Ice Cream Desserts," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 5 pages |
| | 166. | "Innovation at Its Best: 5 Years of Food Valley Awards," Food Valley, retrieved on 3/7/2014, http://www.foodvalley.nl/English/Afbeeldingen/FVAjubileumuitgave/Innovation%20at%20Its%20Best%20-%205%20Years%20of%20Food%20Valley%20Awards.pdf, 51 pages |
| | 167. | "Low Methylester Amidated Pectins," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 13 pages |
| | 168. | "Stabilisation of Whey and Whey Mix Products with Pectin," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 6 Pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 169. | "Texturising of Fermented Milk Products," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 6 pages |
| | 170. | Asgar et al., "Nonmeat Protein Alternatives as Meat Extenders and Meat Analogs," Comprehensive Reviews in Food Science and Food Safety, 2010, 9:513-529 |
| | 171. | Australian Patent Examination Report No. 1 in Australian Application No. 2012281064, dated January 25, 2016, 5 pages |
| | 172. | Australian Patent Examination Report No. 1 in Australian Application No. 2012281069, dated September 25, 2015, 5 pages |
| | 173. | Baek, "Process Flavors," Handbook of Meat, Poultry and Seafood Quality, Second Edition, 2012, Chapter 7, 91-104 |
| | 174. | Battaglia et al., "The Enigmatic LEA Proteins and Other HydroPhilins1[W]," Plant Physiology, September 2008, 148:6-24 |
| | 175. | Belitz et al., "Aroma Compounds," Food Chemistry, Springer 2009, pp. 340-402 |
| | 176. | Belitz et al., Food Chemistry, 3rd revised edition. Springer-Verlag, Berlin (2006), p. 368 |
| | 177. | Beuchat et al., "Fermentation of Peanut Milk with Lactobacillus bulgaricus and L. acidophilus," J. Food Sci, 1978, 43:1109-1112 |
| | 178. | Beyond Better Order page and Nutritional Facts, retrieved on 2/6/2014, http://www.beyond-better.com/order.html, 8 pages |
| | 179. | Beyond Meat, posted on or before 2/24/2001, accessed 1/7/2014, http://beyondmeat.com/, 2 pages |
| | 180. | Boca Bruschetta Tomato Basil Parmesan Veggie Patties Package Ingredients, posted on or before 7/22/2008, accessed on 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928360103, 1 page |
| | 181. | Boca Flame Grilled Meatless Burgers Package Ingredients, posted on or before 7/14/2008, accessed on 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928367321, 1 page |
| | 182. | Boca Original Meatless Chik'n Nuggets Package Ingredients, posted on or before7/22/2008, accessed 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928360012, 1 page |
| | 183. | Boca Original Vegan Meatless Burgers Package Ingredients, posted on or before 7/14/2008, accessed 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928333445, 1 page |
| | 184. | Boral and Bohidar , "Effect Of Ionic Strength On Surface-Selective Patch Binding-Induced Phase Separation And Coacervation In Similarly Charged Gelatin-Agar Molecular Systems," Journal of Physical Chemistry B, 2010, 114(37): 12027-35 |
| | 185. | Bradshaw, "Food 2.0: the future of what we eat," FT Magazine, October 31, 2014, retrieved on 11/11/2014, http://www.ft.com/cms/s/2/bfa6fca0-5fbb-11e4-8c27-00144feabdc0.html#axzz3InGaCIdL, 6 pages |
| | 186. | Brewer, "The Chemistry of Beef Flavor," December, 2006, retrieved on August 30, 2016, <http://beefresearch.org/CMDocs/BeefResearch/The%20Chemistry%20of%20Beef%20Flavor.pdf>, 16 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 187. | Brooks et al., "Prediction of beef flavor by precursor and volatile compounds Principal Investigators: Funded by The Beef Checkoff," Texas Tech University, May 31, 2012, retreived August 30, 2016, <http://www.beefresearch.org/CMDocs/BeefResearch/PE_Project_Summaries_FY11Prediction_of_beef_flavor.pdf> |
| | 188. | Bunge et al., "Quest Heats up for Alternatives to Beef," The Wall Street Journal, Business News, November 4, 2016, page B5 |
| | 189. | Burdock, "Fenaroli's handbook of flavor ingredients," CRC press, 17 pages (2016) |
| | 190. | Bute Island Foods, "Sheese," posted on or before 12/5/2006, retrieved on 2/6/2014, http://www.buteisland.com/a_sheese_home.htm, 26 pages |
| | 191. | Cadwallader and Macleod, "16 Instrumental methods for analyzing the flavor of muscle foods," Flavor of Meat, Meat Products and Seafoods, 18 pages (1998) |
| | 192. | Calkins et al., "A fresh look at meat flavor," Meat Science, 77(1):63-80 (2007) |
| | 193. | Chamlee, "Why Do People Want Veggie Burgers That Bleed?," Eater, July 25, 2016, retrieved August 25, 2016, <http://www.eater.com/2016/7/25/12270698/lab-grown-meat-beyond-burger-impossible-foods>, 11 pages |
| | 194. | Chaudhari et al., "The cell biology of taste," 190(3):285-296 (August 2010) |
| | 195. | Chen et al., "Effect of Urea on Volatile Generation from Maillard Reaction of Cysteine and Ribose," J. Agric. Food Chem., 48:3512-3516 (2000) |
| | 196. | Chen et al., "Influence of DNA on Volatile Generation from Maillard Reaction of Cysteine and Ribose," Nutraceutical Beverages, American Chemical Society, pp. 427-442 (December 2003) |
| | 197. | Chicago Vegan Foods, accessed on 1/7/2014, http://chicagoveganfoods.com/products/teese-vegan-cheese/, 8 pages |
| | 198. | Chinese Second Office Action in Chinese Application No. 201280041099.9, dated 10/8/2015, 15 pages (with translation) |
| | 199. | Clare et al., "Effects of Transglutaminase Catalysis on the Functional and Immunoglobulin Binding Properties of Peanut Flour Dispersions Containing Casein," J. Agric. Food Chem., 2008, 56(22):10913-10921 |
| | 200. | Connelly and Piper, "Person of the Year: Tal Ronnen," VegNews, November/December 2013, 29-32 |
| | 201. | Dai, "David Chang Adds Plant Based 'Impossible Burger' to Nishi Menu," July 26, 2016, retrieved July 27, 2016 <http://ny.eater.com/2016/7/26/12277310/david-chang-impossible-burger-nishi>, 6 pages |
| | 202. | Daiya, Deliciously Dairy Free, "Say Cheese, Dairy-Free cheesy deliciousness," posted on or before 1/26/2010, accessed 1/7/2014, http://www.daiyafoods.com, 6 pages |
| | 203. | Davis et al., "Some Rheological Properties of Aqueous Peanut Flour Dispersions," J. Texture Studies, 2007, 38:253-272 |
| | 204. | Deliciously Healthy Nacheez, Products and Nutrition Facts, posted on or before 1/23/2011, retrieved on 2/7/2014, http://nacheez.com/, 9 pages |
| | 205. | Dixie Diner's Club, Cheese (Not!) Sauce Nutrition Facts, posted on or before 9/3/2009, retrieved on 2/7/2014, http://www.dixiediner.com/cheese-notÂ™-sauce-regular-cheese-p-69.html, 2 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 10 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 206. | D'Onfro, "I tried the plant-based meat that Google wanted to buy and I never want to eat a 'real' hamburger again" Business Insider, June 12, 2016, retrieved June 14, 2016, <http://www.businessinsider.com/impossible-burgers-taste-test-2016-6>, 14 pages |
| | 207. | Donnelly, "Meet the Impossible Burget: It Looks and Taskes Like the Real Thing But Is Totally Meat-Free," Vogue, August 1, 2016, retreived August 25, 2016 <http://www.vogue.com/13462891/impossible-burger-meat-free-vegan-david-chang/>, 6 pages |
| | 208. | Door 86 Vegan Cheese, Discover a New World of Vegan Cheese and Menu, posted on or before 12/5/2013, retrieved 2/7/2014, http://door86vegancheese.wix.com/door-86-vegan-cheese#, 14 pages |
| | 209. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Brazil Nut Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-brazil.html, 1 page |
| | 210. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Crystal Algae Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-crystal.html, 1 page |
| | 211. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Dulse Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-dulse.html, 1 page |
| | 212. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Hemp Seeds Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-hemp.html, 1 page |
| | 213. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew Nut Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-nut-cheese.html, 1 page |
| | 214. | Dr. Cow, Natural Living & Organic Foods, "Aged Macadamia & Hemp Seeds Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-macadam-hemp.html, 1 page |
| | 215. | Dr. Cow, Natural Living & Organic Foods, "Aged Macadamia Nut Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-macadam-nut-cheese.html, 1 page |
| | 216. | Dr. Cow, Natural Living & Organic Foods, "Cashew Nut Cream Cheese," posted on or before 9/22/2008, accessed 1/7/2014, http://www.dr-cow.com/products/cashew-nut-cream-cheese.html, 1 page |
| | 217. | Duane, "Engineering the Future of Artisanal Vegan Cheese," Food & Wine, November 2013, http://www.foodandwine.com/articles/engineering-the-future-of-artisanal-vegan-cheese, 5 pages |
| | 218. | Ellis et al., "Structure of ferric soybean leghemoglobin a nicotinate at 2.3 A resolution," Acta Crystallographica, May 1997, Section D, 53(3):302-310 |
| | 219. | Elmore et al., "Effect of the Polyunsaturated Fatty Acid Composition of Beef Muscle on the Profile of Aroma Volatiles," J. Agric. Food Chem. 47:1619-1625 (1999) |
| | 220. | Etienne, "Eating the plant-derived Impossible Burget cooked by Momofuku's David Chang," Tech Crunch, July 26, 2016, retrieved August 25, 2016, <https://techcrunch.com/2016/07/26/eating-the-plant-derived-impossible-burger-cooked-by-momofukus-david-chang/>, 9 pages |
| | 221. | European Search Report (Supplementary) in European Application No. 12810661.4, dated March 12, 2015, 14 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 11 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 222. | European Search Report (Supplementary) in European Application No. 12811683.7, dated March 12, 2015, 9 pages |
| | 223. | European Search Report for International Application No. EP 14737766, dated July 15, 2016, 11 pages |
| | 224. | Fantastic World Foods, "Fantastic Foods Nature's Burger (Meatless Burger Mix)," posted on or before 1/6/2009, accessed on 1/7/2014, http://fantasticfoods.elsstore.com/view/product/?id=8715&cid=1967, 2 pages |
| | 225. | Felt, "Raw Vegan Almond Ricotta Cheese," FeedYourSkull, March 12, 2012, https://feedyourskull.com/2012/03/12/raw-vegan-almond-ricotta-cheese/, 15 pages |
| | 226. | Follow Your Heart Homepage, posted on or before 11/28/1999, accessed 1/7/2014, http://www.followyourheart.com, 3 pages |
| | 227. | Follow Your Heart, Products and Nutrition Facts, posted on or before 11/28/1999, accessed 2/7/2014, http://www.followyourheart.com/products/, 26 pages |
| | 228. | Foo, "Beef and Scallop Stir-Fry," Food & Wine, July 2001, retrieved on 9/10/2015, http://www.foodandwine.com/recipes/beef-and-scallop-stir-fry/print, 3 pages |
| | 229. | Food for Lovers, Vegan Queso Original & Vegan Queso Mild, posted on or before 10/27/2011, retrieved 2/7/2014, http://www.foodforlovers.com/products, 3 pages |
| | 230. | Free & Easy Dairy Free Cheese Flavour Sauce Mix, Holland & Barrett, posted on or before 6/22/2013, retrieved 2/7/2014, http://www.hollandandbarrett.com/pages/product_detail.asp?pid=2686, 2 pages |
| | 231. | Fromson, "The Race to Build a Fake-Meat Burger That Just Might Save the World, Free the cows!" New York Magazine, June 1-7, 2015, 46-48 |
| | 232. | Galaxy Foods Vegan Soy Grated Parmesan, ShopRite, retrieved 2/7/2014, http://www.shoprite.com/pd/Galaxy-Nutritional-Foods/Vegan-Grated-Soy-Topping-Parmesan-Flavor/4-oz/077172640006/, 6 pages |
| | 233. | Gardein The Ultimate Beefless Burger Package Ingredients, posted on or before 2013, accessed 1/7/2014, http://gardein.com/products/beefless-burger/, 12 pages |
| | 234. | Gardenburger The Original Veggie Burger Package Ingredients, posted on or before 10/5/2008, accessed 1/7/2014, http://www.gardenburger.com/product.aspx?id=11630, 1 page |
| | 235. | GenBank Accession No. AFK42304.1, "unknown [Medicago truncatula], May 25, 2012, 1 page |
| | 236. | GHARST, "Biochemical and Rheological Characteristics of Peanut Proteins Crosslinked with Microbial Transglutaminase," A dissertation submitted to the Graduate Faculty of North Carolina State University, Raleigh NC, 2007, 149 pages |
| | 237. | Gharst, "Effects of Transglutaminase Catalysis on the Functional and Immunoglobulin Binding Properties of Peanut Flour Dispersions Containing Casein," J. Agric. Food Chem., 2008, 56:10913-10921 |
| | 238. | Gharst, "The Effect of Transglutaminase Crosslinking on the Rheological Characteristics of Heated Peanut Flour Dispersions," J. Food Sci., 2007, 72(7):C369-C375 |
| | 239. | Gilbert et al., "The revolutionary meatless burger from Impossible Foods is perfect for begtarians and carnivores alike," Tech Insider, August 4, 2016, retrieved on August 25, 2016, <http://www.techinsider.io/the-impossible-foods-burger-review-vegetarian-2016-8>, 9 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 12 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 240. | Go Veggie!, "O% Dairy. 100% Yum.," posted on or before 2013, accessed 1/7/2014, http://goveggiefoods.com/our-products/dairy-free-cheese-alternative-products/, 1 page |
| | 241. | Go Veggie!, Dairy Free Products and Nutrition Facts, posted on or before 2013, accessed 2/7/2014, http://goveggiefoods.com/our-products/dairy-free-cheese-alternative-products/, 13 pages |
| | 242. | Gordinier, "Masters of Disguise Among Meatless Burgers," The New York Times, 3/22/2011, accessed 1/7/2014, http://www.nytimes.com/2011/03/23/dining/23meatless.html?pagewanted=all&_r=0, 5 pages |
| | 243. | Grigorakis et al., "Organoleptic and volatile aroma compounds comparison of wild and cultured gilthead sea bream (*Sparus aurata*): sensory differences and possible chemical basis," Aquaculture 225:109-119 (2003) |
| | 244. | Grobart, "Making a Steak Without a Cow," Bloomberg Technology, June 21, 2016, retrieved June 23, 2016 <http://www.bloomberg.com/news/articles/2016-06-21/making-a-steak-without-the-cow>, 2 pages |
| | 245. | Grosch, "Evaluation of the Key Odorants of Food by Dilution Experiments, Aroma Models and Omission," Chem. Senses 26:533-545 (June 2001) |
| | 246. | Hanlon, "Fake Meat: is science fiction on the verge of becoming fact?," The Guardian, June 22, 2012, http://www.theguardian.com/science/2012/jun/22/fake-meat-scientific-breakthroughs-research, 7 pages |
| | 247. | Hannah, "A fermented feast," Bittersweet, retrieved on November 3, 2016, retrieved from <https://bittersweetblog.com/2010/06/09/a-fermented-feast/>, 2 pages |
| | 248. | Heller, "Barbecued Soybeans," Vegetarian Soybean Recipes, Mother Earth News, January/February 1985, http://motherearthnews.com/real-food/vegetarian-soybean-recipes-zmaz85asie.aspx |
| | 249. | Heme Protein Database, "Welcome to the Heme Protein Database," posted on or before 4/14/2013, accessed 12/18/2013, http://hemeprotein.info/heme.php, 1 page |
| | 250. | Heritage Health Food Creamy Veeta Cheeze Sauce Mix, Vegan Essentials, posted on or before 8/13/2013, retrieved 2/7/2014, http://store.veganessentials.com/creamy-veeta-cheeze-sauce-mix-by-heritage-health-food-p3945.aspx, 1 page |
| | 251. | Herper, "Mission Impossible Burger: Tasting The Fake Meat That Wants To Save The World," Forbes, July 28, 2016, retrieved on August 25, 2016, <http://www.forbes.com/sites/matthewherper/2016/07/28/mission-impossible-burger-tasting-the-fake-meat-that-wants-to-save-the-world/#57781d823c43>, 6 pages |
| | 252. | Herper, "Drop that Burger," Forbes Online, November 12, 2009, http://www.forbes.com/forbes/2009/1130/thought-leaders-mcdonalds-global-warming-drop-that-burger.html, 4 pages |
| | 253. | Homma et al. "Cheese-like food production from various nuts," Food Preservation Science, Japan 2009, ABSTRACT |
| | 254. | Hoshaw, "Silicon Valley's Bloody Plant Burger Smells, Tastes and Sizzles Like Meat" the salt, June 21, 2016, retrieved June 21, 2016 <http://www.npr.org/sections/thesalt/2016/06/21/482322571/silicon-valley-s-bloody-plant-burger-smells-tastes-and-sizzles-like-meat>, 8 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 13 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 255. | Hui et al., "Handbook of meat and meat processing," CRC Press, 2012, retrieved on December 05, 2016, retrieved from <https://www.crcpress.com/Handbook-of-Meat-and-Meat-Processing-Second-Edition/Hui/p/book/9781439836835>, 3 pages |
| | 256. | International Preliminary Report on Patentability in International Application No. PCT/US14/11347, dated July 14, 2015, 10 pages |
| | 257. | International Search Report and Written Opinion in International Application No. PCT/US14/11347, dated July 3, 2014, 20 pages |
| | 258. | Jamieson, "Iroquois Stew with Beef, Chicken and Pork," Epicurious, November 1995, retrieved on 9/10/2015, http://www.epicurious.com/recipes/food/printerfriendly/iroquois-stew-with-beef-chicken-and-pork-865, 2 pages |
| | 259. | Jensen, "Comparative Analysis of Autoxidation of Haemoglobin," J. Experimental Biology, 2001, 204:2029-2033 |
| | 260. | Ju and Kilara, "Textural Properties of Cold-set Gels Induced from Heat-denatured Whey Protein Isolates," J. Food Science, 1998, 63(2): 288-292 |
| | 261. | Jublot et al., "Quantitation of sulphur aroma compounds in maillard model reaction systems of different composition," Expression of Multidisciplinary Flavour Science, 4 pages (2010) |
| | 262. | Kanani, "The Future of Meat is Meatless, Just as Tasty, And About to Change the World," Forbes, 3/6/2014, retrieved on 9/11/2015, http://www.forbes.com/sites/rahimkanani/2014/03/06/the-future-of-meat-is-meatless-just-as-tasty-and-about-to-change-the-world/, 8 pages |
| | 263. | Karahadian et al., "Action of Tocopherol-Type Compounds in Directing Reactions Forming Flavor Compounds in Autoxidizing Fish Oils," J. Amer. Oil Chem. Soc., 66:1302-8 (1989) |
| | 264. | Kerscher et al., "Quantification of 2-Methyl-3-furnathiol, 2-Furfurylthiol, 3-Mercapto-2-pentanone in Heated Meat," J. Agric. Food Chem. 46:1954-1958 (1996) |
| | 265. | Kerth and Miller, "Beef flavor: a review from chemistry to consumer," White Paper: Product Quality, Texas A&M University Dept of Animal Sciences, 25 pages (2013) |
| | 266. | Khan et al., "Meat flavor precursors and factors influencing flavor precursors- A systematic review," Meat Science, 110:278-284 (December 2010) |
| | 267. | Kraft American Singles Package Ingredients, posted on or before 6/27/2012, accessed on 1/7/2014, http://www.kraftrecipes.com/Products/ProductInfoDisplay.aspx?SiteId=1&Product=2100060473, 1 page |
| | 268. | Kummer, "The Problem with Fake Meat," MIT Technology Review, March 31, 2015, retrieved April 20, 2016, <https://www.technologyreview.com/s/536296/the-problem-with-fake-meat/>, 11 pages |
| | 269. | Kung et al., "Tobacco as a Potential Food Source and Smoke Material: Nutritional Evaluation of Tobacco Leaf Protein," J. Food Sci., 1980, 45(2):320-322, 327 |
| | 270. | Lane et al., "The Variety of Odors Produced in Maillard Model Systems and How They are Influenced by Reaction Conditions," The Maillard Reaction in Foods and Nutrition, American Chemical Society, pp. 141-158 (April 1983) |
| | 271. | Leahy Gardens Vegan & Delicious, Macaroni & Cheese and Cheese Flavored Sauce Mix Product and Nutrition Facts, posted on or before 2/8/2010, retrieved 2/7/2014, http://www.leaheyfoods.com/products/MacCheese.aspx, 3 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 272. | Leduc et al., "Differentiation of fresh and frozen/thawed fish, European sea bass (Dicentrarchus labrax), gilthead seabream (Sparus aurata), cod (Gadus morhua) and salmon (Salmo salar), using volatile compounds by SPME/GC/MS," J. Sci. Food Agric., 92:2560-80 (2012) |
| | 273. | Lisanatti Foods, Vegan Cheeze Products and Nutrition Facts, posted on or before 3/26/2013, retrieved 2/7/2014, http://www.lisanatti.com/index.php?option=com_zoo&view=category&layout=category&Itemid=22, 5 pages |
| | 274. | Liu et al., "Intermolecular Interactions During Complex Coacervation Of Pea Protein Isolate And Gum Arabic," Journal of Agricultural and Food Chemistry, 2010, 58:552-556 |
| | 275. | Lopez, "We just tried the 'Impossible Burger' - the meatless burger NYC has been waiting for," Business Insider, July 27, 2016, retrieved on August 25, 2016, <http://www.businessinsider.com/what-the-impossible-burger-tastes-like-2016-7>, 5 pages |
| | 276. | Lugay and Kim, "Freeze alignment: A novel method for protein texturization," Utilization of Protein Resources, 1981, Page 177-187 |
| | 277. | Luteness, "The Richest Source of Protein," MOSAIC, May/June 1979, 39-45 |
| | 278. | Maltais et al., "Formation of Soy Protein Isolate Cold-Set Gels: Proteins and Salt Effects," J. Food Science, 2005, 70 (1): C67-C73 |
| | 279. | Marshall et al., "We Tried the "Bleeding" Vegetarian Burger And It Was Actually Good," July 27, 2016, retrieved July 28, 2016 <https://www.buzzfeed.com/chelseamarshall/bleeding-vegetable-burger?utm_term=.jaa03Kyo7#.ogV0m7MAW>, 10 pages |
| | 280. | McGorrin, "Advances in Dairy Flavor Chemistry," FoodFlavors and Chemistry: Advances of the New Millennium, Spanier, A. M.; Shahidi,F.; Parliment, T. H.; Mussinan, C. J.; Ho, C.-T.; Contis, E. T., Eds., RoyalSociety of Chemistry, Cambridge, pp. 67-84 (2001) |
| | 281. | McGorrin, "Character-impact flavor and off-flavor compounds in foods," Flavor, Fragrance, and Odor Analysis, 2nd, 207-262 (2012). |
| | 282. | McGorrin, "The significance of volatile sulfur compounds in food flavors," Volatile sulfur compounds in food 1068, 29 pages (2011). |
| | 283. | Moon et al., "Odour-active components of simulated beef flavour analyzed by solid phase microextraction and gas chromatography-mass spectrometry and -olfactometry," Food Research International, 39:294-308 (April 2006) |
| | 284. | Morita, "Comparison of aroma characteristics of 16 fish species by sensory evaluation and gas chromatographic analysis," J. Sci. Food Agric., 83:289-297 (2003) |
| | 285. | Morningstar Farms Garden Veggie Patties Package Ingredients, posted on or before 6/26/2013, accessed 1/7/2014, https://www.morningstarfarms.com/products/burgers/garden-veggie-patties, 6 pages |
| | 286. | Mottram et al., "Formation of Sulfer Aroma Compounds in Reaction Mixtures Containing Cysteine and Three Different Forms of Ribose," J. Agric. Food Chem., 50:4080-4086 (2002) |
| | 287. | Mottram, "Flavour formation in meat and meat products: a review," Food Chemistry, 62(4):415-24 (August 1998) |
| | 288. | Mottram,"An Overview of the Contribution of Sulfur-Containing Compounds to the Aroma in Heated Foods," Heteroatomic Aroma Compounds, American Chemical Society, pp. 73-92 (August 2002) |

| Examiner Signature | Date Considered |
|---|---|
| | |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 289. | Nacho Mom's Vegan Queso, Products and Nutrition Facts, posted on or before 9/20/2010, retrieved on 2/7/2014, http://fatgoblin.com/Home.html, 6 pages |
| | 290. | Nielson, Introduction to the Chemical Analysis of Foods, Jones & Bartlett Publishers, 1994 |
| | 291. | Nutty Cow Nut Cheeses, Products and Nutrition Facts, posted on or before 7/23/2012, retrieved 2/7/2014, http://www.nuttycow.com/, 6 pages |
| | 292. | Parmela Parmesan Style Aged Nut Cheese, Product and Nutrition Facts, 2012, retrieved 2/7/2014, http://www.parmelafoods.com/your-health.html, 4 pages |
| | 293. | Peace Cheese 100% Plant-based Cheese Alternative, Product and Nutrition Facts, posted on or before 6/6/2012, retrieved 2/7/2014, http://www.ilovepeacecheese.com/#/products/4571642621, 3 pages |
| | 294. | Proulx et al., "Iron Bioavailability of Hemoglobin from Soy Root Nodules Using a Caco-2 Cell Culture Model," J. Agricultural and Food Chemistry, February 2006, 54(4):1519-1522 |
| | 295. | Proulx, "Diversified strategies for improving iron bioavalibility of maize," Iowa State University - Retrospective Theses and Dissertations, 2007 retrieved on September 19, 2016, retreived from <http://lib.dr.iastate.edu/rtd/15852/>, 144 pages |
| | 296. | Punk Rawk Labs: an ongoing experiment in optimal health, Nut Milk Cheese Products, posted on or before 6/8/2011, retrieved 2/7/2014, http://www.punkrawklabs.net/cheeses.html, 4 pages |
| | 297. | Ramos et al., "What is Masa? - Ingredient Intelligence," The Kitchn, retrieved on 12/01/2016, http://www.thekitchn.com/whats-the-difference-between-masa-and-masa-harina-226434, 5 pages |
| | 298. | Reedy et al., "Development of a heme protein structure-electrochemical function database," Nucleic Acids Research, 2008, 36:307-313 |
| | 299. | Richins et al., "Effect of Iron Source on Color and Appearance of Micronutrient-Fortified Corn Flour Toritallas," Cereal Chem., 85:561-5 (2008) |
| | 300. | Road's End Organics, Cheese Sauce Mix Products and Nutrition Facts, posted on or before 10/28/2009, retrieved 2/7/2014, http://www.edwardandsons.com/reo_shop_chreese.itml, 6 pages |
| | 301. | Road's End Organics, Mac & Chreese Products and Nutrition Facts, posted on or before 10/28/2009, retrieved 2/7/2014, http://www.edwardandsons.com/reo_shop_pastas.itml, 7 pages |
| | 302. | Rochet and Chaintreau, "Carbonyl Odorants Contributing to the In-Oven Roast Beef Top Note," J. Agric. Food Chem., 53:9578-9585 (November 2005) |
| | 303. | Rowe, "Chemistry and technology of flavors and fragrances," Oxford:: Blackwell; 2005, 351 pages |
| | 304. | Rusli, "The Secret of These New Veggie Burgers: Plant Blood," The Wall Street Journal, October 7, 2014, retrieved on 10/9/2014, http://online.wsj.com/articles/the-secret-of-these-new-veggie-burgers-plant-blood-1412725267, 5 pages |
| | 305. | Schieberle et al., "Characterization of Key Odorants in Dry-Heated Cysteine-Carbohydrate Mixtures: Comparison with Aqueous Reaction Systems," Flavor Analysis, American Chemical Society, pp. 320-330 (Setpember 1998) |
| | 306. | Schwartz, "Meet the Silicon Valley-Backed Vegan Cheese That You Might Actually Eat," Fast Company, February 26, 2014, retrieved 9/11/2015, http://www.fastcoexist.com/3025648/meet-the-silicon-valley-backed-vegan-cheese-that-you-might-actually-eat, 6 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 307. | Segner, "Meatless burger made possible with local effort," July 29, 2016, retrieved August 1, 2016 <http://www.southernminn.com/owatonna_peoples_press/news/article_3d414149-1040-534d-b1af-bf4f8c486788.html>, 5 pages |
| | 308. | Selli et al., "Odour-active and off-odour components in rainbow trout (Oncorhynchus mykiss) extracts obtained by microwave assisted distillation-solvent extraction," Food Chemistry, 114:317-322 (2009) |
| | 309. | Shahidi et al., "Meat flavor volatiles: A review of the composition, techniques of analysis, and sensory evaluation," CRC Critical Reviews in Food Science and Nutrition, 24(2):141-243 (January 1986) |
| | 310. | Shi et al., "Identification of characteristic flavour precursors from enzymatic hydrolysis-mild thermal oxidation tallow by descriptive sensory analysis and gas chromatography–olfactometry and partial least squares regression," Journal of Chromatography B, 913-914:96-76 (January 2013) |
| | 311. | Shu et al., "Parameter Effects on the Thermal Reaction of Cystine and 2,5-Dimethyl-4-hydroxy-3(2*H*)-furanone," Thermal Generation of Aromas, American Chemical Society, pp. 229-241 (October 1989) |
| | 312. | Sister River Foods Parma!, Products and Nutrition Facts, Posted on or before 6/2/2012, retrieved 2/11/2014, http://www.veganstore.com/product/parma-vegan-parmesan/vegan-cheese-and-dairy-alternatives, 6 pages |
| | 313. | Soller, "The Impossible Burger is Ready for Its (Meatless) Close-Up," The Wall Street Journal, June 14, 2016, retrieved June 21, 2016 <http://www.wsj.com/articles/the-impossible-burger-is-ready-for-its-meatless-close-up-1465912323>, 8 pages |
| | 314. | Song, et al., "Contribution of oxidized tallow to aroma characteristics of beeflike process flavour assessed by gas chromatography-mass spectrometry and partial least squares regression," Journal of Chromatography A, 1254:115-124 (September 2012) |
| | 315. | Soy Kaas, Products, posted on or before 1/20/2011, retrieved 2/11/2014, http://www.soykaas.com/products, 1 page |
| | 316. | Soyco Cheese Products, Natural Pantry, retrieved 2/11/2014, http://www.natural-pantry.com/search_results.asp?ct=All&site_search_qu=soyco&storeID=D92VLAQVMPDL9L5UHTS2WLU67NADEHUA, 10 pages |
| | 317. | Soymage Cheese Products, Good Earth Natural Foods, retrieved on 2/11/2014, http://www.goodearthnaturalfoods.com/shop/brand2.asp?storeID=PJ102JRNHNGT8G0QMPEQ7LDC7GX6C2W2&alpha=S&brand=Soymage&brand_id=805, 6 pages |
| | 318. | Spence et al., "Multisensory Flavor Perception," Cell 161: 24-35 (2015) |
| | 319. | Ste Martaen Cheese, Products and Nutrition Facts, posted on or before 5/28/2009, retrieved 2/11/2014, http://stemartaen.bigcartel.com/, 14 pages |
| | 320. | Sterling, "Welcome to the Era of Plant -Based Meat," Food & Wine, April 13, 2016, Retrieved April 20, 2016, <http://www.foodandwine.com/blogs/welcome-era-plant-based-meat>, 3 pages |
| | 321. | Supplementary Partial European Search Report in European Application No. 14738061 dated November 7, 2016, 11 pages |
| | 322. | Swanson, "Patenting the Quest for a More Perfect Veggie Burger," JDSUPRA Business Advisor, June 21, 2016, retrieved June 23, 2016 <http://www.jdsupra.com/legalnews/patenting-the-quest-for-a-more-perfect-72212/>. 13 pages |

| Examiner Signature | Date Considered |
|---|---|
| | |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

Sheet 17 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 323. | Tang et al., "Flavor chemistry of 2-methyl-3-furanthiol, an intense meaty aroma compound," Journal of Sulfur Chemistry, 11 pages, (2012) |
| | 324. | The Daiya Advantage, Products and Nutrition Facts, posted on or before 1/26/2010, retrieved on 2/7/2014, http://us.daiyafoods.com/our-products, 126 pages |
| | 325. | The Good Scents Company, "The Good Scents Company Information System," 2015, retrieved on December 1, 2016, http://www.thegoodscentscompany.com/, 2 pages |
| | 326. | The Vegetarian Express Parma Zaan Sprinkles, posted on or about 10/17/2009, retrieved 2/11/2014, http://www.thevegetarianexpress.com/cart/home.php?cat=250, 2 pages |
| | 327. | Tofu Rella Mozzarella Cheese, Natural Pantry, retrieved 2/11/2014, http://www.natural-pantry.com/shop/product_view.asp?id=24684&StoreID=D92VLAQVMPDL9L5UHTS2WLU67NADEHUA&private_product=0, 2 pages |
| | 328. | Tofutti Cheese Products and Nutrition, posted on or before 6/26/2013, retrieved 2/11/2014, http://www.tofutti.com/dairy-free-cheeses/, 18 pages |
| | 329. | Tofutti Milk Free, "Premium Dairy Free Cheeses,", posted on or before 6/26/2013, accessed 1/7/2014, http://www.tofutti.com/dairy-free-cheeses/, 2 pages |
| | 330. | Trader Joe's Sliced Soy Cheese Alternative, Fotki, posted 10/27/2008, retrieved 2/11/2014, http://public.fotki.com/harwons/food/tj-sliced-soy-cheese.html, 1 pages |
| | 331. | Trader Joe's Vegan Mozzarella, A(soy) Bean, posted 6/7/2013, retrieved 2/11/2014, http://a-soy-bean.blogspot.com/2013/06/showdown-trader-joes-vegan-mozzarella.html, 13 pages |
| | 332. | Treeline Treenut Cheese, Products and Nutrition Facts, posted on or before 12/10/2013, retrieved on 2/11/2014, http://www.treelinecheese.com/treeline-cheese-products.html, 3 pages |
| | 333. | Tressl et al., "Formation of Amino Acid Specific Maillard Products and Their Contribution to Thermally Generated Aromas," Thermal Generation of Aromas, American Chemical Society, pp. 156-171 (October 1989) |
| | 334. | Uauy et al., "Iron Fortification of Foods: Overcoming Technical and Practical Barriers," J. Nutr. 132:849S-852S (2002) |
| | 335. | Van Ba et al., "Principles of Meat Aroma flavors and Future Prospect," INTECH Open Science, Open Minds, 2012, Chapter 7, 145-176 |
| | 336. | Van Den Ouweland et al., "Process Meat Flavor Development and the Maillard Reaction," In Thermal Generation of Aromas, ACS Symposium Series, American Chemical Society, 1989, 433-441 |
| | 337. | VBites, "Cheezly," posted on or before 2013 , accessed 1/7/2014, http://www.vbitesfoods.com/meat-free/cheezly.html, 2 pages |
| | 338. | Vegan Sun Artisan Aged Raw Cheese, Vegan Essentials, retrieved 2/11/2014, http://store.veganessentials.com/vegan-sun-artisan-aged-raw-cheese-p4201.aspx, 3 pages |
| | 339. | VegCuisine Soy Cheese Products, The Vegan Store, retrieved on 2/11/2014, http://www.veganstore.com/category/s?keyword=vegcuisine, 5 pages |
| | 340. | Veggie Brothers Mozzarella Sticks, Vegan Essentials, 11/9/2013, retrieved 2/11/2014, http://store.veganessentials.com/vegan-mozzarella-sticks-by-veggie-brothers-p3761.aspx, 2 pages |
| | 341. | Victoria Vegan Sauces, Products and Nutrition Facts, posted on or about 9/16/2012, retrieved 2/11/2014, http://www.victoriafinefoods.com/products/specialty-sauces/victoria-vegan, 9 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Sheet 18 of 18

| Substitute Disclosure Form<br>U.S. Department of Commerce<br>Patent and Trademark Office | Attorney Docket No.<br>38767-0015002 | Application No. |
|---|---|---|
| **Information Disclosure Statement by Applicant**<br>(Use several sheets if necessary) | Applicant<br>Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 342. | Wayfare We Can't say It's Cheese Spread, Products and Nutrition Facts, posted on or about 10/12/2013, retrieved 2/11/2014, http://www.wayfarefoods.com/we-cant-say-its-cheese/, 5 pages |
| | 343. | Welcome to Bute Island Foods, "100% Vegan Cheese – 100% Tasty," posted on or before 12/5/2006, accessed 1/7/2014, http://www.buteisland.com, 2 pages |
| | 344. | Welcome to VBites Foods, Cheezly Products and Nutrition Facts, 2013, retrieved on 2/7/2014, http://www.vbitesfoods.com/meat-free/cheezly.html, 26 pages |
| | 345. | Withycombe et al., "Identification of 2-Methyl-3-Furanthiol in the Steam Distillate from Canned Tuna Fish," Journal of Food Science, 53(2):658-660 (1988) |
| | 346. | Wortham and Miller, "Venture Capitalists Are Making Bigger Bets on Food Start-Ups," The New York Times Online, April 28, 2013, http://www.nytimes.com/2013/04/29/business/venture-capitalists-are-making-bigger-bets-on-food-start-ups.html?pagewanted=all&_r=1&, 4 pages |
| | 347. | Yancey et al., "Effects of total iron, myoglobin, hemoglobin, and lipid oxidation of uncooked muscles on livery flavor development and volatiles of cooked beef steaks," Meat Science, 73:680-686 (2006) |
| | 348. | Yves Veggie Cuisine The Good Slice, ShopWell, retrieved on 2/11/2014, http://www.shopwell.com/yves-veggie-cuisine-the-good-slice-cheese-alternative-cheddar-style/soy-foods/p/6082260001, 1 page |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

Attorney Docket No.: 38767-0015001 / Client Ref: M3CON-Track 1

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

| Title of Invention | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
|---|---|

As the below named inventor, I hereby declare that:

This declaration is directed to:
[ ] The attached application, or
[X] United States application or PCT international application number 14/797,006
filed on July 10, 2015.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

## WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Rachel Fraser Date (Optional): 2/10/16

Signature: Rachel Fraser

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

61187971.doc

American LegalNet, Inc.
www.FormsWorkFlow.com

Attorney Docket No.: 36767-0015001 / Client Ref: M3CON-Track 1

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

| | |
|---|---|
| **Title of Invention** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |

As the below named inventor, I hereby declare that:

This declaration is directed to:

[ ] The attached application, or

[ X ] United States application or PCT international application number 14/797,006

filed on July 10, 2015.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

## WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Patrick O'Reilly Brown M.D., Ph.D. Date (Optional) : _____

Signature: _____

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

61187971.doc

American LegalNet, Inc.
www.FormsWorkFlow.com

Attorney Docket No.: 38767-0015001 / Client Ref: M3CON-Track 1

PTO/AIA/01 (05-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

| | |
|---|---|
| **Title of Invention** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |

As the below named inventor, I hereby declare that:

This declaration is directed to: [ ] The attached application, or

[ X ] United States application or PCT international application number 14/797,006

filed on July 10, 2015.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

## WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Jessica Karr Date (Optional) : 9.21.15

Signature:

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

61187971.doc

American LegalNet, Inc.
www.FormsWorkFlow.com

Attorney Docket No.: 38767-0015001 / Client Ref: M3CON-Track 1

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

| | |
|---|---|
| **Title of Invention** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |

As the below named inventor, I hereby declare that:

This declaration is directed to:

[ ] The attached application, or

[X] United States application or PCT international application number 14/797,006

filed on July 10, 2015.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

## WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Celeste Holz-Schietinger Date (Optional) :

Signature:

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

61187971.doc

American LegalNet, Inc.
www.FormsWorkflow.com

Attorney Docket No.: 38767-0015001 / Client Ref: M3CON-Track 1

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

| | |
|---|---|
| **Title of Invention** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |

As the below named inventor, I hereby declare that:

This declaration is directed to:

[ ] The attached application, or

[ X ] United States application or PCT international application number 14/797,006

filed on July 10, 2015.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

## WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Elysia Cohn Date (Optional): 10/14/15

Signature:

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

61187971.doc

American LegalNet, Inc.
www.FormsWorkflow.com

# TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

| | |
|---|---|
| Application Number | |
| Filing Date | |
| First Named Inventor | Rachel Fraser |
| Title | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| Art Unit | |
| Examiner Name | |
| Attorney Docket Number | 38767-0015002 |

**SIGNATURE of Applicant or Patent Practitioner**

| | | | |
|---|---|---|---|
| Signature | /Ian J.S. Lodovice, Reg. No. 59,749/ | Date (Optional) | January 4, 2017 |
| Name | Ian J. Lodovice | Registration Number | 59,749 |
| Title (if Applicant is a juristic entity) | | | |
| Applicant Name (if Applicant is a juristic entity) | | | |

**NOTE:** This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ *Total of _____ forms are submitted.

# POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

| Application Number | Filing Date |
|---|---|
| 14/797,006 | July 10, 2015 |

(Note: The boxes above may be left blank if information is provided on the Transmittal.)

☐ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter, which may be an application filed after the date of this power of attorney, or identified above:

**OR**

☒ I hereby appoint Practitioner(s) named in the attached list as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter, which may be an application filed after the date of this power of attorney, or identified above.

**Please recognize or change the correspondence address for the application identified in the attached transmittal letter to:**

☐ The address associated with the above-mentioned Customer Number

**OR**

☒ The address associated with Customer Number: **26191**

**OR**

| | | | | | |
|---|---|---|---|---|---|
| Firm or Individual Name | | | | | |
| Address | | | | | |
| City | | State | | Zip | |
| Country | | | | | |
| Telephone | | Email | | | |

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

Impossible Foods Inc.

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☒ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

**SIGNATURE of Applicant for Patent**

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

| | | | |
|---|---|---|---|
| Signature | Myra Pasek | Date (Optional) | Oct 17, 2016 |
| Name | Myra Pasek | | |
| Title | General Counsel | | |

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ *Total of _____ forms are submitted.

61383281.doc

# POWER OF ATTORNEY BY APPLICANT

No more than ten (10) patent practitioners total may be appointed as set forth below by name and registration number. This page need not be submitted if appointing the Patent Practitioner(s) associated with a Customer Number:

| Name | Registration Number |
|---|---|
| Teresa Lavoie | 42,782 |
| Ian Lodovice | 59,749 |
| M. Angela Parsons | 44,282 |
| Elizabeth Kaytor | 53,103 |
| Cameron Lutijens | 58,674 |
| Monica McCormick Graham | 42,600 |
| Andrea Dorigo | 47,532 |
| Angela Follett | 60,365 |
| Michael Fleming | 67,933 |
| | |

Document in ProLaw

DocCode - SCORE

# SCORE Placeholder Sheet for IFW Content

Application Number: 15398479 Document Date: 01/04/2017

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

- Drawings – Other than Black and White Line Drawings

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

To access the documents in the SCORE database, refer to instructions below.

At the time of document entry (noted above):

- Examiners may access SCORE content via the eDAN interface.
- Other USPTO employees can bookmark the current SCORE URL (http://Score.uspto.gov/ScoreAccessWeb/).
- External customers may access SCORE content via the Public and Private PAIR interfaces.

Form Revision Date: September 30, 2013

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

| PATENT APPLICATION FEE DETERMINATION RECORD<br>Substitute for Form PTO-875 | Application or Docket Number<br>15/398,479 | Filing Date<br>01/04/2017 | ☐ To be Mailed |
|---|---|---|---|

**ENTITY**: ☒ LARGE ☐ SMALL ☐ MICRO

## APPLICATION AS FILED – PART I

| FOR | (Column 1) NUMBER FILED | (Column 2) NUMBER EXTRA | RATE ($) | FEE ($) |
|---|---|---|---|---|
| ☐ BASIC FEE (37 CFR 1.16(a), (b), or (c)) | N/A | N/A | N/A | |
| ☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m)) | N/A | N/A | N/A | |
| ☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q)) | N/A | N/A | N/A | |
| TOTAL CLAIMS (37 CFR 1.16(i)) | minus 20 = | * | X $ = | |
| INDEPENDENT CLAIMS (37 CFR 1.16(h)) | minus 3 = | * | X $ = | |
| ☐ APPLICATION SIZE FEE (37 CFR 1.16(s)) | If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s). | | | |
| ☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j)) | | | | |
| * If the difference in column 1 is less than zero, enter "0" in column 2. | | | TOTAL | |

## APPLICATION AS AMENDED – PART II

| AMENDMENT 01/04/2017 | (Column 1) CLAIMS REMAINING AFTER AMENDMENT | | (Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR | (Column 3) PRESENT EXTRA | RATE ($) | ADDITIONAL FEE ($) |
|---|---|---|---|---|---|---|
| Total (37 CFR 1.16(i)) | * 30 | Minus | ** 30 | = 0 | X $80 = | 0 |
| Independent (37 CFR 1.16(h)) | * 2 | Minus | ***3 | = 0 | X $420 = | 0 |
| ☐ Application Size Fee (37 CFR 1.16(s)) | | | | | | |
| ☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j)) | | | | | | |
| | | | | | TOTAL ADD'L FEE | 0 |

| AMENDMENT | (Column 1) CLAIMS REMAINING AFTER AMENDMENT | | (Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR | (Column 3) PRESENT EXTRA | RATE ($) | ADDITIONAL FEE ($) |
|---|---|---|---|---|---|---|
| Total (37 CFR 1.16(i)) | * | Minus | ** | = | X $ = | |
| Independent (37 CFR 1.16(h)) | * | Minus | *** | = | X $ = | |
| ☐ Application Size Fee (37 CFR 1.16(s)) | | | | | | |
| ☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j)) | | | | | | |
| | | | | | TOTAL ADD'L FEE | |

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
ROZENIA HARMON

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

==========
Sequence Listing was accepted.
If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).
Reviewer: Saleem, Syed (ASRC)
Timestamp: [year=2017; month=1; day=11; hr=7; min=55; sec=25; ms=458; ]
==========

**Validated By CRFValidator v 1.0.5**

Application No: 15398479 Version No: 1.0

**Input Set:**

**Output Set:**

**Started:** 2017-01-04 17:40:04.548
**Finished:** 2017-01-04 17:40:05.198
**Elapsed:** 0 hr(s) 0 min(s) 0 sec(s) 650 ms
**Total Warnings:** 4
**Total Errors:** 0
**No. of SeqIDs Defined:** 27
**Actual SeqID Count:** 27

| Error code | Error Description |
|---|---|
| W 402 | Undefined organism found in <213> in SEQ ID (6) |
| W 402 | Undefined organism found in <213> in SEQ ID (14) |
| W 402 | Undefined organism found in <213> in SEQ ID (24) |
| W 402 | Undefined organism found in <213> in SEQ ID (25) |

SEQUENCE LISTING

<110> Impossible Foods Inc.

<120> METHODS AND COMPOSITIONS FOR AFFECTING
THE FLAVOR AND AROMA PROFILE OF CONSUMABLES

<130> 38767-0015001

<140> US 15/398,479
<141> 2017-01-04

<150> PCT/US2014/011347
<151> 2014-01-13

<150> 13/941,211
<151> 2013-07-12

<150> 61/908,634
<151> 2013-11-25

<150> 61/751,816
<151> 2013-01-11

<160> 27

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 161
<212> PRT
<213> Vigna radiata

<400> 1
Met Thr Thr Thr Leu Glu Arg Gly Phe Thr Glu Glu Gln Glu Ala Leu
1 5 10 15
Val Val Lys Ser Trp Asn Val Met Lys Lys Asn Ser Gly Glu Leu Gly
20 25 30
Leu Lys Phe Phe Leu Lys Ile Phe Glu Ile Ala Pro Ser Ala Gln Lys
35 40 45
Leu Phe Ser Phe Leu Arg Asp Ser Thr Val Pro Leu Glu Gln Asn Pro
50 55 60
Lys Leu Lys Pro His Ala Val Ser Val Phe Val Met Thr Cys Asp Ser
65 70 75 80
Ala Val Gln Leu Arg Lys Ala Gly Lys Val Thr Val Arg Glu Ser Asn
85 90 95
Leu Lys Lys Leu Gly Ala Thr His Phe Arg Thr Gly Val Ala Asn Glu
100 105 110
His Phe Glu Val Thr Lys Phe Ala Leu Leu Glu Thr Ile Lys Glu Ala
115 120 125
Val Pro Glu Met Trp Ser Pro Ala Met Lys Asn Ala Trp Gly Glu Ala
130 135 140
Tyr Asp Gln Leu Val Asp Ala Ile Lys Tyr Glu Met Lys Pro Pro Ser
145 150 155 160
Ser

<210> 2
<211> 133
<212> PRT
<213> Methylacidiphilum infernorum

<400> 2
Met Ile Asp Gln Lys Glu Lys Glu Leu Ile Lys Glu Ser Trp Lys Arg
1 5 10 15
Ile Glu Pro Asn Lys Asn Glu Ile Gly Leu Leu Phe Tyr Ala Asn Leu
20 25 30
Phe Lys Glu Glu Pro Thr Val Ser Val Leu Phe Gln Asn Pro Ile Ser
35 40 45
Ser Gln Ser Arg Lys Leu Met Gln Val Leu Gly Ile Leu Val Gln Gly
50 55 60
Ile Asp Asn Leu Glu Gly Leu Ile Pro Thr Leu Gln Asp Leu Gly Arg
65 70 75 80
Arg His Lys Gln Tyr Gly Val Val Asp Ser His Tyr Pro Leu Val Gly
85 90 95
Asp Cys Leu Leu Lys Ser Ile Gln Glu Tyr Leu Gly Gln Gly Phe Thr
100 105 110
Glu Glu Ala Lys Ala Ala Trp Thr Lys Val Tyr Gly Ile Ala Ala Gln
115 120 125
Val Met Thr Ala Glu
130

<210> 3
<211> 139
<212> PRT
<213> Aquifex aeolicus

<400> 3
Met Leu Ser Glu Glu Thr Ile Arg Val Ile Lys Ser Thr Val Pro Leu
1 5 10 15
Leu Lys Glu His Gly Thr Glu Ile Thr Ala Arg Met Tyr Glu Leu Leu
20 25 30
Phe Ser Lys Tyr Pro Lys Thr Lys Glu Leu Phe Ala Gly Ala Ser Glu
35 40 45
Glu Gln Pro Lys Lys Leu Ala Asn Ala Ile Ile Ala Tyr Ala Thr Tyr
50 55 60
Ile Asp Arg Leu Glu Glu Leu Asp Asn Ala Ile Ser Thr Ile Ala Arg
65 70 75 80
Ser His Val Arg Arg Asn Val Lys Pro Glu His Tyr Pro Leu Val Lys
85 90 95
Glu Cys Leu Leu Gln Ala Ile Glu Glu Val Leu Asn Pro Gly Glu Glu
100 105 110
Val Leu Lys Ala Trp Glu Glu Ala Tyr Asp Phe Leu Ala Lys Thr Leu
115 120 125
Ile Thr Leu Glu Lys Lys Leu Tyr Ser Gln Pro
130 135

<210> 4
<211> 145

<212> PRT
<213> Glycine max

<400> 4
Met Gly Ala Phe Thr Glu Lys Gln Glu Ala Leu Val Ser Ser Ser Phe
1 5 10 15
Glu Ala Phe Lys Ala Asn Ile Pro Gln Tyr Ser Val Val Phe Tyr Thr
20 25 30
Ser Ile Leu Glu Lys Ala Pro Ala Ala Lys Asp Leu Phe Ser Phe Leu
35 40 45
Ser Asn Gly Val Asp Pro Ser Asn Pro Lys Leu Thr Gly His Ala Glu
50 55 60
Lys Leu Phe Gly Leu Val Arg Asp Ser Ala Gly Gln Leu Lys Ala Asn
65 70 75 80
Gly Thr Val Val Ala Asp Ala Ala Leu Gly Ser Ile His Ala Gln Lys
85 90 95
Ala Ile Thr Asp Pro Gln Phe Val Val Val Lys Glu Ala Leu Leu Lys
100 105 110
Thr Ile Lys Glu Ala Val Gly Asp Lys Trp Ser Asp Glu Leu Ser Ser
115 120 125
Ala Trp Glu Val Ala Tyr Asp Glu Leu Ala Ala Ala Ile Lys Lys Ala
130 135 140
Phe
145

<210> 5
<211> 162
<212> PRT
<213> Hordeum vulgare

<400> 5
Met Ser Ala Ala Glu Gly Ala Val Val Phe Ser Glu Glu Lys Glu Ala
1 5 10 15
Leu Val Leu Lys Ser Trp Ala Ile Met Lys Lys Asp Ser Ala Asn Leu
20 25 30
Gly Leu Arg Phe Phe Leu Lys Ile Phe Glu Ile Ala Pro Ser Ala Arg
35 40 45
Gln Met Phe Pro Phe Leu Arg Asp Ser Asp Val Pro Leu Glu Thr Asn
50 55 60
Pro Lys Leu Lys Thr His Ala Val Ser Val Phe Val Met Thr Cys Glu
65 70 75 80
Ala Ala Ala Gln Leu Arg Lys Ala Gly Lys Ile Thr Val Arg Glu Thr
85 90 95
Thr Leu Lys Arg Leu Gly Gly Thr His Leu Lys Tyr Gly Val Ala Asp
100 105 110
Gly His Phe Glu Val Thr Arg Phe Ala Leu Leu Glu Thr Ile Lys Glu
115 120 125
Ala Leu Pro Ala Asp Met Trp Gly Pro Glu Met Arg Asn Ala Trp Gly
130 135 140
Glu Ala Tyr Asp Gln Leu Val Ala Ala Ile Lys Gln Glu Met Lys Pro
145 150 155 160
Ala Glu

<210> 6

<211> 1153
<212> PRT
<213> Magnaporthe oryzae

<400> 6
Met Asp Gly Ala Val Arg Leu Asp Trp Thr Gly Leu Asp Leu Thr Gly
1 5 10 15
His Glu Ile His Asp Gly Val Pro Ile Ala Ser Arg Val Gln Val Met
20 25 30
Val Ser Phe Pro Leu Phe Lys Asp Gln His Ile Ile Met Ser Ser Lys
35 40 45
Glu Ser Pro Ser Arg Lys Ser Ser Thr Ile Gly Gln Ser Thr Arg Asn
50 55 60
Gly Ser Cys Gln Ala Asp Thr Gln Lys Gly Gln Leu Pro Pro Val Gly
65 70 75 80
Glu Lys Pro Lys Pro Val Lys Glu Asn Pro Met Lys Lys Leu Lys Glu
85 90 95
Met Ser Gln Arg Pro Leu Pro Thr Gln His Gly Asp Gly Thr Tyr Pro
100 105 110
Thr Glu Lys Lys Leu Thr Gly Ile Gly Glu Asp Leu Lys His Ile Arg
115 120 125
Gly Tyr Asp Val Lys Thr Leu Leu Ala Met Val Lys Ser Lys Leu Lys
130 135 140
Gly Glu Lys Leu Lys Asp Asp Lys Thr Met Leu Met Glu Arg Val Met
145 150 155 160
Gln Leu Val Ala Arg Leu Pro Thr Glu Ser Lys Lys Arg Ala Glu Leu
165 170 175
Thr Asp Ser Leu Ile Asn Glu Leu Trp Glu Ser Leu Asp His Pro Pro
180 185 190
Leu Asn Tyr Leu Gly Pro Glu His Ser Tyr Arg Thr Pro Asp Gly Ser
195 200 205
Tyr Asn His Pro Phe Asn Pro Gln Leu Gly Ala Ala Gly Ser Arg Tyr
210 215 220
Ala Arg Ser Val Ile Pro Thr Val Thr Pro Pro Gly Ala Leu Pro Asp
225 230 235 240
Pro Gly Leu Ile Phe Asp Ser Ile Met Gly Arg Thr Pro Asn Ser Tyr
245 250 255
Arg Lys His Pro Asn Asn Val Ser Ser Ile Leu Trp Tyr Trp Ala Thr
260 265 270
Ile Ile Ile His Asp Ile Phe Trp Thr Asp Pro Arg Asp Ile Asn Thr
275 280 285
Asn Lys Ser Ser Ser Tyr Leu Asp Leu Ala Pro Leu Tyr Gly Asn Ser
290 295 300
Gln Glu Met Gln Asp Ser Ile Arg Thr Phe Lys Asp Gly Arg Met Lys
305 310 315 320
Pro Asp Cys Tyr Ala Asp Lys Arg Leu Ala Gly Met Pro Pro Gly Val
325 330 335
Ser Val Leu Leu Ile Met Phe Asn Arg Phe His Asn His Val Ala Glu
340 345 350
Asn Leu Ala Leu Ile Asn Glu Gly Gly Arg Phe Asn Lys Pro Ser Asp
355 360 365
Leu Leu Glu Gly Glu Ala Arg Glu Ala Ala Trp Lys Lys Tyr Asp Asn
370 375 380
Asp Leu Phe Gln Val Ala Arg Leu Val Thr Ser Gly Leu Tyr Ile Asn
385 390 395 400
Ile Thr Leu Val Asp Tyr Val Arg Asn Ile Val Asn Leu Asn Arg Val
405 410 415

Asp Thr Thr Trp Thr Leu Asp Pro Arg Gln Asp Ala Gly Ala His Val
420 425 430
Gly Thr Ala Asp Gly Ala Glu Arg Gly Thr Gly Asn Ala Val Ser Ala
435 440 445
Glu Phe Asn Leu Cys Tyr Arg Trp His Ser Cys Ile Ser Glu Lys Asp
450 455 460
Ser Lys Phe Val Glu Ala Gln Phe Gln Asn Ile Phe Gly Lys Pro Ala
465 470 475 480
Ser Glu Val Arg Pro Asp Glu Met Trp Lys Gly Phe Ala Lys Met Glu
485 490 495
Gln Asn Thr Pro Ala Asp Pro Gly Gln Arg Thr Phe Gly Gly Phe Lys
500 505 510
Arg Gly Pro Asp Gly Lys Phe Asp Asp Asp Asp Leu Val Arg Cys Ile
515 520 525
Ser Glu Ala Val Glu Asp Val Ala Gly Ala Phe Gly Ala Arg Asn Val
530 535 540
Pro Gln Ala Met Lys Val Val Glu Thr Met Gly Ile Ile Gln Gly Arg
545 550 555 560
Lys Trp Asn Val Ala Gly Leu Asn Glu Phe Arg Lys His Phe His Leu
565 570 575
Lys Pro Tyr Ser Thr Phe Glu Asp Ile Asn Ser Asp Pro Gly Val Ala
580 585 590
Glu Ala Leu Arg Arg Leu Tyr Asp His Pro Asp Asn Val Glu Leu Tyr
595 600 605
Pro Gly Leu Val Ala Glu Glu Asp Lys Gln Pro Met Val Pro Gly Val
610 615 620
Gly Ile Ala Pro Thr Tyr Thr Ile Ser Arg Val Val Leu Ser Asp Ala
625 630 635 640
Val Cys Leu Val Arg Gly Asp Arg Phe Tyr Thr Thr Asp Phe Thr Pro
645 650 655
Arg Asn Leu Thr Asn Trp Gly Tyr Lys Glu Val Asp Tyr Asp Leu Ser
660 665 670
Val Asn His Gly Cys Val Phe Tyr Lys Leu Phe Ile Arg Ala Phe Pro
675 680 685
Asn His Phe Lys Gln Asn Ser Val Tyr Ala His Tyr Pro Met Val Val
690 695 700
Pro Ser Glu Asn Lys Arg Ile Leu Glu Ala Leu Gly Arg Ala Asp Leu
705 710 715 720
Phe Asp Phe Glu Ala Pro Lys Tyr Ile Pro Pro Arg Val Asn Ile Thr
725 730 735
Ser Tyr Gly Gly Ala Glu Tyr Ile Leu Glu Thr Gln Glu Lys Tyr Lys
740 745 750
Val Thr Trp His Glu Gly Leu Gly Phe Leu Met Gly Glu Gly Gly Leu
755 760 765
Lys Phe Met Leu Ser Gly Asp Asp Pro Leu His Ala Gln Gln Arg Lys
770 775 780
Cys Met Ala Ala Gln Leu Tyr Lys Asp Gly Trp Thr Glu Ala Val Lys
785 790 795 800
Ala Phe Tyr Ala Gly Met Met Glu Glu Leu Leu Val Ser Lys Ser Tyr
805 810 815
Phe Leu Gly Asn Asn Lys His Arg His Val Asp Ile Ile Arg Asp Val
820 825 830
Gly Asn Met Val His Val His Phe Ala Ser Gln Val Phe Gly Leu Pro
835 840 845
Leu Lys Thr Ala Lys Asn Pro Thr Gly Val Phe Thr Glu Gln Glu Met
850 855 860
Tyr Gly Ile Leu Ala Ala Ile Phe Thr Thr Ile Phe Phe Asp Leu Asp

865 870 875 880
Pro Ser Lys Ser Phe Pro Leu Arg Thr Lys Thr Arg Glu Val Cys Gln
885 890 895
Lys Leu Ala Lys Leu Val Glu Ala Asn Val Lys Leu Ile Asn Lys Ile
900 905 910
Pro Trp Ser Arg Gly Met Phe Val Gly Lys Pro Ala Lys Asp Glu Pro
915 920 925
Leu Ser Ile Tyr Gly Lys Thr Met Ile Lys Gly Leu Lys Ala His Gly
930 935 940
Leu Ser Asp Tyr Asp Ile Ala Trp Ser His Val Val Pro Thr Ser Gly
945 950 955 960
Ala Met Val Pro Asn Gln Ala Gln Val Phe Ala Gln Ala Val Asp Tyr
965 970 975
Tyr Leu Ser Pro Ala Gly Met His Tyr Ile Pro Glu Ile His Met Val
980 985 990
Ala Leu Gln Pro Ser Thr Pro Glu Thr Asp Ala Leu Leu Leu Gly Tyr
995 1000 1005
Ala Met Glu Gly Ile Arg Leu Ala Gly Thr Phe Gly Ser Tyr Arg Glu
1010 1015 1020
Ala Ala Val Asp Asp Val Val Lys Glu Asp Asn Gly Arg Gln Val Pro
1025 1030 1035 1040
Val Lys Ala Gly Asp Arg Val Phe Val Ser Phe Val Asp Ala Ala Arg
1045 1050 1055
Asp Pro Lys His Phe Pro Asp Pro Glu Val Val Asn Pro Arg Arg Pro
1060 1065 1070
Ala Lys Lys Tyr Ile His Tyr Gly Val Gly Pro His Ala Cys Leu Gly
1075 1080 1085
Arg Asp Ala Ser Gln Ile Ala Ile Thr Glu Met Phe Arg Cys Leu Phe
1090 1095 1100
Arg Arg Arg Asn Val Arg Arg Val Pro Gly Pro Gln Gly Glu Leu Lys
1105 1110 1115 1120
Lys Val Pro Arg Pro Gly Gly Phe Tyr Val Tyr Met Arg Glu Asp Trp
1125 1130 1135
Gly Gly Leu Phe Pro Phe Pro Val Thr Met Arg Val Met Trp Asp Asp
1140 1145 1150
Glu

<210> 7
<211> 530
<212> PRT
<213> Fusarium oxysporum

<400> 7
Met Lys Gly Ser Ala Thr Leu Ala Phe Ala Leu Val Gln Phe Ser Ala
1 5 10 15
Ala Ser Gln Leu Val Trp Pro Ser Lys Trp Asp Glu Val Glu Asp Leu
20 25 30
Leu Tyr Met Gln Gly Gly Phe Asn Lys Arg Gly Phe Ala Asp Ala Leu
35 40 45
Arg Thr Cys Glu Phe Gly Ser Asn Val Pro Gly Thr Gln Asn Thr Ala
50 55 60
Glu Trp Leu Arg Thr Ala Phe His Asp Ala Ile Thr His Asp Ala Lys
65 70 75 80
Ala Gly Thr Gly Gly Leu Asp Ala Ser Ile Tyr Trp Glu Ser Ser Arg
85 90 95

```
Pro Glu Asn Pro Gly Lys Ala Phe Asn Asn Thr Phe Gly Phe Phe Ser
            100                 105                 110
Gly Phe His Asn Pro Arg Ala Thr Ala Ser Asp Leu Thr Ala Leu Gly
        115                 120                 125
Thr Val Leu Ala Val Gly Ala Cys Asn Gly Pro Arg Ile Pro Phe Arg
    130                 135                 140
Ala Gly Arg Ile Asp Ala Tyr Lys Ala Gly Pro Ala Gly Val Pro Glu
145                 150                 155                 160
Pro Ser Thr Asn Leu Lys Asp Thr Phe Ala Ala Phe Thr Lys Ala Gly
                165
```

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NUMBER | FILING or 371(c) DATE | GRP ART UNIT | FIL FEE REC'D | ATTY.DOCKET.NO | TOT CLAIMS | IND CLAIMS |
|---|---|---|---|---|---|---|
| 15/398,479 | 01/04/2017 | 1791 | 2400 | 38767-0015002 | 30 | 2 |

**CONFIRMATION NO. 2358**

26191
FISH & RICHARDSON P.C. (TC)
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

**FILING RECEIPT**

OC000000088498332

Date Mailed: 01/17/2017

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

**Inventor(s)**

Rachel Fraser, San Francisco, CA;
Patrick O'Reilly Brown, Stanford, CA;
Jessica Karr, San Francisco, CA;
Celeste Holz-Schietinger, East Palo Alto, CA;
Elysia Cohn, Sunnyvale, CA;

**Applicant(s)**

Impossible Foods Inc., Redwood City, CA;

**Power of Attorney:**

Monica Graham--42600
Teresa Lavoie--42782
M. Parsons--44282
Andrea Dorigo--47532
Elizabeth Kaytor--53103
Cameron Luitjens--58674
Ian Lodovice--59749
Angela Follett--60365
Michael Fleming--67933

**Domestic Priority data as claimed by applicant**

This application is a CON of 14/797,006 07/10/2015
which is a CON of PCT/US2014/011347 01/13/2014
which is a CON of 13/941,211 07/12/2013
and claims benefit of 61/908,634 11/25/2013
and claims benefit of 61/751,816 01/11/2013

**Foreign Applications** for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
*Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.*

**Permission to Access Application via Priority Document Exchange:** Yes

**Permission to Access Search Results:** Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

**If Required, Foreign Filing License Granted:** 01/13/2017
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/398,479**
**Projected Publication Date:** 04/27/2017
**Non-Publication Request:** No
**Early Publication Request:** No
**Title**

METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES

**Preliminary Class**

426

**Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications:** No

## PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

## LICENSE FOR FOREIGN FILING UNDER

## Title 35, United States Code, Section 184

## Title 37, Code of Federal Regulations, 5.11 & 5.15

**GRANTED**

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

---

## *SelectUSA*

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor

community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

# PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number
15/398,479

## APPLICATION AS FILED - PART I

| FOR | (Column 1) NUMBER FILED | (Column 2) NUMBER EXTRA | SMALL ENTITY RATE($) | SMALL ENTITY FEE($) | OR | OTHER THAN SMALL ENTITY RATE($) | OTHER THAN SMALL ENTITY FEE($) |
|---|---|---|---|---|---|---|---|
| BASIC FEE (37 CFR 1.16(a), (b), or (c)) | N/A | N/A | N/A | | | N/A | 280 |
| SEARCH FEE (37 CFR 1.16(k), (i), or (m)) | N/A | N/A | N/A | | | N/A | 600 |
| EXAMINATION FEE (37 CFR 1.16(o), (p), or (q)) | N/A | N/A | N/A | | | N/A | 720 |
| TOTAL CLAIMS (37 CFR 1.16(i)) | 30 minus 20 = | * 10 | | | OR | x 80 = | 800 |
| INDEPENDENT CLAIMS (37 CFR 1.16(h)) | 2 minus 3 = | * | | | | x 420 = | 0.00 |
| APPLICATION SIZE FEE (37 CFR 1.16(s)) | If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s). | | | | | | 0.00 |
| MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j)) | | | | | | | 0.00 |
| * If the difference in column 1 is less than zero, enter "0" in column 2. | | | TOTAL | | | TOTAL | 2400 |

## APPLICATION AS AMENDED - PART II

| | | (Column 1) CLAIMS REMAINING AFTER AMENDMENT | | (Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR | (Column 3) PRESENT EXTRA | SMALL ENTITY RATE($) | SMALL ENTITY ADDITIONAL FEE($) | OR | OTHER THAN SMALL ENTITY RATE($) | OTHER THAN SMALL ENTITY ADDITIONAL FEE($) |
|---|---|---|---|---|---|---|---|---|---|---|
| AMENDMENT A | Total (37 CFR 1.16(i)) | * | Minus | ** | = | x = | | OR | x = | |
| AMENDMENT A | Independent (37 CFR 1.16(h)) | * | Minus | *** | = | x = | | OR | x = | |
| AMENDMENT A | Application Size Fee (37 CFR 1.16(s)) | | | | | | | | | |
| AMENDMENT A | FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j)) | | | | | | | OR | | |
| | | | | | | TOTAL ADD'L FEE | | OR | TOTAL ADD'L FEE | |

| | | (Column 1) CLAIMS REMAINING AFTER AMENDMENT | | (Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR | (Column 3) PRESENT EXTRA | RATE($) | ADDITIONAL FEE($) | OR | RATE($) | ADDITIONAL FEE($) |
|---|---|---|---|---|---|---|---|---|---|---|
| AMENDMENT B | Total (37 CFR 1.16(i)) | * | Minus | ** | = | x = | | OR | x = | |
| AMENDMENT B | Independent (37 CFR 1.16(h)) | * | Minus | *** | = | x = | | OR | x = | |
| AMENDMENT B | Application Size Fee (37 CFR 1.16(s)) | | | | | | | | | |
| AMENDMENT B | FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j)) | | | | | | | OR | | |
| | | | | | | TOTAL ADD'L FEE | | OR | TOTAL ADD'L FEE | |

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

FISH & RICHARDSON P.C. (TC)
PO BOX 1022
MINNEAPOLIS MN 55440-1022

MAILED
JAN 18 2017
OFFICE OF PETITIONS

Doc Code: TRACK1.GRANT

| ***Decision Granting Request for Prioritized Examination (Track I or After RCE)*** | Application No.: 15/398,479 |
|---|---|

1. THE REQUEST FILED January 4, 2017 IS **GRANTED**.

The above-identified application has met the requirements for prioritized examination
A. ☒ for an original nonprovisional application (Track I).
B. ☐ for an application undergoing continued examination (RCE).

2. **The above-identified application will undergo prioritized examination.** The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:

A. filing a **petition for extension of time** to extend the time period for filing a reply;
B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims**, or a multiple dependent claim;
C. filing a **request for continued examination**;
D. filing a notice of appeal;
E. filing a request for suspension of action;
F. mailing of a notice of allowance;
G. mailing of a final Office action;
H. completion of examination as defined in 37 CFR 41.102; or
I. abandonment of the application.

Telephone inquiries with regard to this decision should be directed to Brian W. Brown at 571-272-5338.

/Brian W. Brown/
[*Signature*]

Petitions Examiner, Office of Petitions
(Title)

U.S. Patent and Trademark Office
PTO-2298 (Rev. 02-2012)

Attorney Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | 15/398,479 | Examiner | : | Unknown |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

**MAIL STOP AMENDMENT**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Please consider the references listed on the enclosed PTO-1449 Form. Foreign patent documents and non-patent literature are enclosed. A copy of a Communication from a foreign Patent Office in a counterpart application also is enclosed.

This statement is being filed before the receipt of a first Office Action on the merits. Therefore, no fees are believed due. If this is incorrect, please apply any charges, or credits, to Deposit Account No. 06-1050, referencing the above-indicated Attorney Docket Number.

Please contact the undersigned if there are any questions regarding this statement.

Respectfully submitted,

Date: /January 19, 2017/

/M. Angela Parsons/
M. Angela Parsons, Ph.D.
Reg. No. 44,282

Customer Number 26191
Fish & Richardson P.C.
Telephone: (612) 335-5070
Facsimile: (877) 769-7945

61426015.doc

Sheet 1 of 1

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. 15/398,479 |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date January 4, 2017 | Group Art Unit |

| U.S. Patent Documents | | | | | | | |
|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |

| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation | |
| | | | | | | | Yes | No |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 1. | Cott et al., "The 'Impossible' Veggie Burger: A Tech Industry Answer to the Big Mac," Business Day, January 13, 2017, retrieved on 01/17/2017, <https://mobile.nytimes.com/2017/01/13/business/veggie-burger-impossible-burger.html?referer=http://www.drudgereport.com/>, 7 pages |
| | 2. | Fang et al., "Food Nutrition health theory and technology," China light industry press, p. 448, January 31, 1997 (Chinese Version) |
| | 3. | Fourth Chinese Office Action in Chinese Application No. 201280041713.1, dated 11/11/2016, 18 pages (with translation) |
| | 4. | Supplementary European Search Report for International No. EP 14737909.3, dated October 07, 2016, 10 pages |
| | 5. | Zhengnong et al., "Cihai biological fascicle," Shanghai Lexicographical Publishing House, P.243, December 31, 1987 (Chinese Version) |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 28106927 |
| **Application Number:** | 15398479 |
| **International Application Number:** | |
| **Confirmation Number:** | 2358 |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Customer Number:** | 26191 |
| **Filer:** | M. Angela Parsons/Shannon Glaeser |
| **Filer Authorized By:** | M. Angela Parsons |
| **Attorney Docket Number:** | 38767-0015002 |
| **Receipt Date:** | 19-JAN-2017 |
| **Filing Date:** | 04-JAN-2017 |
| **Time Stamp:** | 13:33:30 |
| **Application Type:** | Utility under 35 USC 111(a) |

## Payment information:

| | |
|---|---|
| Submitted with Payment | no |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | Information Disclosure Statement (IDS) Form (SB08) | Transmittal.pdf | 68369<br>fe22330428b665d568ef5489df831df4ffe80692 | no | 1 |

**Warnings:**

| | | | | | |
|---|---|---|---|---|---|
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 2 | Information Disclosure Statement (IDS) Form (SB08) | 1449.pdf | 125226<br>19d51d65d5e98b49482f6aed0d65e364ee95d98b | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 3 | Non Patent Literature | Cott_2017.pdf | 1529112<br>0b1c2aeb0d196de1168e72e6075717b5995245db | no | 7 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 4 | Non Patent Literature | Fang_1997.pdf | 53006<br>f70b5af11e0d2686e304268ee39a5d40aa8b07d3 | no | 3 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 5 | Non Patent Literature | CNOA_2012800417131_2016_11_11.pdf | 749892<br>0e4b56819fa08b1bdfa8ccc319b4ca60513cdd18 | no | 18 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 6 | Non Patent Literature | ESSR_147379093_2016_10_07.pdf | 992849<br>4ff7ba99061f456b4273e9e36cceec9916c993f8 | no | 10 |
| **Warnings:** | | | | | |
| The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing | | | | | |
| **Information:** | | | | | |
| 7 | Non Patent Literature | Zhengnong_1987.pdf | 327331<br>7aca2d50a1665f1d35052a979258bd867755fe5e | no | 3 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | | **Total Files Size (in bytes):** | 3845785 | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**New Applications Under 35 U.S.C. 111**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**National Stage of an International Application under 35 U.S.C. 371**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**New International Application Filed with the USPTO as a Receiving Office**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

Sheet 1 of 1

| Substitute Disclosure Form<br>U.S. Department of Commerce<br>Patent and Trademark Office | Attorney Docket No.<br>38767-0015002 | Application No.<br>15/398,479 |
|---|---|---|
| **Information Disclosure Statement by Applicant**<br>(Use several sheets if necessary) | Applicant<br>Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | Filing Date<br>January 4, 2017 | Group Art Unit |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | -- | -- | | | | | |

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | -- | -- | | | | | | |

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| | 1. | Lombardi et al., "Total Heme and Non-heme Iron in Raw and Cooked Meats," Journal of Food Science, 67(5):1738-1741 (2002) |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 28282562 |
| **Application Number:** | 15398479 |
| **International Application Number:** | |
| **Confirmation Number:** | 2358 |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Customer Number:** | 26191 |
| **Filer:** | M. Angela Parsons/Shannon Glaeser |
| **Filer Authorized By:** | M. Angela Parsons |
| **Attorney Docket Number:** | 38767-0015002 |
| **Receipt Date:** | 07-FEB-2017 |
| **Filing Date:** | 04-JAN-2017 |
| **Time Stamp:** | 10:32:18 |
| **Application Type:** | Utility under 35 USC 111(a) |

## Payment information:

| | |
|---|---|
| Submitted with Payment | no |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | Information Disclosure Statement (IDS) Form (SB08) | Transmittal.pdf | 68260<br>5c7d804c5bc7ca011c02fdcead4d837966a193fa | no | 1 |

**Warnings:**

| | | | | | |
|---|---|---|---|---|---|
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 2 | Information Disclosure Statement (IDS) Form (SB08) | 1449.pdf | 120256<br>0183e25cd5a76ad9d98a17b7c4e5ec2e8da1d3c0 | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 3 | Non Patent Literature | Lombardi_2002.pdf | 379677<br>34d54e0dc988193a4deb437a7cc9b4aa9992d49c | no | 4 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | | **Total Files Size (in bytes):** | 568193 | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**New Applications Under 35 U.S.C. 111**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**National Stage of an International Application under 35 U.S.C. 371**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**New International Application Filed with the USPTO as a Receiving Office**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

Attorney Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | 15/398,479 | Examiner | : | Unknown |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

**MAIL STOP AMENDMENT**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Please consider the references listed on the enclosed PTO-1449 Form. A non-patent literature reference is enclosed.

This statement is being filed before the mailing date of a first Office Action on the merits. Therefore, no fees are believed due. If this is incorrect, please apply any charges, or credits, to Deposit Account No. 06-1050, referencing the above-indicated Attorney Docket Number.

Please contact the undersigned if there are any questions regarding this statement.

Respectfully submitted,

Date: /February 7, 2017/

/M. Angela Parsons/
M. Angela Parsons, Ph.D.
Reg. No. 44,282

Customer Number 26191
Fish & Richardson P.C.
Telephone: (612) 335-5070
Facsimile: (877) 769-7945

61434599.doc

Attorney Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | 15/398,479 | Examiner | : | Unknown |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

**MAIL STOP AMENDMENT**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Please consider the reference listed on the enclosed PTO-1449 Form. A non-patent literature reference is enclosed.

This statement is being filed before receipt of a first Office Action on the merits. Therefore, no fees are believed due. If this is incorrect, please apply any charges, or credits, to Deposit Account No. 06-1050, referencing the above-indicated Attorney Docket Number.

Please contact the undersigned if there are any questions regarding this statement.

Respectfully submitted,

Date: /February 15, 2017/

/M. Angela Parsons/
M. Angela Parsons, Ph.D.
Reg. No. 44,282

Customer Number 26191
Fish & Richardson P.C.
Telephone: (612) 335-5070
Facsimile: (877) 769-7945

61439338.doc

Sheet 1 of 1

| Substitute Disclosure Form<br>U.S. Department of Commerce<br>Patent and Trademark Office | Attorney Docket No.<br>38767-0015002 | Application No.<br>15/398,479 |
|---|---|---|
| **Information Disclosure Statement by Applicant**<br>(Use several sheets if necessary) | Applicant<br>Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | Filing Date<br>January 4, 2017 | Group Art Unit |

| U.S. Patent Documents | | | | | | | |
|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |

| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation | |
| | | | | | | | Yes | No |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 1. | Aubrey, "Food For Thought: Saving The Planet, One Burger At A Time: This Juicy Patty Is Meat-Free," The Salt, February 11, 2017, retrieved on February 14, 2017, retrieved from <http://www.npr.org/sections/thesalt/2017/02/11/514544431/saving-the-planet-one-burger-at-a-time-this-juicy-patty-is-meat-free>, 14 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 28360066 |
| **Application Number:** | 15398479 |
| **International Application Number:** | |
| **Confirmation Number:** | 2358 |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Customer Number:** | 26191 |
| **Filer:** | M. Angela Parsons/Shannon Glaeser |
| **Filer Authorized By:** | M. Angela Parsons |
| **Attorney Docket Number:** | 38767-0015002 |
| **Receipt Date:** | 15-FEB-2017 |
| **Filing Date:** | 04-JAN-2017 |
| **Time Stamp:** | 11:10:04 |
| **Application Type:** | Utility under 35 USC 111(a) |

## Payment information:

| | |
|---|---|
| Submitted with Payment | no |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | Information Disclosure Statement (IDS) Form (SB08) | Transmittal.pdf | 68253<br>df4721a2b7af0013a12c42846ce5422d6fa24dde | no | 1 |

**Warnings:**

| | | | | | |
|---|---|---|---|---|---|
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 2 | Information Disclosure Statement (IDS) Form (SB08) | 1449.pdf | 121286<br>d17bf2e8ed6249ee433723c0b66d85f3eb6661ed | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 3 | Non Patent Literature | Aubrey_2017.pdf | 2445147<br>deb5daf624d276cf4d4048a1c2780a0ee5585e63 | no | 14 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | | **Total Files Size (in bytes):** | 2634686 | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**<u>New Applications Under 35 U.S.C. 111</u>**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**<u>National Stage of an International Application under 35 U.S.C. 371</u>**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**<u>New International Application Filed with the USPTO as a Receiving Office</u>**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

Attorney Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | 15/398,479 | Examiner | : | Unknown |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

**MAIL STOP AMENDMENT**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Please consider the reference listed on the enclosed PTO-1449 Form. A non-patent literature reference is enclosed.

This statement is being filed before receipt of a first Office Action on the merits. Therefore, no fees are believed due. If this is incorrect, please apply any charges, or credits, to Deposit Account No. 06-1050, referencing the above-indicated Attorney Docket Number.

Please contact the undersigned if there are any questions regarding this statement.

Respectfully submitted,

Date: /March 3, 2017/

/M. Angela Parsons/
M. Angela Parsons, Ph.D.
Reg. No. 44,282

Customer Number 26191
Fish & Richardson P.C.
Telephone: (612) 335-5070
Facsimile: (877) 769-7945

61445101.doc

Sheet 1 of 1

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. 15/398,479 |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date January 4, 2017 | Group Art Unit |

| U.S. Patent Documents | | | | | | | |
|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |

| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation | |
| | | | | | | | Yes | No |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 1. | Chau, "Uncanny Patty," The Ringer, February 27, 2017, retrieved on February 28, 2017, retrieved from <https://theringer.com/impossible-burger-last-meal-on-earth-week-food-f9f14acdb99d#.vocb2hi6e>, 19 pages |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 28523669 |
| **Application Number:** | 15398479 |
| **International Application Number:** | |
| **Confirmation Number:** | 2358 |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Customer Number:** | 26191 |
| **Filer:** | M. Angela Parsons/Adam Schunk |
| **Filer Authorized By:** | M. Angela Parsons |
| **Attorney Docket Number:** | 38767-0015002 |
| **Receipt Date:** | 03-MAR-2017 |
| **Filing Date:** | 04-JAN-2017 |
| **Time Stamp:** | 09:54:00 |
| **Application Type:** | Utility under 35 USC 111(a) |

## Payment information:

| | |
|---|---|
| Submitted with Payment | no |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | Information Disclosure Statement (IDS) Form (SB08) | IDS_Transmittal.pdf | 52501<br>22d8b4bdfb627de07809125dc7dfbc7cfd4c4ab1 | no | 1 |

**Warnings:**

| | | | | | |
|---|---|---|---|---|---|
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 2 | Information Disclosure Statement (IDS) Form (SB08) | IDS-1449.pdf | 89310<br>ca120cbad6eea4068f8a81961821286e5b6b44ca | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 3 | Non Patent Literature | Chau_UnCanny_Patty_2017.pdf | 4480589<br>7c86f34b9ee0a712a025ede571552518136cf873 | no | 19 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | | **Total Files Size (in bytes):** | 4622400 | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**<u>New Applications Under 35 U.S.C. 111</u>**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**<u>National Stage of an International Application under 35 U.S.C. 371</u>**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**<u>New International Application Filed with the USPTO as a Receiving Office</u>**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

Attorney Docket No.: 38767-0015002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | Unknown |
| Serial No. | : | 15/398,479 | Examiner | : | Unknown |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

**MAIL STOP AMENDMENT**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Please consider the references listed on the enclosed PTO-1449 Form. Non-patent literature references are enclosed.

This statement is being filed before the receipt of a first Office Action on the merits. Therefore, no fees are believed due. If this is incorrect, please apply any charges, or credits, to Deposit Account No. 06-1050, referencing the above-indicated Attorney Docket Number.

Please contact the undersigned if there are any questions regarding this statement.

Respectfully submitted,

Date: /March 20, 2017/

/M. Angela Parsons/
M. Angela Parsons, Ph.D.
Reg. No. 44,282

Customer Number 26191
Fish & Richardson P.C.
Telephone: (612) 335-5070
Facsimile: (877) 769-7945

61452754.doc

Sheet 1 of 1

| Substitute Disclosure Form<br>U.S. Department of Commerce<br>Patent and Trademark Office | Attorney Docket No.<br>38767-0015002 | Application No.<br>15/398,479 |
|---|---|---|
| **Information Disclosure Statement by Applicant**<br>(Use several sheets if necessary) | Applicant<br>Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | Filing Date<br>January 4, 2017 | Group Art Unit |

| U.S. Patent Documents | | | | | | | |
|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |

| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation | |
| | | | | | | | Yes | No |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 1. | Fang et al., "Food Nutrition health theory and technology," China light industry press, p. 448, January 31, 1997 (English Translation) |
| | 2. | Zhengnong et al., "Cihai biological fascicle," Shanghai Lexicographical Publishing House, P.243, December 31, 1987 (English Translation) |

| Examiner Signature | Date Considered |
|---|---|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 28673335 |
| **Application Number:** | 15398479 |
| **International Application Number:** | |
| **Confirmation Number:** | 2358 |
| **Title of Invention:** | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES |
| **First Named Inventor/Applicant Name:** | Rachel Fraser |
| **Customer Number:** | 26191 |
| **Filer:** | M. Angela Parsons/Shannon Glaeser |
| **Filer Authorized By:** | M. Angela Parsons |
| **Attorney Docket Number:** | 38767-0015002 |
| **Receipt Date:** | 20-MAR-2017 |
| **Filing Date:** | 04-JAN-2017 |
| **Time Stamp:** | 11:23:46 |
| **Application Type:** | Utility under 35 USC 111(a) |

## Payment information:

| | |
|---|---|
| Submitted with Payment | no |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | Information Disclosure Statement (IDS) Form (SB08) | Transmittal.pdf | 68246<br>dfa3eab2438a4ac78440f8e29878eb4407f67155 | no | 1 |

**Warnings:**

| | | | | | |
|---|---|---|---|---|---|
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 2 | Information Disclosure Statement (IDS) Form (SB08) | 1449.pdf | 120466<br>65d1c2dfa3d441157d76d4dbf1df99ea9ca41e48 | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| This is not an USPTO supplied IDS fillable form | | | | | |
| 3 | Non Patent Literature | Fang_1997_transl.pdf | 2255629<br>ab1d1d4b888473da91b59370e6f63f5801b68883 | no | 7 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 4 | Non Patent Literature | Zhengnong_1987_transl.pdf | 6204157<br>8b4ed646ebd51c58f3303cbdb3cef23d65adc075 | no | 8 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | | **Total Files Size (in bytes):** | 8648498 | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**<u>New Applications Under 35 U.S.C. 111</u>**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**<u>National Stage of an International Application under 35 U.S.C. 371</u>**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**<u>New International Application Filed with the USPTO as a Receiving Office</u>**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

UNITED STATES PATENT AND TRADEMARK OFFICE

**UNITED STATES DEPARTMENT OF COMMERCE**
**United States Patent and Trademark Office**
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 15/398,479 | 01/04/2017 | Rachel Fraser | 38767-0015002 | 2358 |

26191 7590 04/14/2017
FISH & RICHARDSON P.C. (TC)
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

| EXAMINER |
|---|
| GWARTNEY, ELIZABETH A |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1791 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 04/14/2017 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

| Office Action Summary | Application No. 15/398,479 | Applicant(s) FRASER ET AL. | |
|---|---|---|---|
| | Examiner ELIZABETH GWARTNEY | Art Unit 1791 | AIA (First Inventor to File) Status No |

***-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims***

5)☒ Claim(s) 31-60 is/are pending in the application.

5a) Of the above claim(s) 59 and 60 is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) 31-58 is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

**Application Papers**

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on 1/4/2017 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

**Certified copies:**

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

## DETAILED ACTION

1. The present application is being examined under the pre-AIA first to invent provisions.

2. U.S. Application No. 15/398,479 is a continuation of U.S. Application No. 14/797,006, now allowed.

### *Election/Restrictions*

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. **Claims 31-58**, drawn to a food flavor additive comprising an isolated heme-containing protein, a sugar, sugar alcohol, sugar acid, or sugar derivative classified in A23L27/00.

II. **Claims 59 and 60**, drawn to a process of imparting a meaty flavor and/or meaty aroma to a consumable food product, classified in A23L13/426.

The inventions are distinct, each from the other because of the following reasons: Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the process for using the product as claimed can be practiced with another materially different product, for example, aroma compounds associated with meat flavor are known to be generated by a reaction of ribose and cysteine when heated (Cerny et al. "Formation of Aroma Compounds from Ribose and Cysteine during the Maillard Reaction" - *J. Agric. Food Chem.* 51, 2003, pp. 2714-2721).

4. Restriction for examination purposes as indicated is proper because all the inventions listed in this action are independent or distinct for the reasons given above <u>and</u> there would be a

serious search and/or examination burden if restriction were not required because one or more of the following reasons apply:

- the inventions have acquired a separate status in the art in view of their different classification

-the inventions have acquired a separate status in the art due to their recognized divergent subject matter

-the inventions require a different field of search (e.g. searching different classes/subclasses or electronic resources, or employing different search strategies or search queries

5. **Applicant is advised that the reply to this requirement to be complete must include (i) an election of an invention to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either

instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 or pre-AIA 35 U.S.C. 103(a) of the other invention.

6. During a telephone conversation with Ian Lodovice on April 6, 2017 a provisional election was made without traverse to prosecute the invention of Group I, claims 31-58.

7. Affirmation of this election must be made by applicant in replying to this Office action. Claims 59 and 60 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

***Specification***

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code; references to websites should be limited to the top-level domain name without any prefix such as http:// or other browser-executable code. See MPEP § 608.01.

***Drawings***

9. The drawings are objected to because Figure 2 does not contain a label for the Y-axis. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be

renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 112***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. The following is a quotation of 35 U.S.C. 112(b):

> (b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. **Claims 31-58 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s)**

**contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention.**

**Claims 31 and 41** recite "wherein the flavor additive composition contains no animal tissue derived components." While there is support to claim that the food products comprising the components of the food additive are non-animal based or free of animal products and that the heme protein can be extracted from animal tissue (page 4/L15-26, page 7/L5-6, page 17/L7-8), there is no support to claim that the flavor additive composition contains no animal tissue derived components.

**Claim 31** recites "wherein the flavor additive composition is packaged and is in the form of a liquid, a gel, an emulsion, a powder or a bouillon cube." While there is support for claiming that the flavor additive is in the form of soup or stew bases, bouillon, e.g. powder or cubes, flavor packets or seasoning packets or shakers (page 5/L10-12), there is no support for claiming a flavor additive in the form of a liquid, a gel, a powder or an emulsion. Note, while there is support to claim the flavor additive is in the form of a soup or stew base and powdered bouillon, there is not support for claiming an additive that is in ***any*** liquid or powder form.

**Claim 32** recites "wherein the heme-containing protein is present in an amount between about 0.01% to about 5%. While there is support to claim a food product comprising 0.01% to 5% by weight of a heme protein (*see* page 18/L16-27 of specification for U.S. Application No. 14/979,006), there is not support for claiming a food additive (which can be added to a food product) comprising 0.01% to 5% by weight of a heme protein.

**Claim 53** recites "further comprising an ingredient selected from an emulsifier and a gelling agent and **claim 54** recites "adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b). While there is support for claiming a product comprising the food flavor additive may include additional ingredients, including emulsifiers and gelling agents, there is no support to say both an emulsifier and gelling agent are added ingredients to the food flavor additive (*see* page 26/L17-23).

13. **Claims 31-58 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.**

Regarding **claims 31 and 41**, the recitation “wherein the flavor additive composition contains no animal tissue derived components” renders the claims indefinite. It is not clear what properties are encompassed by components that are specifically animal tissue derived. Given, for example, water could be derived from animal tissue. Therefore, it is not clear that the phrase "animal tissue derived" is any more than a source indicator.

Regarding **claims 31 and 41**, the recitation “a sugar, sugar, alcohol, sugar acid, or sugar derivative selective from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose and mixture of two or more thereof renders the claim indefinite because there are no sugar acids in the list of compounds listed in the Markush group.

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. **Claims 31, 33-36, 38 and 40 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Tong et al. ("Blood Composition of Different Beef Breed Types" – *Can. J. Anim. Sci*, 66, Dec. 1986, pp. 915-924) as evidenced by Shimbayashi et al. ("Free Amino Acids and Phsphorylethanolamine in Milk Whey of Cow" – *Agr. Biol. Chem*, Vol. 29, No. 1, 1965, pp. 13-19).**

Regarding **claims 31, 33, 35, 36, 38 and 40**, Tong et al. disclose blood from cattle comprising hemoglobin, glucose, protein, and albumin (p. 917/Table 1).

As evidenced by Shimbayashi et al., blood from cattle was known to comprise free amino acids including methionine, taurine, threonine, serine, glutamic acid, proline, glycine, alanine, valine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, and arginine (p. 18/Table IV).

With regards to the limitations of "an isolated heme-containing protein" and "no animal tissue derived components," it is noted "even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself" (*see* MPEP §2113). "The patentability of a product does not depend on its method of product. If the product in the product-by process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.d 695, 698, 227 USPQ 964,966 (Fed. Cir. 1985) (*see* MPEP §2113).

Regarding **claim 34**, Tong et al. disclose all of the claim limitations as set forth above. Given Tong et al. disclose wherein the heme-containing protein is hemoglobin from cattle blood, inherently the protein would comprise an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID no. 18 (*Bos Taurus).*

16. **Claims 31-36 and 38 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Koutsidis et al. ("Water-soluble precursors of beef flavor: I. Effect of diet and breed"- *Meat Science*, 79, 2008, pp. 124-130) as evidenced by Field et al. ("Heme Pgiment Content of Bovine Hemopoietic Marrow and Muscle" – *J. Food Sci*., Volume 45, 1980, pp. 1109-1112).**

Regarding **claims 31-33, 35, 36 and 38,** Koutsidis et al. disclose beef comprising: (a) sugars and sugar phosphates including mannose, fructose, glucose, mannose 6-phosphate, fructose 6-phosphate, glucose 6-phosphate, maltose, ribose and inositol; and (b) free amino acids including glycine, alanine, valine, isoleucine, leucine, threonine, serine, proline, asparagine, aspartic acid, methionine, glutamic acid, phenylalanine, cysteine, glutamine, ornithine, lysine, histidine, tyrosine, tryptophan, arginine, and β-alanine (p. 127/Table 1, p. 128/Table 3).

As evidenced by Field et al., beef muscle is known to comprise about 0.06 % by weight hemoglobin (p. 1109/Table 1).

With regards to the limitations of "an isolated heme-containing protein" and "no animal tissue derived components," it is noted "even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself" (*see* MPEP §2113). "The patentability of a product does not depend on its method of product. If the

product in the product-by process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.d 695, 698, 227 USPQ 964,966 (Fed. Cir. 1985) (*see* MPEP §2113). In this case, Koutsidis et al. discloses beef which is known to comprise heme-containing protein, hemoglobin. Although the heme-containing protein is not isolated, the burden shifts to establish an unobvious difference between the claimed product and the prior art product.

Regarding **claim 34**, Koutsidis et al. disclose all of the claim limitations as set forth above. Given Koutsidis et al. disclose beef, which is known to comprise a heme-containing protein, hemoglobin, inherently the protein would comprise an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID no. 18 (*Bos Taurus).*

17. **Claims 31, 33-36, 38, 39-45, 50, 51 and 58 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Jamieson ("Iroquois Stew With Beef, Chicken and Pork"– Bon Appétit, November 1995, http://www.epicurious.com/recipes/food/views/iroquois-stew-with-beef-chicken-and-pork-865) as evidenced by Koutsidis et al. ("Water-soluble precursors of beef flavor: I. Effect of diet and breed"- *Meat Science*, 79, 2008, pp. 124-130), Field et al. ("Heme Pgiment Content of Bovine Hemopoietic Marrow and Muscle" – *J. Food Sci.*, Volume 45, 1980, pp. 1109-1112) and Griffiths ("XCIII. The Action of Gastric Juice on Beef Muscle-Globulin, With Reference to Anaemia" – *Biochemistry Journal*, Vol. 28, 1934, pp. 671-675)**

Regarding **claims 31, 33, 35, 36, 38, 39, 40-42, 50 and 58**, Jamieson discloses Iroquois stew with beef and method for making the stew comprising adding beef to a composition of

pork, chicken, flour, vegetable oil, onion, chicken broth, carrots, bay leaves, all spice and potatoes (Ingredients, Preparation). Jamieson disclose heating the ingredients (Preparation). Given Jamieson disclose heating the ingredients for time periods of over 30 minutes at temperatures of medium-high and medium-low, it follows that the stew would be heated at least 150°C for at least 1 minute (Preparation).

As evidenced by Koutsidis et al. beef is known to comprise: (a) sugars and sugar phosphates including mannose, fructose, glucose, mannose 6-phosphate, fructose 6-phosphate, glucose 6-phosphate, maltose, ribose and inositol; and (b) free amino acids including glycine, alanine, valine, isoleucine, leucine, threonine, serine, proline, asparagine, aspartic acid, methionine, glutamic acid, phenylalanine, cysteine, glutamine, ornithine, lysine, histidine, tyrosine, tryptophan, arginine, and β-alanine (p. 127/Table 1, p. 128/Table 3).

Moreover, as evidenced by Field et al., beef muscle is known to comprise about 0.06 % by weight hemoglobin (p. 1109/Table 1).

As evidenced by Griffiths, beef is known to comprise globulin.

While Jamieson discloses a heme-containing protein (in the form of beef), the reference is silent with respect to an isolated or animal tissue derived products.

However, it is noted that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process", *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (*see* MPEP §2113). In this case, Jamieson

discloses a beef comprising a heme-containing protein. Although the heme-containing protein is obtained from a different source (i.e. beef, non-purified), the burden shifts to establish an unobvious difference between the claimed product and the prior art product.

Regarding **claims 34 and 51**, Jamieson discloses all of the claim limitations as set forth above. Given Jamieson discloses beef which is known to comprise hemoglobin, a heme-containing protein, inherently the protein would comprise an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID no. 18 (*Bos Taurus).*

Regarding **claims 43-45**, Jamieson discloses all of the claim limitations as set forth above. Given Jamieson discloses heating the claimed components as presently claimed, inherently the stew of Jamieson would display a meaty flavor and/or meaty aroma, including a compounds of claim 44, in the headspace during or after heating.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELIZABETH GWARTNEY whose telephone number is (571)270-3874. The examiner can normally be reached on M-F.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, D. Lawrence Tarazano can be reached on (571) 272-1515. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ELIZABETH GWARTNEY/
Primary Examiner, Art Unit 1791

| Notice of References Cited | Application/Control No. 15/398,479 | Applicant(s)/Patent Under Reexamination FRASER ET AL. | |
|---|---|---|---|
| | Examiner ELIZABETH GWARTNEY | Art Unit 1791 | Page 1 of 2 |

**U.S. PATENT DOCUMENTS**

| * | | Document Number Country Code-Number-Kind Code | Date MM-YYYY | Name | CPC Classification | US Classification |
|---|---|---|---|---|---|---|
| | A | US- | | | | |
| | B | US- | | | | |
| | C | US- | | | | |
| | D | US- | | | | |
| | E | US- | | | | |
| | F | US- | | | | |
| | G | US- | | | | |
| | H | US- | | | | |
| | I | US- | | | | |
| | J | US- | | | | |
| | K | US- | | | | |
| | L | US- | | | | |
| | M | US- | | | | |

**FOREIGN PATENT DOCUMENTS**

| * | | Document Number Country Code-Number-Kind Code | Date MM-YYYY | Country | Name | CPC Classification |
|---|---|---|---|---|---|---|
| | N | | | | | |
| | O | | | | | |
| | P | | | | | |
| | Q | | | | | |
| | R | | | | | |
| | S | | | | | |
| | T | | | | | |

**NON-PATENT DOCUMENTS**

| * | | Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages) |
|---|---|---|
| | U | Cerny et al. "Formation of Aroma Compounds from Ribose and Cysteine during the Maillard Reaction" - J. Agric. Food Chem. 51, 2003, pp. 2714-2721. |
| | V | Tong et al. ,"Blood Composition of Different Beef Breed Types" - Can. J. Anim. Sci, 66, Dec. 1986, pp. 915-924. |
| | W | Shimbayashi et al.,"Free Amino Acids and Phsphorylethanolamine in Milk Whey of Cow" - Agr. Biol. Chem, Vol. 29, No. 1, 1965, pp. 13-19. |
| | X | Koutsidis et al., "Water-soluble precursors of beef flavor: I. Effect of diet and breed"- Meat Science, 79, 2008, pp. 124-130. |

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

| Notice of References Cited | Application/Control No. 15/398,479 | Applicant(s)/Patent Under Reexamination FRASER ET AL. | |
|---|---|---|---|
| | Examiner ELIZABETH GWARTNEY | Art Unit 1791 | Page 2 of 2 |

**U.S. PATENT DOCUMENTS**

| * | | Document Number Country Code-Number-Kind Code | Date MM-YYYY | Name | CPC Classification | US Classification |
|---|---|---|---|---|---|---|
| | A | US- | | | | |
| | B | US- | | | | |
| | C | US- | | | | |
| | D | US- | | | | |
| | E | US- | | | | |
| | F | US- | | | | |
| | G | US- | | | | |
| | H | US- | | | | |
| | I | US- | | | | |
| | J | US- | | | | |
| | K | US- | | | | |
| | L | US- | | | | |
| | M | US- | | | | |

**FOREIGN PATENT DOCUMENTS**

| * | | Document Number Country Code-Number-Kind Code | Date MM-YYYY | Country | Name | Classification |
|---|---|---|---|---|---|---|
| | N | | | | | |
| | O | | | | | |
| | P | | | | | |
| | Q | | | | | |
| | R | | | | | |
| | S | | | | | |
| | T | | | | | |

**NON-PATENT DOCUMENTS**

| * | | Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages) |
|---|---|---|
| | U | Field et al., “Heme Pgiment Content of Bovine Hemopoietic Marrow and Muscle” – J. Food Sci., Volume 45, 1980, pp. 1109-1112. |
| | V | Jamieson, “Iroquois Stew With Beef, Chicken and Pork”– Bon Appétit, November 1995, http://www.epicurious.com/recipes/food/views/iroquois-stew-with-beef-chicken-and-pork-865. |
| | W | Griffiths, W., “XCIII. The Action of Gastric Juice on Beef Muscle-Globulin, With Reference to Anaemia” – Biochemistry Journal, Vol. 28, 1934, pp. 671-675. |
| | X | |

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

| Index of Claims | Application/Control No. | Applicant(s)/Patent Under Reexamination |
|---|---|---|
| | 15398479 | FRASER ET AL. |
| | **Examiner** | **Art Unit** |
| | ELIZABETH GWARTNEY | 1791 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ✓ | Rejected | - | Cancelled | N | Non-Elected | A | Appeal |
| = | Allowed | ÷ | Restricted | I | Interference | O | Objected |

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

| CLAIM | | DATE | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Final | Original | 04/10/2017 | | | | | | | | |
| | 1 | - | | | | | | | | |
| | 2 | - | | | | | | | | |
| | 3 | - | | | | | | | | |
| | 4 | - | | | | | | | | |
| | 5 | - | | | | | | | | |
| | 6 | - | | | | | | | | |
| | 7 | - | | | | | | | | |
| | 8 | - | | | | | | | | |
| | 9 | - | | | | | | | | |
| | 10 | - | | | | | | | | |
| | 11 | - | | | | | | | | |
| | 12 | - | | | | | | | | |
| | 13 | - | | | | | | | | |
| | 14 | - | | | | | | | | |
| | 15 | - | | | | | | | | |
| | 16 | - | | | | | | | | |
| | 17 | - | | | | | | | | |
| | 18 | - | | | | | | | | |
| | 19 | - | | | | | | | | |
| | 20 | - | | | | | | | | |
| | 21 | - | | | | | | | | |
| | 22 | - | | | | | | | | |
| | 23 | - | | | | | | | | |
| | 24 | - | | | | | | | | |
| | 25 | - | | | | | | | | |
| | 26 | - | | | | | | | | |
| | 27 | - | | | | | | | | |
| | 28 | - | | | | | | | | |
| | 29 | - | | | | | | | | |
| | 30 | - | | | | | | | | |
| | 31 | ✓ | | | | | | | | |
| | 32 | ✓ | | | | | | | | |
| | 33 | ✓ | | | | | | | | |
| | 34 | ✓ | | | | | | | | |
| | 35 | ✓ | | | | | | | | |
| | 36 | ✓ | | | | | | | | |

| Index of Claims | Application/Control No. | Applicant(s)/Patent Under Reexamination |
|---|---|---|
| | 15398479 | FRASER ET AL. |
| | **Examiner** | **Art Unit** |
| | ELIZABETH GWARTNEY | 1791 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ✓ | Rejected | - | Cancelled | N | Non-Elected | A | Appeal |
| = | Allowed | ÷ | Restricted | I | Interference | O | Objected |

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

| CLAIM | | DATE | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Final | Original | 04/10/2017 | | | | | | | | |
| | 37 | ✓ | | | | | | | | |
| | 38 | ✓ | | | | | | | | |
| | 39 | ✓ | | | | | | | | |
| | 40 | ✓ | | | | | | | | |
| | 41 | ✓ | | | | | | | | |
| | 42 | ✓ | | | | | | | | |
| | 43 | ✓ | | | | | | | | |
| | 44 | ✓ | | | | | | | | |
| | 45 | ✓ | | | | | | | | |
| | 46 | ✓ | | | | | | | | |
| | 47 | ✓ | | | | | | | | |
| | 48 | ✓ | | | | | | | | |
| | 49 | ✓ | | | | | | | | |
| | 50 | ✓ | | | | | | | | |
| | 51 | ✓ | | | | | | | | |
| | 52 | ✓ | | | | | | | | |
| | 53 | ✓ | | | | | | | | |
| | 54 | ✓ | | | | | | | | |
| | 55 | ✓ | | | | | | | | |
| | 56 | ✓ | | | | | | | | |
| | 57 | ✓ | | | | | | | | |
| | 58 | ✓ | | | | | | | | |
| | 59 | N | | | | | | | | |
| | 60 | N | | | | | | | | |

| Search Notes | Application/Control No. | Applicant(s)/Patent Under Reexamination |
|---|---|---|
| | 15398479 | FRASER ET AL. |
| | **Examiner** | **Art Unit** |
| | ELIZABETH GWARTNEY | 1791 |

## CPC- SEARCHED

| Symbol | Date | Examiner |
|---|---|---|
| A23L1/221, 231, 31427 (text limited) | 4/10/2017 | EG |

## CPC COMBINATION SETS - SEARCHED

| Symbol | Date | Examiner |
|---|---|---|
| | | |

## US CLASSIFICATION SEARCHED

| Class | Subclass | Date | Examiner |
|---|---|---|---|
| | | | |

## SEARCH NOTES

| Search Notes | Date | Examiner |
|---|---|---|
| PALM inventor search completed | 4/7/2017 | EG |
| Review of search history for 14/797,006 | 4/7/2017 | EG |
| Google/Google Scholar - composition of blood from cow/cattle, composition of cow muscle, hemoglobin content of cow blood and muscle | 4/7/2017 | EG |
| A23L1/221, 231, 31427 (text limited) | 4/10/2017 | EG |

## INTERFERENCE SEARCH

| US Class/ CPC Symbol | US Subclass / CPC Group | Date | Examiner |
|---|---|---|---|
| | | | |

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## U.S. Patent Documents

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 1. | 2001/0024677 | 9/27/2001 | Bringe | | | |
| | 2. | 2001/0049132 | 12/6/2001 | Kringelum et al. | | | |
| | 3. | 2003/0198700 | 10/23/2003 | Gruber | | | |
| | 4. | 2003/0224476 | 12/4/2003 | Chou | | | |
| | 5. | 2004/0151778 | 8/5/2004 | Richard et al. | | | |
| | 6. | 2004/0161513 | 8/19/2004 | Akashe et al. | | | |
| | 7. | 2005/0037111 | 2/17/2005 | Berry | | | |
| | 8. | 2006/0035003 | 2/16/2006 | McMindes et al. | | | |
| | 9. | 2006/0035006 | 2/16/2006 | McMindes et al. | | | |
| | 10. | 2006/0233721 | 10/19/2006 | Tamarkin et al. | | | |
| | 11. | 2007/0269567 | 11/22/2007 | McMindes et al. | | | |
| | 12. | 2007/0269571 | 11/22/2007 | Akita et al. | | | |
| | 13. | 2007/0269583 | 11/22/2007 | McMindes et al. | | | |
| | 14. | 2008/0226810 | 9/18/2008 | Passe et al. | | | |
| | 15. | 2008/0254168 | 10/16/2008 | Mueller et al. | | | |
| | 16. | 2008/0268112 | 10/30/2008 | Rolan et al. | | | |
| | 17. | 2008/0292749 | 11/27/2008 | Goodwins et al. | | | |
| | 18. | 2008/0299254 | 12/4/2008 | Kim et al. | | | |
| | 19. | 2009/0264520 | 10/22/2009 | Bhagat et al. | | | |
| | 20. | 2009/0274817 | 11/5/2009 | Yamaguchi et al. | | | |
| | 21. | 2010/0074998 | 3/25/2010 | Vega et al. | | | |
| | 22. | 2010/0136201 | 6/3/2010 | Bigeard et al. | | | |
| | 23. | 2010/0233347 | 9/16/2010 | Uhrhan | | | |
| | 24. | 2010/0249560 | 9/30/2010 | Levinson et al. | | | |
| | 25. | 2010/0281765 | 11/11/2010 | Schwartz | | | |
| | 26. | 2010/0311950 | 12/9/2010 | Kugitani | | | |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## U.S. Patent Documents

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 27. | 2011/0008502 | 1/13/2011 | Hosomi et al. | | | |
| | 28. | 2011/0064862 | 3/17/2011 | McCready et al | | | |
| | 29. | 2011/0065847 | 3/17/2011 | Miwa et al. | | | |
| | 30. | 2011/0081386 | 4/7/2011 | Guth et al. | | | |
| | 31. | 2011/0081435 | 4/7/2011 | Guth et al. | | | |
| | 32. | 2011/0117180 | 5/19/2011 | Yan et al. | | | |
| | 33. | 2011/0286992 | 11/24/2012 | Gruber et al. | | | |
| | 34. | 2011/0288389 | 11/24/2011 | Levinson et al. | | | |
| | 35. | 2012/0059150 | 3/8/2012 | Moloney et al. | | | |
| | 36. | 2012/0093994 | 4/19/2012 | Hsieh et al. | | | |
| | 37. | 2013/0004617 | 1/3/2013 | Zhang et al. | | | |
| | 38. | 2015/0366233 | 12/24/2015 | Brown et al. | | | |
| | 39. | 3,658,550 | 4/25/1972 | Hawley | | | |
| | 40. | 3,693,533 | 9/26/1972 | Liepa | | | |
| | 41. | 3,829,582 | 8/13/1974 | Guadagni et al. | | | |
| | 42. | 3,870,801 | 3/11/1975 | Tombs | | | |
| | 43. | 3,973,043 | 8/3/1976 | Lynn | | | |
| | 44. | 3,966,985 | 6/29/1976 | Jonas | | | |
| | 45. | 4,045,587 | 8/30/1977 | Katz et al. | | | |
| | 46. | 4,094,997 | 6/13/1978 | Aishima et al. | | | |
| | 47. | 4,218,487 | 8/19/1980 | Jaeggi | | | |
| | 48. | 4,435,438 | 3/6/1984 | Lehnhardt et al. | | | |
| | 49. | 4,604,290 | 8/5/1986 | Lee et al. | | | |
| | 50. | 4,678,676 | 7/7/1987 | Ishizuka et al. | | | |
| | 51. | 4,994,285 | 2/19/1991 | Hisano et al. | | | |
| | 52. | 5,055,310 | 10/18/1991 | Nonaka et al. | | | |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017

Sheet 3 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 53. | 5,264,239 | 11/23/1993 | Cornet et al. | | | |
| | 54. | 5,443,852 | 8/22/1995 | Shahidi et al. | | | |
| | 55. | 5,650,554 | 7/22/1997 | Moloney et al. | | | |
| | 56. | 5,753,295 | 5/19/1998 | Goldman | | | |
| | 57. | 5,807,601 | 9/15/1998 | Carpenter et al | | | |
| | 58. | 5,856,452 | 1/5/1999 | Moloney et al. | | | |
| | 59. | 5,922,392 | 7/13/1999 | Kelly et al. | | | |
| | 60. | 6,093,424 | 7/25/2000 | Han et al. | | | |
| | 61. | 6,146,645 | 11/14/2000 | Deckers et al. | | | |
| | 62. | 6,183,762 | 2/6/2001 | Deckers et al. | | | |
| | 63. | 6,210,742 | 4/3/2001 | Deckers et al. | | | |
| | 64. | 6,228,418 | 5/8/2001 | Gluck | | | |
| | 65. | 6,242,036 | 6/5/2001 | Han et al. | | | |
| | 66. | 6,287,620 | 9/11/2001 | Van Den Ouweland et al. | | | |
| | 67. | 6,372,234 | 4/16/2002 | Deckers et al. | | | |
| | 68. | 6,372,961 | 4/16/2002 | Tarczynski | | | |
| | 69. | 6,379,738 | 4/30/2002 | Dingman et al. | | | |
| | 70. | 6,383,531 | 5/7/2002 | Gottemoller | | | |
| | 71. | 6,399,135 | 6/4/2002 | Gottemoller | | | |
| | 72. | 6,413,569 | 7/2/2002 | Borders et al. | | | |
| | 73. | 6,416,797 | 7/9/2002 | Han et al. | | | |
| | 74. | 6,420,148 | 7/16/2002 | Yamaguchi | | | |
| | 75. | 6,495,184 | 12/17/2002 | Zheng et al. | | | |
| | 76. | 6,495,187 | 12/17/2002 | Borders et al. | | | |
| | 77. | 6,509,453 | 1/21/2003 | Moloney | | | |
| | 78. | 6,582,710 | 6/24/2003 | Deckers et al. | | | |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## U.S. Patent Documents

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | 79. | 6,596,287 | 7/22/2003 | Deckers et al. | | | |
| | 80. | 6,599,513 | 7/29/2003 | Deckers et al. | | | |
| | 81. | 6,692,788 | 2/17/2004 | Mottram et al. | | | |
| | 82. | 6,761,914 | 7/13/2004 | Deckers et al. | | | |
| | 83. | 6,908,634 | 6/21/2005 | Hwang | | | |
| | 84. | 6,936,749 | 8/30/2005 | Guy et al. | | | |
| | 85. | 7,052,879 | 5/30/2006 | Shaw et al. | | | |
| | 86. | 7,332,587 | 2/19/2008 | Moloney | | | |
| | 87. | 7,407,786 | 8/5/2008 | Giver et al. | | | |
| | 88. | 7,479,472 | 1/20/2009 | Harbury et al. | | | |
| | 89. | 7,585,645 | 9/8/2009 | Deckers et al. | | | |
| | 90. | 7,622,290 | 11/24/2009 | Brunstedt et al. | | | |
| | 91. | 7,666,618 | 2/23/2010 | Miasnikov et al. | | | |
| | 92. | 7,666,628 | 2/23/2010 | Moloney | | | |
| | 93. | 7,674,953 | 3/9/2010 | Mulet Salort et al. | | | |
| | 94. | 7,709,044 | 5/4/2010 | Ishimoto | | | |
| | 95. | 7,807,870 | 10/5/2010 | Geigenberger et al. | | | |
| | 96. | 7,931,925 | 4/26/2011 | Nielsen | | | |
| | 97. | 8,012,732 | 9/6/2011 | Brunstedt et al. | | | |
| | 98. | 8,021,695 | 9/20/2011 | Gruber et al. | | | |
| | 99. | 8,188,415 | 5/29/2012 | Kats et al. | | | |
| | 100. | 8,304,522 | 11/6/2012 | Kungitani | | | |
| | 101. | 8,597,694 | 12/3/2013 | Guth et al. | | | |
| | 102. | 9,011,949 | 4/21/2015 | Brown et al. | | | |

## Foreign Patent Documents or Published Foreign Patent Applications

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

## Foreign Patent Documents or Published Foreign Patent Applications

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | 103. | CN 101138405 | 3/12/2008 | CHINA | | | | |
| | 104. | CN 101541187A | 9/23/2009 | CHINA | | | | |
| | 105. | CN 101606574A | 12/23/2009 | CHINA | | | | |
| | 106. | CN 1252231A | 5/10/2000 | CHINA | | | | |
| | 107. | CN 1301811A | 7/4/2001 | CHINA | | | | |
| | 108. | CN 1407108A | 4/2/2003 | CHINA | | | | |
| | 109. | CN 1593223A | 3/16/2005 | CHINA | | | | |
| | 110. | CN 1634524A | 7/6/2005 | CHINA | | | | |
| | 111. | CN1466903 | 1/14/2004 | CHINA | | | | |
| | 112. | CN1557188 | 12/29/2004 | CHINA | | | | |
| | 113. | DE 102007061256 | 6/25/2009 | GERMANY | | | | |
| | 114. | DE 202011002097 | 3/24/2011 | GERMANY | | | | |
| | 115. | EP 0500132 | 8/26/1992 | EPO | | | | |
| | 116. | EP 0680751 | 11/24/2004 | EPO | | | | |
| | 117. | EP 0815736 | 1/7/1998 | EPO | | | | |
| | 118. | EP 1166653 | 1/2/2002 | EPO | | | | |
| | 119. | EP 1254601 | 11/6/2002 | EPO | | | | |
| | 120. | EP 1361264 | 4/18/2007 | EPO | | | | |
| | 121. | EP 1529444 | 5/11/2005 | EPO | | | | |
| | 122. | EP 1952695 | 8/6/2008 | EPO | | | | |
| | 123. | EP 2138052 | 12/30/2009 | EPO | | | | |
| | 124. | EP1759593 | 3/7/2007 | EPO | | | | |
| | 125. | GB 2016255 | 9/26/1979 | GB | | | | |
| | 126. | JP 2009171877 | 8/6/2009 | JAPAN | | | | |
| | 127. | JP 2011000073 | 1/6/2011 | JAPAN | | | | |
| | 128. | JP 52156962 | 12/27/1977 | JAPAN | | | | |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | 129. | JP S54122766 | 9/22/1979 | JAPAN | | | | |
| | 130. | JP S573338 | 01/21/1982 | JAPAN | | | | |
| | 131. | WO 1993/025697 | 12/23/1993 | WIPO | | | | |
| | 132. | WO 1994/017673 | 8/18/1994 | WIPO | | | | |
| | 133. | WO 1996/017981 | 6/13/1996 | WIPO | | | | |
| | 134. | WO 1997/01961 | 1/23/1997 | WIPO | | | | |
| | 135. | WO 1998/012913 | 4/2/1998 | WIPO | | | | |
| | 136. | WO 1998/053698 | 12/3/1998 | WIPO | | | | |
| | 137. | WO 2001/022829 | 4/5/2001 | WIPO | | | | |
| | 138. | WO 2001/022830 | 4/5/2001 | WIPO | | | | |
| | 139. | WO 2003/070172 | 8/28/2003 | WIPO | | | | |
| | 140. | WO 2004/113543 | 12/29/2004 | WIPO | | | | |
| | 141. | WO 2005/013713 | 2/17/2005 | WIPO | | | | |
| | 142. | WO 2005/097059 | 10/20/2005 | WIPO | | | | |
| | 143. | WO 2006/042608 | 4/27/2006 | WIPO | | | | |
| | 144. | WO 2007/060288 | 5/31/2007 | WIPO | | | | |
| | 145. | WO 2007/115899 | 10/18/2007 | WIPO | | | | |
| | 146. | WO 2007/118751 | 12/21/2007 | WIPO | | | | |
| | 147. | WO 2007/137125 | 11/29/2007 | WIPO | | | | |
| | 148. | WO 2008/017499 | 2/14/2008 | WIPO | | | | |
| | 149. | WO 2008/030089 | 3/13/2008 | WIPO | | | | |
| | 150. | WO 2008/083117 | 7/10/2008 | WIPO | | | | |
| | 151. | WO 2009/060678 | 5/14/2009 | WIPO | | | | |
| | 152. | WO 2010/101625 | 9/10/2010 | WIPO | | | | |
| | 153. | WO 2012/106751 | 8/16/2012 | WIPO | | | | |
| | 154. | WO 2012/110797 | 8/23/2012 | WIPO | | | | |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017

Sheet 7 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|
| | 155. | WO 2012/116703 | 9/7/2012 | WIPO | | | | |
| | 156. | WO 2013/010037 | 1/17/2013 | WIPO | | | | |
| | 157. | WO 2013/010042 | 1/17/2013 | WIPO | | | | |
| | 158. | WO 2013/138793 | 9/19/2013 | WIPO | | | | |

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| | 159. | "Heterlolgous," Merriam-Webster Dictionary, retrieved on 9/10/2015, http://www.merriam-webster.com/dictionary/heterologous, 1 page |
| | 160. | "Rethink Meat," Presented at the 6th Annual Sustainable Innovation Forum, Paris, France, December 7-8, 2015, retrieved on 2/1/2016, https://amp.twimg.com/v/7c7f7084-b173-42cb-bc12-723f35994dff, 1 page (Video Submission) |
| | 161. | "Silicon Valley gets a taste for food," The Economist Technology Quarterly, March 7, 2015, http://cdn.static-economist.com/sites/default/files/sponsorships/accenture_tq_march2015/20150307_tq_mailout.pdf, pages 11-13 |
| | 162. | "Veggie burgers that look, taste, and bleed like real meat," CBS News, August 9, 2016, retrieved August 25, 2016 <http://www.cbsnews.com/news/food-trend-veggie-burgers-that-look-bleed-taste-like-real-meat/>, 4 pages |
| | 163. | "Watch Momofuku Cook Impossible Foods' Plant-Based Burger that 'Bleeds'," Vice, July 27, 2016, retrieved August 25, 2016, <https://munchies.vice.com/en/videos/watch-momofuku-cook-impossible-foods-plant-based-burger-that-bleeds>, 3 pages |
| | 164. | "Acidified Milk Products and Protein Stabilisation," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 15 pages |
| | 165. | "Ice Cream and Ice Cream Desserts," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 5 pages |
| | 166. | "Innovation at Its Best: 5 Years of Food Valley Awards," Food Valley, retrieved on 3/7/2014, http://www.foodvalley.nl/English/Afbeeldingen/FVAjubileumuitgave/Innovation%20at%20Its%20Best%20-%205%20Years%20of%20Food%20Valley%20Awards.pdf, 51 pages |
| | 167. | "Low Methylester Amidated Pectins," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 13 pages |
| | 168. | "Stabilisation of Whey and Whey Mix Products with Pectin," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 6 Pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 169. | "Texturising of Fermented Milk Products," Herbstreith & Fox, retrieved on 3/3/2014, http://www.herbstreith-fox.de/en/informative-literature/informative-literature-from-rd-and-tech-application.html, 6 pages |
| | 170. | Asgar et al., "Nonmeat Protein Alternatives as Meat Extenders and Meat Analogs," Comprehensive Reviews in Food Science and Food Safety, 2010, 9:513-529 |
| | 171. | Australian Patent Examination Report No. 1 in Australian Application No. 2012281064, dated January 25, 2016, 5 pages |
| | 172. | Australian Patent Examination Report No. 1 in Australian Application No. 2012281069, dated September 25, 2015, 5 pages |
| | 173. | Baek, "Process Flavors," Handbook of Meat, Poultry and Seafood Quality, Second Edition, 2012, Chapter 7, 91-104 |
| | 174. | Battaglia et al., "The Enigmatic LEA Proteins and Other HydroPhilins1[W]," Plant Physiology, September 2008, 148:6-24 |
| | 175. | Belitz et al., "Aroma Compounds," Food Chemistry, Springer 2009, pp. 340-402 |
| | 176. | Belitz et al., Food Chemistry, 3rd revised edition. Springer-Verlag, Berlin (2006), p. 368 |
| | 177. | Beuchat et al., "Fermentation of Peanut Milk with Lactobacillus bulgaricus and L. acidophilus," J. Food Sci, 1978, 43:1109-1112 |
| | 178. | Beyond Better Order page and Nutritional Facts, retrieved on 2/6/2014, http://www.beyond-better.com/order.html, 8 pages |
| | 179. | Beyond Meat, posted on or before 2/24/2001, accessed 1/7/2014, http://beyondmeat.com/, 2 pages |
| | 180. | Boca Bruschetta Tomato Basil Parmesan Veggie Patties Package Ingredients, posted on or before 7/22/2008, accessed on 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928360103, 1 page |
| | 181. | Boca Flame Grilled Meatless Burgers Package Ingredients, posted on or before 7/14/2008, accessed on 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928367321, 1 page |
| | 182. | Boca Original Meatless Chik'n Nuggets Package Ingredients, posted on or before7/22/2008, accessed 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928360012, 1 page |
| | 183. | Boca Original Vegan Meatless Burgers Package Ingredients, posted on or before 7/14/2008, accessed 1/7/2014, http://www.bocaburger.com/products/nutrition-info.aspx?product=5928333445, 1 page |
| | 184. | Boral and Bohidar , "Effect Of Ionic Strength On Surface-Selective Patch Binding-Induced Phase Separation And Coacervation In Similarly Charged Gelatin-Agar Molecular Systems," Journal of Physical Chemistry B, 2010, 114(37): 12027-35 |
| | 185. | Bradshaw, "Food 2.0: the future of what we eat," FT Magazine, October 31, 2014, retrieved on 11/11/2014, http://www.ft.com/cms/s/2/bfa6fca0-5fbb-11e4-8c27-00144feabdc0.html#axzz3InGaCIdL, 6 pages |
| | 186. | Brewer, "The Chemistry of Beef Flavor," December, 2006, retrieved on August 30, 2016, <http://beefresearch.org/CMDocs/BeefResearch/The%20Chemistry%20of%20Beef%20Flavor.pdf>, 16 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 187. | Brooks et al., "Prediction of beef flavor by precursor and volatile compounds Principal Investigators: Funded by The Beef Checkoff," Texas Tech University, May 31, 2012, retreived August 30, 2016, <http://www.beefresearch.org/CMDocs/BeefResearch/PE_Project_Summaries_FY11Prediction_of_beef_flavor.pdf> |
| | 188. | Bunge et al., "Quest Heats up for Alternatives to Beef," The Wall Street Journal, Business News, November 4, 2016, page B5 |
| | 189. | Burdock, "Fenaroli's handbook of flavor ingredients," CRC press, 17 pages (2016) |
| | 190. | Bute Island Foods, "Sheese," posted on or before 12/5/2006, retrieved on 2/6/2014, http://www.buteisland.com/a_sheese_home.htm, 26 pages |
| | 191. | Cadwallader and Macleod, "16 Instrumental methods for analyzing the flavor of muscle foods," Flavor of Meat, Meat Products and Seafoods, 18 pages (1998) |
| | 192. | Calkins et al., "A fresh look at meat flavor," Meat Science, 77(1):63-80 (2007) |
| | 193. | Chamlee, "Why Do People Want Veggie Burgers That Bleed?," Eater, July 25, 2016, retrieved August 25, 2016, <http://www.eater.com/2016/7/25/12270698/lab-grown-meat-beyond-burger-impossible-foods>, 11 pages |
| | 194. | Chaudhari et al., "The cell biology of taste," 190(3):285-296 (August 2010) |
| | 195. | Chen et al., "Effect of Urea on Volatile Generation from Maillard Reaction of Cysteine and Ribose," J. Agric. Food Chem., 48:3512-3516 (2000) |
| | 196. | Chen et al., "Influence of DNA on Volatile Generation from Maillard Reaction of Cysteine and Ribose," Nutraceutical Beverages, American Chemical Society, pp. 427-442 (December 2003) |
| | 197. | Chicago Vegan Foods, accessed on 1/7/2014, http://chicagoveganfoods.com/products/teese-vegan-cheese/, 8 pages |
| | 198. | Chinese Second Office Action in Chinese Application No. 201280041099.9, dated 10/8/2015, 15 pages (with translation) |
| | 199. | Clare et al., "Effects of Transglutaminase Catalysis on the Functional and Immunoglobulin Binding Properties of Peanut Flour Dispersions Containing Casein," J. Agric. Food Chem., 2008, 56(22):10913-10921 |
| | 200. | Connelly and Piper, "Person of the Year: Tal Ronnen," VegNews, November/December 2013, 29-32 |
| | 201. | Dai, "David Chang Adds Plant Based 'Impossible Burger' to Nishi Menu," July 26, 2016, retrieved July 27, 2016 <http://ny.eater.com/2016/7/26/12277310/david-chang-impossible-burger-nishi>, 6 pages |
| | 202. | Daiya, Deliciously Dairy Free, "Say Cheese, Dairy-Free cheesy deliciousness," posted on or before 1/26/2010, accessed 1/7/2014, http://www.daiyafoods.com, 6 pages |
| | 203. | Davis et al., "Some Rheological Properties of Aqueous Peanut Flour Dispersions," J. Texture Studies, 2007, 38:253-272 |
| | 204. | Deliciously Healthy Nacheez, Products and Nutrition Facts, posted on or before 1/23/2011, retrieved on 2/7/2014, http://nacheez.com/, 9 pages |
| | 205. | Dixie Diner's Club, Cheese (Not!) Sauce Nutrition Facts, posted on or before 9/3/2009, retrieved on 2/7/2014, http://www.dixiediner.com/cheese-notÂ™-sauce-regular-cheese-p-69.html, 2 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 206. | D'Onfro, "I tried the plant-based meat that Google wanted to buy and I never want to eat a 'real' hamburger again" Business Insider, June 12, 2016, retrieved June 14, 2016, <http://www.businessinsider.com/impossible-burgers-taste-test-2016-6>, 14 pages |
| | 207. | Donnelly, "Meet the Impossible Burget: It Looks and Taskes Like the Real Thing But Is Totally Meat-Free," Vogue, August 1, 2016, retreived August 25, 2016 <http://www.vogue.com/13462891/impossible-burger-meat-free-vegan-david-chang/>, 6 pages |
| | 208. | Door 86 Vegan Cheese, Discover a New World of Vegan Cheese and Menu, posted on or before 12/5/2013, retrieved 2/7/2014, http://door86vegancheese.wix.com/door-86-vegan-cheese#, 14 pages |
| | 209. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Brazil Nut Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-brazil.html, 1 page |
| | 210. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Crystal Algae Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-crystal.html, 1 page |
| | 211. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Dulse Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-dulse.html, 1 page |
| | 212. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew & Hemp Seeds Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-hemp.html, 1 page |
| | 213. | Dr. Cow, Natural Living & Organic Foods, "Aged Cashew Nut Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-cashew-nut-cheese.html, 1 page |
| | 214. | Dr. Cow, Natural Living & Organic Foods, "Aged Macadamia & Hemp Seeds Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-macadam-hemp.html, 1 page |
| | 215. | Dr. Cow, Natural Living & Organic Foods, "Aged Macadamia Nut Cheese," posted on or before 9/22/2008, accessed 2/7/2014, http://www.dr-cow.com/products/aged-macadam-nut-cheese.html, 1 page |
| | 216. | Dr. Cow, Natural Living & Organic Foods, "Cashew Nut Cream Cheese," posted on or before 9/22/2008, accessed 1/7/2014, http://www.dr-cow.com/products/cashew-nut-cream-cheese.html, 1 page |
| | 217. | Duane, "Engineering the Future of Artisanal Vegan Cheese," Food & Wine, November 2013, http://www.foodandwine.com/articles/engineering-the-future-of-artisanal-vegan-cheese, 5 pages |
| | 218. | Ellis et al., "Structure of ferric soybean leghemoglobin a nicotinate at 2.3 A resolution," Acta Crystallographica, May 1997, Section D, 53(3):302-310 |
| | 219. | Elmore et al., "Effect of the Polyunsaturated Fatty Acid Composition of Beef Muscle on the Profile of Aroma Volatiles," J. Agric. Food Chem. 47:1619-1625 (1999) |
| | 220. | Etienne, "Eating the plant-derived Impossible Burget cooked by Momofuku's David Chang," Tech Crunch, July 26, 2016, retrieved August 25, 2016, <https://techcrunch.com/2016/07/26/eating-the-plant-derived-impossible-burger-cooked-by-momofukus-david-chang/>, 9 pages |
| | 221. | European Search Report (Supplementary) in European Application No. 12810661.4, dated March 12, 2015, 14 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 222. | European Search Report (Supplementary) in European Application No. 12811683.7, dated March 12, 2015, 9 pages |
| | 223. | European Search Report for International Application No. EP 14737766, dated July 15, 2016, 11 pages |
| | 224. | Fantastic World Foods, "Fantastic Foods Nature's Burger (Meatless Burger Mix)," posted on or before 1/6/2009, accessed on 1/7/2014, http://fantasticfoods.elsstore.com/view/product/?id=8715&cid=1967, 2 pages |
| | 225. | Felt, "Raw Vegan Almond Ricotta Cheese," FeedYourSkull, March 12, 2012, https://feedyourskull.com/2012/03/12/raw-vegan-almond-ricotta-cheese/, 15 pages |
| | 226. | Follow Your Heart Homepage, posted on or before 11/28/1999, accessed 1/7/2014, http://www.followyourheart.com, 3 pages |
| | 227. | Follow Your Heart, Products and Nutrition Facts, posted on or before 11/28/1999, accessed 2/7/2014, http://www.followyourheart.com/products/, 26 pages |
| | 228. | Foo, "Beef and Scallop Stir-Fry," Food & Wine, July 2001, retrieved on 9/10/2015, http://www.foodandwine.com/recipes/beef-and-scallop-stir-fry/print, 3 pages |
| | 229. | Food for Lovers, Vegan Queso Original & Vegan Queso Mild, posted on or before 10/27/2011, retrieved 2/7/2014, http://www.foodforlovers.com/products, 3 pages |
| | 230. | Free & Easy Dairy Free Cheese Flavour Sauce Mix, Holland & Barrett, posted on or before 6/22/2013, retrieved 2/7/2014, http://www.hollandandbarrett.com/pages/product_detail.asp?pid=2686, 2 pages |
| | 231. | Fromson, "The Race to Build a Fake-Meat Burger That Just Might Save the World, Free the cows!" New York Magazine, June 1-7, 2015, 46-48 |
| | 232. | Galaxy Foods Vegan Soy Grated Parmesan, ShopRite, retrieved 2/7/2014, http://www.shoprite.com/pd/Galaxy-Nutritional-Foods/Vegan-Grated-Soy-Topping-Parmesan-Flavor/4-oz/077172640006/, 6 pages |
| | 233. | Gardein The Ultimate Beefless Burger Package Ingredients, posted on or before 2013, accessed 1/7/2014, http://gardein.com/products/beefless-burger/, 12 pages |
| | 234. | Gardenburger The Original Veggie Burger Package Ingredients, posted on or before 10/5/2008, accessed 1/7/2014, http://www.gardenburger.com/product.aspx?id=11630, 1 page |
| | 235. | GenBank Accession No. AFK42304.1, "unknown [Medicago truncatula], May 25, 2012, 1 page |
| | 236. | GHARST, "Biochemical and Rheological Characteristics of Peanut Proteins Crosslinked with Microbial Transglutaminase," A dissertation submitted to the Graduate Faculty of North Carolina State University, Raleigh NC, 2007, 149 pages |
| | 237. | Gharst, "Effects of Transglutaminase Catalysis on the Functional and Immunoglobulin Binding Properties of Peanut Flour Dispersions Containing Casein," J. Agric. Food Chem., 2008, 56:10913-10921 |
| | 238. | Gharst, "The Effect of Transglutaminase Crosslinking on the Rheological Characteristics of Heated Peanut Flour Dispersions," J. Food Sci., 2007, 72(7):C369-C375 |
| | 239. | Gilbert et al., "The revolutionary meatless burger from Impossible Foods is perfect for begtarians and carnivores alike," Tech Insider, August 4, 2016, retrieved on August 25, 2016, <http://www.techinsider.io/the-impossible-foods-burger-review-vegetarian-2016-8>, 9 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017

Sheet 12 of 18

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 240. | Go Veggie!, "O% Dairy. 100% Yum.," posted on or before 2013, accessed 1/7/2014, http://goveggiefoods.com/our-products/dairy-free-cheese-alternative-products/, 1 page |
| | 241. | Go Veggie!, Dairy Free Products and Nutrition Facts, posted on or before 2013, accessed 2/7/2014, http://goveggiefoods.com/our-products/dairy-free-cheese-alternative-products/, 13 pages |
| | 242. | Gordinier, "Masters of Disguise Among Meatless Burgers," The New York Times, 3/22/2011, accessed 1/7/2014, http://www.nytimes.com/2011/03/23/dining/23meatless.html?pagewanted=all&_r=0, 5 pages |
| | 243. | Grigorakis et al., "Organoleptic and volatile aroma compounds comparison of wild and cultured gilthead sea bream (*Sparus aurata*): sensory differences and possible chemical basis," Aquaculture 225:109-119 (2003) |
| | 244. | Grobart, "Making a Steak Without a Cow," Bloomberg Technology, June 21, 2016, retrieved June 23, 2016 <http://www.bloomberg.com/news/articles/2016-06-21/making-a-steak-without-the-cow>, 2 pages |
| | 245. | Grosch, "Evaluation of the Key Odorants of Food by Dilution Experiments, Aroma Models and Omission," Chem. Senses 26:533-545 (June 2001) |
| | 246. | Hanlon, "Fake Meat: is science fiction on the verge of becoming fact?," The Guardian, June 22, 2012, http://www.theguardian.com/science/2012/jun/22/fake-meat-scientific-breakthroughs-research, 7 pages |
| | 247. | Hannah, "A fermented feast," Bittersweet, retrieved on November 3, 2016, retrieved from <https://bittersweetblog.com/2010/06/09/a-fermented-feast/>, 2 pages |
| | 248. | Heller, "Barbecued Soybeans," Vegetarian Soybean Recipes, Mother Earth News, January/February 1985, http://motherearthnews.com/real-food/vegetarian-soybean-recipes-zmaz85asie.aspx |
| | 249. | Heme Protein Database, "Welcome to the Heme Protein Database," posted on or before 4/14/2013, accessed 12/18/2013, http://hemeprotein.info/heme.php, 1 page |
| | 250. | Heritage Health Food Creamy Veeta Cheeze Sauce Mix, Vegan Essentials, posted on or before 8/13/2013, retrieved 2/7/2014, http://store.veganessentials.com/creamy-veeta-cheeze-sauce-mix-by-heritage-health-food-p3945.aspx, 1 page |
| | 251. | Herper, "Mission Impossible Burger: Tasting The Fake Meat That Wants To Save The World," Forbes, July 28, 2016, retrieved on August 25, 2016, <http://www.forbes.com/sites/matthewherper/2016/07/28/mission-impossible-burger-tasting-the-fake-meat-that-wants-to-save-the-world/#57781d823c43>, 6 pages |
| | 252. | Herper, "Drop that Burger," Forbes Online, November 12, 2009, http://www.forbes.com/forbes/2009/1130/thought-leaders-mcdonalds-global-warming-drop-that-burger.html, 4 pages |
| | 253. | Homma et al. "Cheese-like food production from various nuts," Food Preservation Science, Japan 2009, ABSTRACT |
| | 254. | Hoshaw, "Silicon Valley's Bloody Plant Burger Smells, Tastes and Sizzles Like Meat" the salt, June 21, 2016, retrieved June 21, 2016 <http://www.npr.org/sections/thesalt/2016/06/21/482322571/silicon-valley-s-bloody-plant-burger-smells-tastes-and-sizzles-like-meat>, 8 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 255. | Hui et al., "Handbook of meat and meat processing," CRC Press, 2012, retrieved on December 05, 2016, retrieved from <https://www.crcpress.com/Handbook-of-Meat-and-Meat-Processing-Second-Edition/Hui/p/book/9781439836835>, 3 pages |
| | 256. | International Preliminary Report on Patentability in International Application No. PCT/US14/11347, dated July 14, 2015, 10 pages |
| | 257. | International Search Report and Written Opinion in International Application No. PCT/US14/11347, dated July 3, 2014, 20 pages |
| | 258. | Jamieson, "Iroquois Stew with Beef, Chicken and Pork," Epicurious, November 1995, retrieved on 9/10/2015, http://www.epicurious.com/recipes/food/printerfriendly/iroquois-stew-with-beef-chicken-and-pork-865, 2 pages |
| | 259. | Jensen, "Comparative Analysis of Autoxidation of Haemoglobin," J. Experimental Biology, 2001, 204:2029-2033 |
| | 260. | Ju and Kilara, "Textural Properties of Cold-set Gels Induced from Heat-denatured Whey Protein Isolates," J. Food Science, 1998, 63(2): 288-292 |
| | 261. | Jublot et al., "Quantitation of sulphur aroma compounds in maillard model reaction systems of different composition," Expression of Multidisciplinary Flavour Science, 4 pages (2010) |
| | 262. | Kanani, "The Future of Meat is Meatless, Just as Tasty, And About to Change the World," Forbes, 3/6/2014, retrieved on 9/11/2015, http://www.forbes.com/sites/rahimkanani/2014/03/06/the-future-of-meat-is-meatless-just-as-tasty-and-about-to-change-the-world/, 8 pages |
| | 263. | Karahadian et al., "Action of Tocopherol-Type Compounds in Directing Reactions Forming Flavor Compounds in Autoxidizing Fish Oils," J. Amer. Oil Chem. Soc., 66:1302-8 (1989) |
| | 264. | Kerscher et al., "Quantification of 2-Methyl-3-furnathiol, 2-Furfurylthiol, 3-Mercapto-2-pentanone in Heated Meat," J. Agric. Food Chem. 46:1954-1958 (1996) |
| | 265. | Kerth and Miller, "Beef flavor: a review from chemistry to consumer," White Paper: Product Quality, Texas A&M University Dept of Animal Sciences, 25 pages (2013) |
| | 266. | Khan et al., "Meat flavor precursors and factors influencing flavor precursors- A systematic review," Meat Science, 110:278-284 (December 2010) |
| | 267. | Kraft American Singles Package Ingredients, posted on or before 6/27/2012, accessed on 1/7/2014, http://www.kraftrecipes.com/Products/ProductInfoDisplay.aspx?SiteId=1&Product=2100060473, 1 page |
| | 268. | Kummer, "The Problem with Fake Meat," MIT Technology Review, March 31, 2015, retrieved April 20, 2016, <https://www.technologyreview.com/s/536296/the-problem-with-fake-meat/>, 11 pages |
| | 269. | Kung et al., "Tobacco as a Potential Food Source and Smoke Material: Nutritional Evaluation of Tobacco Leaf Protein," J. Food Sci., 1980, 45(2):320-322, 327 |
| | 270. | Lane et al., "The Variety of Odors Produced in Maillard Model Systems and How They are Influenced by Reaction Conditions," The Maillard Reaction in Foods and Nutrition, American Chemical Society, pp. 141-158 (April 1983) |
| | 271. | Leahy Gardens Vegan & Delicious, Macaroni & Cheese and Cheese Flavored Sauce Mix Product and Nutrition Facts, posted on or before 2/8/2010, retrieved 2/7/2014, http://www.leaheyfoods.com/products/MacCheese.aspx, 3 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 272. | Leduc et al., "Differentiation of fresh and frozen/thawed fish, European sea bass (Dicentrarchus labrax), gilthead seabream (Sparus aurata), cod (Gadus morhua) and salmon (Salmo salar), using volatile compounds by SPME/GC/MS," J. Sci. Food Agric., 92:2560-80 (2012) |
| | 273. | Lisanatti Foods, Vegan Cheeze Products and Nutrition Facts, posted on or before 3/26/2013, retrieved 2/7/2014, http://www.lisanatti.com/index.php?option=com_zoo&view=category&layout=category&Itemid=22, 5 pages |
| | 274. | Liu et al., "Intermolecular Interactions During Complex Coacervation Of Pea Protein Isolate And Gum Arabic," Journal of Agricultural and Food Chemistry, 2010, 58:552-556 |
| | 275. | Lopez, "We just tried the 'Impossible Burger' - the meatless burger NYC has been waiting for," Business Insider, July 27, 2016, retrieved on August 25, 2016, <http://www.businessinsider.com/what-the-impossible-burger-tastes-like-2016-7>, 5 pages |
| | 276. | Lugay and Kim, "Freeze alignment: A novel method for protein texturization," Utilization of Protein Resources, 1981, Page 177-187 |
| | 277. | Luteness, "The Richest Source of Protein," MOSAIC, May/June 1979, 39-45 |
| | 278. | Maltais et al., "Formation of Soy Protein Isolate Cold-Set Gels: Proteins and Salt Effects," J. Food Science, 2005, 70 (1): C67-C73 |
| | 279. | Marshall et al., "We Tried the "Bleeding" Vegetarian Burger And It Was Actually Good," July 27, 2016, retrieved July 28, 2016 <https://www.buzzfeed.com/chelseamarshall/bleeding-vegetable-burger?utm_term=.jaa03Kyo7#.ogV0m7MAW>, 10 pages |
| | 280. | McGorrin, "Advances in Dairy Flavor Chemistry," FoodFlavors and Chemistry: Advances of the New Millennium, Spanier, A. M.; Shahidi,F.; Parliment, T. H.; Mussinan, C. J.; Ho, C.-T.; Contis, E. T., Eds., RoyalSociety of Chemistry, Cambridge, pp. 67-84 (2001) |
| | 281. | McGorrin, "Character-impact flavor and off-flavor compounds in foods," Flavor, Fragrance, and Odor Analysis, 2nd, 207-262 (2012). |
| | 282. | McGorrin, "The significance of volatile sulfur compounds in food flavors," Volatile sulfur compounds in food 1068, 29 pages (2011). |
| | 283. | Moon et al., "Odour-active components of simulated beef flavour analyzed by solid phase microextraction and gas chromatography-mass spectrometry and -olfactometry," Food Research International, 39:294-308 (April 2006) |
| | 284. | Morita, "Comparison of aroma characteristics of 16 fish species by sensory evaluation and gas chromatographic analysis," J. Sci. Food Agric., 83:289-297 (2003) |
| | 285. | Morningstar Farms Garden Veggie Patties Package Ingredients, posted on or before 6/26/2013, accessed 1/7/2014, https://www.morningstarfarms.com/products/burgers/garden-veggie-patties, 6 pages |
| | 286. | Mottram et al., "Formation of Sulfer Aroma Compounds in Reaction Mixtures Containing Cysteine and Three Different Forms of Ribose," J. Agric. Food Chem., 50:4080-4086 (2002) |
| | 287. | Mottram, "Flavour formation in meat and meat products: a review," Food Chemistry, 62(4):415-24 (August 1998) |
| | 288. | Mottram,"An Overview of the Contribution of Sulfur-Containing Compounds to the Aroma in Heated Foods," Heteroatomic Aroma Compounds, American Chemical Society, pp. 73-92 (August 2002) |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 289. | Nacho Mom's Vegan Queso, Products and Nutrition Facts, posted on or before 9/20/2010, retrieved on 2/7/2014, http://fatgoblin.com/Home.html, 6 pages |
| | 290. | Nielson, Introduction to the Chemical Analysis of Foods, Jones & Bartlett Publishers, 1994 |
| | 291. | Nutty Cow Nut Cheeses, Products and Nutrition Facts, posted on or before 7/23/2012, retrieved 2/7/2014, http://www.nuttycow.com/, 6 pages |
| | 292. | Parmela Parmesan Style Aged Nut Cheese, Product and Nutrition Facts, 2012, retrieved 2/7/2014, http://www.parmelafoods.com/your-health.html, 4 pages |
| | 293. | Peace Cheese 100% Plant-based Cheese Alternative, Product and Nutrition Facts, posted on or before 6/6/2012, retrieved 2/7/2014, http://www.ilovepeacecheese.com/#/products/4571642621, 3 pages |
| | 294. | Proulx et al., "Iron Bioavailability of Hemoglobin from Soy Root Nodules Using a Caco-2 Cell Culture Model," J. Agricultural and Food Chemistry, February 2006, 54(4):1519-1522 |
| | 295. | Proulx, "Diversified strategies for improving iron bioavalibility of maize," Iowa State University - Retrospective Theses and Dissertations, 2007 retrieved on September 19, 2016, retreived from <http://lib.dr.iastate.edu/rtd/15852/>, 144 pages |
| | 296. | Punk Rawk Labs: an ongoing experiment in optimal health, Nut Milk Cheese Products, posted on or before 6/8/2011, retrieved 2/7/2014, http://www.punkrawklabs.net/cheeses.html, 4 pages |
| | 297. | Ramos et al., "What is Masa? - Ingredient Intelligence," The Kitchn, retrieved on 12/01/2016, http://www.thekitchn.com/whats-the-difference-between-masa-and-masa-harina-226434, 5 pages |
| | 298. | Reedy et al., "Development of a heme protein structure-electrochemical function database," Nucleic Acids Research, 2008, 36:307-313 |
| | 299. | Richins et al., "Effect of Iron Source on Color and Appearance of Micronutrient-Fortified Corn Flour Toritallas," Cereal Chem., 85:561-5 (2008) |
| | 300. | Road's End Organics, Cheese Sauce Mix Products and Nutrition Facts, posted on or before 10/28/2009, retrieved 2/7/2014, http://www.edwardandsons.com/reo_shop_chreese.itml, 6 pages |
| | 301. | Road's End Organics, Mac & Chreese Products and Nutrition Facts, posted on or before 10/28/2009, retrieved 2/7/2014, http://www.edwardandsons.com/reo_shop_pastas.itml, 7 pages |
| | 302. | Rochet and Chaintreau, "Carbonyl Odorants Contributing to the In-Oven Roast Beef Top Note," J. Agric. Food Chem., 53:9578-9585 (November 2005) |
| | 303. | Rowe, "Chemistry and technology of flavors and fragrances," Oxford:: Blackwell; 2005, 351 pages |
| | 304. | Rusli, "The Secret of These New Veggie Burgers: Plant Blood," The Wall Street Journal, October 7, 2014, retrieved on 10/9/2014, http://online.wsj.com/articles/the-secret-of-these-new-veggie-burgers-plant-blood-1412725267, 5 pages |
| | 305. | Schieberle et al., "Characterization of Key Odorants in Dry-Heated Cysteine-Carbohydrate Mixtures: Comparison with Aqueous Reaction Systems," Flavor Analysis, American Chemical Society, pp. 320-330 (Setpember 1998) |
| | 306. | Schwartz, "Meet the Silicon Valley-Backed Vegan Cheese That You Might Actually Eat," Fast Company, February 26, 2014, retrieved 9/11/2015, http://www.fastcoexist.com/3025648/meet-the-silicon-valley-backed-vegan-cheese-that-you-might-actually-eat, 6 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 307. | Segner, "Meatless burger made possible with local effort," July 29, 2016, retrieved August 1, 2016 <http://www.southernminn.com/owatonna_peoples_press/news/article_3d414149-1040-534d-b1af-bf4f8c486788.html>, 5 pages |
| | 308. | Selli et al., "Odour-active and off-odour components in rainbow trout (Oncorhynchus mykiss) extracts obtained by microwave assisted distillation-solvent extraction," Food Chemistry, 114:317-322 (2009) |
| | 309. | Shahidi et al., "Meat flavor volatiles: A review of the composition, techniques of analysis, and sensory evaluation," CRC Critical Reviews in Food Science and Nutrition, 24(2):141-243 (January 1986) |
| | 310. | Shi et al., "Identification of characteristic flavour precursors from enzymatic hydrolysis-mild thermal oxidation tallow by descriptive sensory analysis and gas chromatography–olfactometry and partial least squares regression," Journal of Chromatography B, 913-914:96-76 (January 2013) |
| | 311. | Shu et al., "Parameter Effects on the Thermal Reaction of Cystine and 2,5-Dimethyl-4-hydroxy-3(2*H*)-furanone," Thermal Generation of Aromas, American Chemical Society, pp. 229-241 (October 1989) |
| | 312. | Sister River Foods Parma!, Products and Nutrition Facts, Posted on or before 6/2/2012, retrieved 2/11/2014, http://www.veganstore.com/product/parma-vegan-parmesan/vegan-cheese-and-dairy-alternatives, 6 pages |
| | 313. | Soller, "The Impossible Burger is Ready for Its (Meatless) Close-Up," The Wall Street Journal, June 14, 2016, retrieved June 21, 2016 <http://www.wsj.com/articles/the-impossible-burger-is-ready-for-its-meatless-close-up-1465912323>, 8 pages |
| | 314. | Song, et al., "Contribution of oxidized tallow to aroma characteristics of beeflike process flavour assessed by gas chromatography-mass spectrometry and partial least squares regression," Journal of Chromatography A, 1254:115-124 (September 2012) |
| | 315. | Soy Kaas, Products, posted on or before 1/20/2011, retrieved 2/11/2014, http://www.soykaas.com/products, 1 page |
| | 316. | Soyco Cheese Products, Natural Pantry, retrieved 2/11/2014, http://www.natural-pantry.com/search_results.asp?ct=All&site_search_qu=soyco&storeID=D92VLAQVMPDL9L5UHTS2WLU67NADEHUA, 10 pages |
| | 317. | Soymage Cheese Products, Good Earth Natural Foods, retrieved on 2/11/2014, http://www.goodearthnaturalfoods.com/shop/brand2.asp?storeID=PJ102JRNHNGT8G0QMPEQ7LDC7GX6C2W2&alpha=S&brand=Soymage&brand_id=805, 6 pages |
| | 318. | Spence et al., "Multisensory Flavor Perception," Cell 161: 24-35 (2015) |
| | 319. | Ste Martaen Cheese, Products and Nutrition Facts, posted on or before 5/28/2009, retrieved 2/11/2014, http://stemartaen.bigcartel.com/, 14 pages |
| | 320. | Sterling, "Welcome to the Era of Plant -Based Meat," Food & Wine, April 13, 2016, Retrieved April 20, 2016, <http://www.foodandwine.com/blogs/welcome-era-plant-based-meat>, 3 pages |
| | 321. | Supplementary Partial European Search Report in European Application No. 14738061 dated November 7, 2016, 11 pages |
| | 322. | Swanson, "Patenting the Quest for a More Perfect Veggie Burger," JDSUPRA Business Advisor, June 21, 2016, retrieved June 23, 2016 <http://www.jdsupra.com/legalnews/patenting-the-quest-for-a-more-perfect-72212/>. 13 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 323. | Tang et al., "Flavor chemistry of 2-methyl-3-furanthiol, an intense meaty aroma compound," Journal of Sulfur Chemistry, 11 pages, (2012) |
| | 324. | The Daiya Advantage, Products and Nutrition Facts, posted on or before 1/26/2010, retrieved on 2/7/2014, http://us.daiyafoods.com/our-products, 126 pages |
| | 325. | The Good Scents Company, "The Good Scents Company Information System," 2015, retrieved on December 1, 2016, http://www.thegoodscentscompany.com/, 2 pages |
| | 326. | The Vegetarian Express Parma Zaan Sprinkles, posted on or about 10/17/2009, retrieved 2/11/2014, http://www.thevegetarianexpress.com/cart/home.php?cat=250, 2 pages |
| | 327. | Tofu Rella Mozzarella Cheese, Natural Pantry, retrieved 2/11/2014, http://www.natural-pantry.com/shop/product_view.asp?id=24684&StoreID=D92VLAQVMPDL9L5UHTS2WLU67NADEHUA&private_product=0, 2 pages |
| | 328. | Tofutti Cheese Products and Nutrition, posted on or before 6/26/2013, retrieved 2/11/2014, http://www.tofutti.com/dairy-free-cheeses/, 18 pages |
| | 329. | Tofutti Milk Free, "Premium Dairy Free Cheeses,", posted on or before 6/26/2013, accessed 1/7/2014, http://www.tofutti.com/dairy-free-cheeses/, 2 pages |
| | 330. | Trader Joe's Sliced Soy Cheese Alternative, Fotki, posted 10/27/2008, retrieved 2/11/2014, http://public.fotki.com/harwons/food/tj-sliced-soy-cheese.html, 1 pages |
| | 331. | Trader Joe's Vegan Mozzarella, A(soy) Bean, posted 6/7/2013, retrieved 2/11/2014, http://a-soy-bean.blogspot.com/2013/06/showdown-trader-joes-vegan-mozzarella.html, 13 pages |
| | 332. | Treeline Treenut Cheese, Products and Nutrition Facts, posted on or before 12/10/2013, retrieved on 2/11/2014, http://www.treelinecheese.com/treeline-cheese-products.html, 3 pages |
| | 333. | Tressl et al., "Formation of Amino Acid Specific Maillard Products and Their Contribution to Thermally Generated Aromas," Thermal Generation of Aromas, American Chemical Society, pp. 156-171 (October 1989) |
| | 334. | Uauy et al., "Iron Fortification of Foods: Overcoming Technical and Practical Barriers," J. Nutr. 132:849S-852S (2002) |
| | 335. | Van Ba et al., "Principles of Meat Aroma flavors and Future Prospect," INTECH Open Science, Open Minds, 2012, Chapter 7, 145-176 |
| | 336. | Van Den Ouweland et al., "Process Meat Flavor Development and the Maillard Reaction," In Thermal Generation of Aromas, ACS Symposium Series, American Chemical Society, 1989, 433-441 |
| | 337. | VBites, "Cheezly," posted on or before 2013 , accessed 1/7/2014, http://www.vbitesfoods.com/meat-free/cheezly.html, 2 pages |
| | 338. | Vegan Sun Artisan Aged Raw Cheese, Vegan Essentials, retrieved 2/11/2014, http://store.veganessentials.com/vegan-sun-artisan-aged-raw-cheese-p4201.aspx, 3 pages |
| | 339. | VegCuisine Soy Cheese Products, The Vegan Store, retrieved on 2/11/2014, http://www.veganstore.com/category/s?keyword=vegcuisine, 5 pages |
| | 340. | Veggie Brothers Mozzarella Sticks, Vegan Essentials, 11/9/2013, retrieved 2/11/2014, http://store.veganessentials.com/vegan-mozzarella-sticks-by-veggie-brothers-p3761.aspx, 2 pages |
| | 341. | Victoria Vegan Sauces, Products and Nutrition Facts, posted on or about 9/16/2012, retrieved 2/11/2014, http://www.victoriafinefoods.com/products/specialty-sauces/victoria-vegan, 9 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/04/2017



| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date | Group Art Unit |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| | 342. | Wayfare We Can't say It's Cheese Spread, Products and Nutrition Facts, posted on or about 10/12/2013, retrieved 2/11/2014, http://www.wayfarefoods.com/we-cant-say-its-cheese/, 5 pages |
| | 343. | Welcome to Bute Island Foods, "100% Vegan Cheese – 100% Tasty," posted on or before 12/5/2006, accessed 1/7/2014, http://www.buteisland.com, 2 pages |
| | 344. | Welcome to VBites Foods, Cheezly Products and Nutrition Facts, 2013, retrieved on 2/7/2014, http://www.vbitesfoods.com/meat-free/cheezly.html, 26 pages |
| | 345. | Withycombe et al., "Identification of 2-Methyl-3-Furanthiol in the Steam Distillate from Canned Tuna Fish," Journal of Food Science, 53(2):658-660 (1988) |
| | 346. | Wortham and Miller, "Venture Capitalists Are Making Bigger Bets on Food Start-Ups," The New York Times Online, April 28, 2013, http://www.nytimes.com/2013/04/29/business/venture-capitalists-are-making-bigger-bets-on-food-start-ups.html?pagewanted=all&_r=1&, 4 pages |
| | 347. | Yancey et al., "Effects of total iron, myoglobin, hemoglobin, and lipid oxidation of uncooked muscles on livery flavor development and volatiles of cooked beef steaks," Meat Science, 73:680-686 (2006) |
| | 348. | Yves Veggie Cuisine The Good Slice, ShopWell, retrieved on 2/11/2014, http://www.shopwell.com/yves-veggie-cuisine-the-good-slice-cheese-alternative-cheddar-style/soy-foods/p/6082260001, 1 page |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /E.G./

Receipt date: 01/19/2017

Sheet 1 of 1

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. 15/398,479 |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date January 4, 2017 | Group Art Unit |

| U.S. Patent Documents | | | | | | | |
|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |

| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| /E.G./ | 1. | Cott et al., "The 'Impossible' Veggie Burger: A Tech Industry Answer to the Big Mac," Business Day, January 13, 2017, retrieved on 01/17/2017, <https://mobile.nytimes.com/2017/01/13/business/veggie-burger-impossible-burger.html?referer=http://www.drudgereport.com/>, 7 pages |
| /E.G./ | 2. | Fang et al., "Food Nutrition health theory and technology," China light industry press, p. 448, January 31, 1997 (Chinese Version) |
| /E.G./ | 3. | Fourth Chinese Office Action in Chinese Application No. 201280041713.1, dated 11/11/2016, 18 pages (with translation) |
| /E.G./ | 4. | Supplementary European Search Report for International No. EP 14737909.3, dated October 07, 2016, 10 pages |
| /E.G./ | 5. | Zhengnong et al., "Cihai biological fascicle," Shanghai Lexicographical Publishing House, P.243, December 31, 1987 (Chinese Version) |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

Receipt date: 02/07/2017

Sheet 1 of 1

| Substitute Disclosure Form<br>U.S. Department of Commerce<br>Patent and Trademark Office | Attorney Docket No.<br>38767-0015002 | Application No.<br>15/398,479 |
|---|---|---|
| **Information Disclosure Statement by Applicant**<br>(Use several sheets if necessary) | Applicant<br>Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | Filing Date<br>January 4, 2017 | Group Art Unit |

| U.S. Patent Documents | | | | | | | |
|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
| | -- | -- | | | | | |

| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation | |
| | | | | | | | Yes | No |
| | -- | -- | | | | | | |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|---|---|---|
| Examiner Initial | Desig. ID | Document |
| /E.G./ | 1. | Lombardi et al., "Total Heme and Non-heme Iron in Raw and Cooked Meats," Journal of Food Science, 67(5):1738-1741 (2002) |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

Receipt date: 02/15/2017

Sheet 1 of 1

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. 15/398,479 |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date January 4, 2017 | Group Art Unit |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| /E.G./ | 1. | Aubrey, "Food For Thought: Saving The Planet, One Burger At A Time: This Juicy Patty Is Meat-Free," The Salt, February 11, 2017, retrieved on February 14, 2017, retrieved from <http://www.npr.org/sections/thesalt/2017/02/11/514544431/saving-the-planet-one-burger-at-a-time-this-juicy-patty-is-meat-free>, 14 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

Receipt date: 03/03/2017

Sheet 1 of 1

| Substitute Disclosure Form<br>U.S. Department of Commerce<br>Patent and Trademark Office | Attorney Docket No.<br>38767-0015002 | Application No.<br>15/398,479 |
|---|---|---|
| **Information Disclosure Statement by Applicant**<br>(Use several sheets if necessary) | Applicant<br>Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | Filing Date<br>January 4, 2017 | Group Art Unit |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| /E.G./ | 1. | Chau, "Uncanny Patty," The Ringer, February 27, 2017, retrieved on February 28, 2017, retrieved from <https://theringer.com/impossible-burger-last-meal-on-earth-week-food-f9f14acdb99d#.vocb2hi6e>, 19 pages |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

Receipt date: 03/20/2017

Sheet 1 of 1

| Substitute Disclosure Form | U.S. Department of Commerce Patent and Trademark Office | Attorney Docket No. 38767-0015002 | Application No. 15/398,479 |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) | | Applicant Impossible Foods Inc. | |
| (37 CFR §1.98(b)) | | Filing Date January 4, 2017 | Group Art Unit |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes | Translation No |
|---|---|---|---|---|---|---|---|---|

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| /E.G./ | 1. | Fang et al., "Food Nutrition health theory and technology," China light industry press, p. 448, January 31, 1997 (English Translation) |
| /E.G./ | 2. | Zhengnong et al., "Cihai biological fascicle," Shanghai Lexicographical Publishing House, P.243, December 31, 1987 (English Translation) |

| Examiner Signature | Date Considered |
|---|---|
| /ELIZABETH GWARTNEY/ | 04/10/2017 |

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Disclosure Form

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

# BIB DATA SHEET

**CONFIRMATION NO. 2358**

| SERIAL NUMBER | FILING or 371(c) DATE | CLASS | GROUP ART UNIT | ATTORNEY DOCKET NO. |
|---|---|---|---|---|
| 15/398,479 | 01/04/2017<br>RULE | 426 | 1791 | 38767-0015002 |

**APPLICANTS**
Impossible Foods Inc., Redwood City, CA;

**INVENTORS**
Rachel Fraser, San Francisco, CA;
Patrick O'Reilly Brown, Stanford, CA;
Jessica Karr, San Francisco, CA;
Celeste Holz-Schietinger, East Palo Alto, CA;
Elysia Cohn, Sunnyvale, CA;

**** CONTINUING DATA ***************************
This application is a CON of 14/797,006 07/10/2015
which is a CON of PCT/US2014/011347 01/13/2014
which is a CON of 13/941,211 07/12/2013
and claims benefit of 61/908,634 11/25/2013
and claims benefit of 61/751,816 01/11/2013

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****
01/13/2017

| | | | | | |
|---|---|---|---|---|---|
| Foreign Priority claimed ☐ Yes ☑ No<br>35 USC 119(a-d) conditions met ☐ Yes ☑ No<br>Verified and Acknowledged /ELIZABETH A GWARTNEY/ Examiner's Signature | ☐ Met after Allowance<br>Initials | STATE OR COUNTRY<br>CA | SHEETS DRAWINGS<br>5 | TOTAL CLAIMS<br>30 | INDEPENDENT CLAIMS<br>2 |

**ADDRESS**
FISH & RICHARDSON P.C. (TC)
PO BOX 1022
MINNEAPOLIS, MN 55440-1022
UNITED STATES

**TITLE**
METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES

| | | |
|---|---|---|
| **FILING FEE RECEIVED**<br>2400 | FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following: | ☐ All Fees<br>☐ 1.16 Fees (Filing)<br>☐ 1.17 Fees (Processing Ext. of time)<br>☐ 1.18 Fees (Issue)<br>☐ Other _____<br>☐ Credit |

BIB (Rev. 05/07).

**EAST Search History**

**EAST Search History (Prior Art)**

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 3 | A23L1/231 AND hemoglobin | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2017/04/10 10:52 |
| L2 | 1 | A23L1/31427 AND heme | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2017/04/10 10:52 |
| L3 | 8 | A23L1/221 AND heme | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2017/04/10 10:53 |
| S1 | 3013 | A23L1/231 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 16:15 |
| S2 | 3 | A23L1/231 AND heme | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 16:15 |
| S3 | 1132 | A23L1/31427 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 16:16 |
| S4 | 20791 | A23L1/221 | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 16:16 |
| S5 | 95 | (heme ADJ containing ADJ protein) | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 16:17 |
| S6 | 1 | "14797006" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 18:04 |
| S7 | 6 | leghemoglobin WITH food | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 18:59 |
| S8 | 67 | leghemoglobin WITH soybean | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 19:00 |
| S9 | 232 | leghemoglobin | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 19:01 |
| S10 | 155 | (soybean WITH monophosphate) | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 19:41 |
| S11 | 42 | (soybean with (meat ADJ substitute)) | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/14 19:43 |
| S12 | 1632 | frozen WITH soybean | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/15 08:25 |
| S13 | 2 | frozen WITH soybean WITH (meat WITH | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; | OR | OFF | 2015/12/15 08:26 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | substitute) | IBM_TDB | | | |
| S14 | 107 | frozen WITH soybean WITH meal | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/15 08:26 |
| S15 | 95 | (heme ADJ containing ADJ protein) | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2015/12/15 08:36 |
| S16 | 1 | "14797006" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 12:28 |
| S17 | 3 | A23L1/231 AND heme | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 12:29 |
| S18 | 913 | heme ADJ protein | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 12:30 |
| S19 | 83 | (heme ADJ protein) AND meat | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 12:30 |
| S20 | 2 | "20030152500" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 15:10 |
| S21 | 44 | "9808603" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 16:00 |
| S22 | 22 | "2008069650" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2016/05/31 20:12 |
| S23 | 8 | "2003059778" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2017/03/10 13:20 |
| S24 | 4 | "20120093994" | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2017/03/14 15:26 |
| S25 | 5 | A23J1/14 AND heme | US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB | OR | OFF | 2017/03/15 12:04 |

**EAST Search History (Interference)**

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| S26 | 0 | A23J1/14 AND heme | USPAT | OR | OFF | 2017/03/15 12:04 |
| S27 | 0 | A23J1/14 AND leghemoglobin | USPAT | OR | OFF | 2017/03/15 12:04 |
| S28 | 77 | A23J1/14 | USPAT | OR | OFF | 2017/03/15 12:05 |
| S29 | 260 | A23J1/14 | US-PGPUB; USPAT | OR | OFF | 2017/03/15 12:05 |
| S30 | 198 | leghemoglobin | US-PGPUB; USPAT | OR | OFF | 2017/03/15 12:05 |
| S31 | 260 | A23J1/14 | US-PGPUB; USPAT | OR | OFF | 2017/03/15 12:40 |
| S32 | 109 | A23J3/14 | US-PGPUB; USPAT | OR | OFF | 2017/03/15 12:40 |

| | | | | | | |
|---|---|---|---|---|---|---|
| S33 | 344 | (heme WITH protein).clm. | US-PGPUB; USPAT | OR | OFF | 2017/03/15 12:41 |

**4/10/2017 10:56:14 AM**
**C:\Users\egwartney\Documents\EAST\Workspaces\14797006.wsp**

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NUMBER | FILING OR 371(C) DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO./TITLE |
|---|---|---|---|
| 15/398,479 | 01/04/2017 | Rachel Fraser | 38767-0015002 |

**CONFIRMATION NO. 2358**

26191
FISH & RICHARDSON P.C. (TC)
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

**PUBLICATION NOTICE**

*OC000000090953841*

**Title:**METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES

**Publication No.**US-2017-0112175-A1
**Publication Date:**04/27/2017

## NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently http://pair.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Attorney Docket No.: 38767-0015002 / Client Ref: Meat3CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | 1791 |
| Serial No. | : | 15/398,479 | Examiner | : | Elizabeth A. Gwartney |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

**Mail Stop Amendment**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY TO ACTION OF APRIL 14, 2017

Please consider the following reply.

Amendments to the Specification:

Please amend the paragraph on page 14, lines 5-29, as follows:

**Marked Up**

Heme-containing proteins that can be used in the compositions and food products described herein can be from mammals (e.g., farms animals such as cows, goats, sheep, pigs, ox, or rabbits), birds, plants, algae, fungi (e.g., yeast or filamentous fungi), ciliates, or bacteria. For example, a heme-containing protein can be from a mammal such as a farm animal (e.g., a cow, goat, sheep, pig, ox, or rabbit) or a bird such as a turkey or chicken. Heme-containing proteins can be from a plant such as *Nicotiana tabacum* or *Nicotiana sylvestris* (tobacco); *Zea mays* (corn), *Arabidopsis thaliana*, a legume such as *Glycine max* (soybean), *Cicer arietinum* (garbanzo or chick pea), *Pisum sativum* (pea) varieties such as garden peas or sugar snap peas, *Phaseolus vulgaris* varieties of common beans such as green beans, black beans, navy beans, northern beans, or pinto beans, *Vigna unguiculata* varieties (cow peas), *Vigna radiata* (Mung beans), *Lupinus albus* (lupin), or *Medicago sativa* (alfalfa); *Brassica napus* (canola); *Triticum* sps. (wheat, including wheat berries, and spelt); *Gossypium hirsutum* (cotton); *Oryza sativa* (rice); *Zizania* sps. (wild rice); *Helianthus annuus* (sunflower); *Beta vulgaris* (sugarbeet); *Pennisetum glaucum* (pearl millet); *Chenopodium* sp. (quinoa); *Sesamum* sp. (sesame); *Linum usitatissimum* (flax); or *Hordeum vulgare* (barley). Heme-containing proteins can be isolated from fungi such as *Saccharomyces cerevisiae*, *Pichia pastoris*, *Magnaporthe oryzae*, *Fusarium graminearum*, *Aspergillus oryzae*, *Trichoderma reesei*, *Myceliopthera thermophile*, *Kluyvera lactis*, or *Fusarium oxysporum*. Heme-containing proteins can be isolated from bacteria such as *Escherichia coli*, *Bacillus subtilis*, *Bacillus licheniformis*, *Bacillus megaterium*, *Synechocistis* sp., *Aquifex aeolicus*, *Methylacidiphilum infernorum*, or thermophilic bacteria such as *Thermophilus*. The sequences and structure of numerous heme-containing proteins are known. See for example, Reedy, et al., *Nucleic Acids Research*, 2008, Vol. 36, Database issue D307–D313 and the Heme Protein Database available on the world wide web at [[http://]] hemeprotein.info/heme.php.

**Clean**

Heme-containing proteins that can be used in the compositions and food products described herein can be from mammals (e.g., farms animals such as cows, goats, sheep, pigs, ox,

or rabbits), birds, plants, algae, fungi (e.g., yeast or filamentous fungi), ciliates, or bacteria. For example, a heme-containing protein can be from a mammal such as a farm animal (e.g., a cow, goat, sheep, pig, ox, or rabbit) or a bird such as a turkey or chicken. Heme-containing proteins can be from a plant such as *Nicotiana tabacum* or *Nicotiana sylvestris* (tobacco); *Zea mays* (corn), *Arabidopsis thaliana*, a legume such as *Glycine max* (soybean), *Cicer arietinum* (garbanzo or chick pea), *Pisum sativum* (pea) varieties such as garden peas or sugar snap peas, *Phaseolus vulgaris* varieties of common beans such as green beans, black beans, navy beans, northern beans, or pinto beans, *Vigna unguiculata* varieties (cow peas), *Vigna radiata* (Mung beans), *Lupinus albus* (lupin), or *Medicago sativa* (alfalfa); *Brassica napus* (canola); *Triticum* sps. (wheat, including wheat berries, and spelt); *Gossypium hirsutum* (cotton); *Oryza sativa* (rice); *Zizania* sps. (wild rice); *Helianthus annuus* (sunflower); *Beta vulgaris* (sugarbeet); *Pennisetum glaucum* (pearl millet); *Chenopodium* sp. (quinoa); *Sesamum* sp. (sesame); *Linum usitatissimum* (flax); or *Hordeum vulgare* (barley). Heme-containing proteins can be isolated from fungi such as *Saccharomyces cerevisiae*, *Pichia pastoris*, *Magnaporthe oryzae*, *Fusarium graminearum*, *Aspergillus oryzae*, *Trichoderma reesei*, *Myceliopthera thermophile*, *Kluyvera lactis*, or *Fusarium oxysporum*. Heme-containing proteins can be isolated from bacteria such as *Escherichia coli*, *Bacillus subtilis*, *Bacillus licheniformis*, *Bacillus megaterium*, *Synechocistis* sp., *Aquifex aeolicus*, *Methylacidiphilum infernorum*, or thermophilic bacteria such as *Thermophilus*. The sequences and structure of numerous heme-containing proteins are known. See for example, Reedy, et al., *Nucleic Acids Research*, 2008, Vol. 36, Database issue D307–D313 and the Heme Protein Database available on the world wide web at hemeprotein.info/heme.php.

Please insert the paragraphs below immediately following page 18, line 23.

In some embodiments, the food product contains between 0.01% and 5% by weight of a heme protein. In some embodiments, the food product contains between 0.01% and 5% by weight of leghemoglobin. Some meat also contains myoglobin, a heme protein, which accounts for most of the red color and iron content of some meat. It is understood that these percentages can vary in meat and the food products can be produced to approximate the natural variation in meat.

In some embodiments, the food product comprises about 0.05%, about 0.1%, about 0.2%, about 0.3%, about 0.4%, about 0.5%, about 0.6%, about 0.7%, about 0.8%, about 0.9%, about 5 1%, about 1.1%, about 1.2%, about 1.3%, about 1.4%, about 1.5%, about 1.6%, about 1.7%, about 1.8%, about 1.9%, about 2%, or more than about 2% of an iron-carrying protein (e.g., a heme-containing protein) by dry weight or total weight. In some cases, the iron carrying protein has been isolated and purified from a source.

Please amend the paragraph on page 52, lines 16-22, as follows:

**Marked Up**

The meat replica sample containing only LegH, was compared to the meat replica sample containing the magic mix and LegH by a sensory panel and GCMS analysis. Five tasters rated the flavored meat replicas for beefiness, bitterness, and levels of savory flavors, and off flavors. Each property was rated on a 7 point scale in which 7 was the highest amount of the specified property (e.g., a standard 80:20 ground beef would be rated 7 on the beefy scale). The Magic Mix flavor was rated one point higher in beefy character than the LegH only sample (~~FIG. 1~~FIG. 2).

**Clean**

The meat replica sample containing only LegH, was compared to the meat replica sample containing the magic mix and LegH by a sensory panel and GCMS analysis. Five tasters rated the flavored meat replicas for beefiness, bitterness, and levels of savory flavors, and off flavors. Each property was rated on a 7 point scale in which 7 was the highest amount of the specified property (e.g., a standard 80:20 ground beef would be rated 7 on the beefy scale). The Magic Mix flavor was rated one point higher in beefy character than the LegH only sample (FIG. 2).

Amendments to the Drawings:

Please replace the original FIG. 2 with the Replacement Sheet filed herewith.

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. – 30. (Canceled)

31. (Currently Amended) A food flavor additive composition comprising:

a) ~~an isolated~~ a heme-containing protein;

b) a ~~sugar, sugar alcohol, sugar acid, or sugar derivative~~ compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose, and mixtures of two or more thereof; and

c) a compound selected from cysteine, cystine, ~~selenocysteine,~~ thiamine, methionine, and mixtures of two or more thereof;

wherein the flavor additive composition contains no animal meat ~~tissue derived components~~; and

wherein the flavor additive composition is packaged and is in the form of a ~~liquid, a gel, an emulsion, a powder or~~ a bouillon ~~cube~~.

32. (Previously Presented) The food flavor additive composition of claim 31, wherein the heme-containing protein is present in an amount between about 0.01% and about 5% by weight.

33. (Previously Presented) The food flavor additive composition of claim 31, wherein the heme-containing protein is selected from the group consisting of a androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a leghemoglobin, an erythrocruorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a

cytoglobin, a histoglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.

34. (Previously Presented) The food flavor additive composition of claim 31, wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.

35. (Currently Amended) The food flavor additive composition of claim 31, wherein the ~~food flavor additive composition~~ bouillon is in the form of a powder or a cube~~, a liquid, an emulsion or a gel composition~~.

36. (Previously Presented) The food flavor additive composition of claim 31, wherein the heme-containing protein is a plant, a mammalian, a yeast or filamentous fungi, or bacterial heme-containing protein.

37. (Previously Presented) The food flavor additive composition of claim 31, further comprising one or more of an extract or hydrolysate selected from a vegetable protein hydrolysate, a soy protein hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate.

38. (Previously Presented) The food flavor additive composition of claim 31, further comprising one or more of a compound selected from alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, maltodextrin, thiamine, IMP, GMP, lactic acid, and creatine.

39. (Previously Presented) The food flavor additive composition of claim 31, further comprising one or more of an oil selected from coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn

oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.

40. (Previously Presented) The food flavor additive composition of claim 31, further comprising one or more of albumin or a globulin.

41. (Currently Amended) A food flavor additive composition prepared by a process of:

a) combining ~~an isolated~~ a heme-containing protein; ~~a sugar, sugar alcohol, sugar acid, or sugar derivative~~ a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, and galactose, and mixtures of two or more thereof; and a compound selected from cysteine, cystine, ~~selenocysteine,~~ thiamine, methionine, and mixtures of two or more thereof, to form a heme flavor reaction mixture, and

b) heating the heme flavor reaction mixture to result in the food flavor additive composition;

wherein the food flavoring additive composition contains no animal meat~~products no animal tissue derived components~~.

42. (Previously Presented) The food flavor additive composition of claim 41, wherein the process further comprises heating the heme flavor reaction mixture to at least 150°C for at least 1 minute.

43. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture has a meaty flavor and/or meaty aroma during the heating of step b) and/or the food flavoring additive composition has a meaty flavor and/or meaty aroma after the heating of step b).

44. (Previously Presented) The food flavor additive composition of claim 42, wherein the food flavoring additive composition further comprises a compound selected from the group consisting of 2-methyl-furan, bis(2-methyl-3-furyl)disulfide, 2-pentyl-furan, 3,3'-dithiobis-2-

methyl-furan, 2,5-dimethyl-pyrazine, 2-methyl-3-furanthiol, bis(2-methyl-4,5-dihydro-3-furyl) disulfide, dihydro-3-(2H)-thiophenone, 5-methyl-2-thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, 2-methyl-thiazole, dimethyl sulfide, decanal, 5-ethyldihydro-2(3H)-furanone, dihydro-5-pentyl-2(3H)-furanone, 2-octanone, 3,5-octadien-2-one, p-Cresol, and hexanoic acid.

45. (Previously Presented) The food flavor additive composition of claim 44, wherein the compound is detectable in the headspace above the heme flavor reaction mixture during the heating of step b) or in the headspace above the food flavoring additive composition after the heating of step b).

46. (Previously Presented) The food flavor additive composition of claim 41, where the process further comprises removing the heme-containing protein from the food flavoring additive composition after the heating in step b) of the heme flavor reaction mixture.

47. (Previously Presented) The food flavor additive composition of claim 41, wherein the process further comprises altering the pH of the heme flavor reaction mixture prior to the heating of step b).

48. (Previously Presented) The food flavor additive composition of claim 41, wherein the process further comprises dehydrating the heme flavor reaction mixture to a powder form after the heating of step b).

49. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme-containing protein is present in an amount between about 0.01% and about 5% by weight in the heme flavor reaction mixture.

50. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme-containing protein is selected from the group consisting of an androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a leghemoglobin, an

erythrocruorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histoglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.

51. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme-containing protein comprises an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.

52. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture further comprises one or more oils selected from coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.

53. (Previously Presented) The food flavor additive composition of claim 41, further comprising an ingredient selected from an emulsifier and a gelling agent.

54. (Previously Presented) The food flavor additive composition of claim 41, the process further comprising adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b).

55. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture is an aqueous solution.

56. (Previously Presented) The food flavor additive composition of claim 41, wherein the heme flavor reaction mixture is an oil-based mixture.

57. (Previously Presented) The food flavor additive composition of claim 41, further comprising removing the heme-containing protein from the food flavor additive composition.

58. (Previously Presented) The food flavor additive composition of claim 41, further comprising one or more of an extract or hydrolysate selected from a vegetable protein hydrolysate, a soy protein hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate, and or an albumin or a globulin.

59. (Withdrawn) A process for imparting a meaty flavor and/or meaty aroma to a consumable food product, comprising:

adding to the consumable food product a food flavor additive composition of claim 31.

60. (Withdrawn) The process of claim 59, further comprising heating the consumable food product.

## REMARKS

Applicants respectfully request entry of the amendments and remarks submitted herein. Upon entry of the above amendment, claims 31-60 will be pending. Claims 59 and 60 were previously withdrawn, so are not currently under examination. Claims 31, 35 and 41 have been amended. Most of the amendments are simply to clarify scope and are supported throughout the specification.

For example, the amendment to claim 1 finds support at least at page 4, line 27 to page 5, line 2; page 5, lines 3-9; page 12, lines 2-5, 15-18 (Table 1, rows 1, 4 and 6); Example 1; Example 4; Example 5; Example 6; Example 7; Example 8; Example 9 Example 10; Example 11 and Table 13; page 7, lines 5-8; Examples 4-12; page 5, lines 10-12; page 7, lines 5-7; and page 25, lines 24-28. Claim 35 finds support at least at page 5, lines 10-12; page 7, lines 5-7; and page 25, lines 24-28. The amendments to claim 41 find support at least at page 3, lines18 – page 4, line 3; page 7, line 9 – page 9, line 28; page 4, lines 16-21; and page 7, lines 5-8; Examples 4-12.

No new matter has been introduced by these amendments. Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Amendments to the Specification

Applicant have amended the Specification for consistency with the amendments made in parent U.S. Application Serial No. 14/797,006. Support for the amendments to the specification can be found at least at page 18, lines 16-27 of U.S. Application Serial No. 14/797,006; at [00354] of U.S. Application Serial No. 13/941,211 (published as US 2014/0220217); and at least at [00258] of U.S. Application Serial No. 61/751,816. The present application claims priority to U.S. Application Serial No. 14/797,006, U.S. Application Serial No. 13/941,211 and to U.S. Application Serial No. 61/751,816, each of which were incorporated by reference. Accordingly, no new matter has been introduced by these amendments.

Interview Request

Applicants respectfully request a telephonic interview to take place after the Examiner has reviewed these amendments and remarks, unless all the claims are then deemed allowable. So that the interview can take place at that point, and prior to preparation of a new Office Action (should that be deemed necessary), Applicants would be grateful if the Examiner would contact Applicants' representative Ian Lodovice at telephone number (617) 956-5972 at the Examiner's convenience, to arrange an appropriate time for the interview.

Election/Restriction

Applicant acknowledges and thanks Examiner Gwartney for the telephone conversation on April 6, 2017 with Applicant's representative Ian Lodovice where the participants discussed Restriction to one of the following inventions is required under 35 U.S.C. 121:

The Examiner restricted the claims into two groups:

**I.** Claims 31-58, drawn to a food flavor additive comprising an isolated heme-containing protein, a sugar, sugar alcohol, sugar acid, or sugar derivative classified in A23L27/00.

**II.** Claims 59 and 60, drawn to a process of imparting a meaty flavor and/or meaty aroma to a consumable food product, classified in A23L13/426.

In a telephone call on April 6, 2017, the undersigned elected Group I, claims 31-58. Applicants affirm this election, without traverse.

Specification

The disclosure is objected to because the Examiner indicated that the specification contains an embedded hyperlink and/or other form of browser-executable code.

Applicants have amended the specification herein to remove the embedded hyperlink. In view of these amendments, Applicants respectfully request that the objections to the specification be withdrawn.

Drawings

The drawings are objected to because the Examiner indicated that Figure 2 does not contain a label for the Y-axis. Filed herewith is a Replacement Sheet for FIG. 2 addressing the present rejection. Reconsideration and withdrawal of the objection is requested.

Claim Rejections - 35 U.S.C. § 112

Claims 31-58 stand rejected under 35 U.S.C. § 112 (pre-AIA), first paragraph, as allegedly failing to comply with the written description requirement. Applicant respectfully disagrees.

The Federal Circuit specifically states that the test for written description under 35 U.S.C. § 112, first paragraph, "is whether the disclosure of the application relied upon *reasonably* conveys to those *skilled in the art* that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm., Inc., 10 v. Eli Lilly & Co.*, 598 F3d 1336, 1351 (Fed. Cir. 2010) (emphasis added). See, also, *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985); and *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983). Whether the description requirement is met is a question of fact. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555 (Fed.Cir.1991). "We have made clear that the written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Ariad Pharm* at 1352 (*citing Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366-67 (Fed.Cir.2006)). "The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not have recognized in the applicant's disclosure a description of the invention defined by the claims." MPEP § 2163.04 (*citing In re Werheim*, 541 F.2d 257, 263 (CCPA 1976)).

The Examiner objected to the phrase "*wherein the flavor additive composition contains no animal tissue derived components*" recited in claims 31 and 41, alleging "there is no support to claim that the flavor additive composition contains no animal tissue derived components." Without conceding the appropriateness of the rejection, and solely in the interested of advancing prosecution, the Applicant has amended claims 31 and 41 to recite "wherein the flavor additive composition contains no animal meat." The amended claim has written description support in the specification as filed at, for example, page 7, lines 5-8; and Examples 4-12. Throughout

Examples 4-12, a number of different flavor additive compositions are described, each of which does not contain animal meat. Further, as the Specification expressly provides that the food products (e.g., food additive compositions) described therein can be prepared in various ways and can be formulated to be free of animal products, including, for example to be free of animal meat.

The Examiner also objected to the phrase "wherein the flavor additive composition is packaged and is in the form of a liquid, a gel, an emulsion, a powder or a bouillon cube." Without out conceding the appropriateness of the rejection, and solely in the interested of advancing prosecution, the Applicant has amended claims 31 to obviate this rejection.

The Examiner also objected to the phrase "wherein the heme-containing protein is present in an amount between about 0.01% to about 5%" recited in claim 32. However, the Examiner acknowledged that "there is support to claim a food product comprising 0.01% to 5% by weight of a heme protein (see page 18/L16-27 of specification for U.S. Application No. 14/979,006)." Applicant thus directs the Examiner's attention to page 4, lines 2-3, of the present specification which provides the "food products for use in the present disclosure can be flavor additive compositions, e.g., for addition to another consumable food product before, during, or after its cooking process." In view of this disclosure at least, Applicant respectfully submits that one of skill in the art would understand that the term "food product" recited at page 18, lines 16-27 includes a "food flavor additive composition" as claimed. Accordingly, based at least on the disclosure cited, claim 32 meets the test for written description under 35 U.S.C. § 112, first paragraph, and reasonably conveys to those skilled in the art that the inventors had possession of the claimed subject matter as of the filing date.

The Examiner also objected to the phrase "further comprising an ingredient selected from an emulsifier and a gelling agent" recited in claim 53, as well as the phrase "adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b)" recited in claim 54. As above, Applicant respectfully that the Specification reasonably conveys that the term "food product" recited in the specification properly includes a "food flavor additive composition" as claimed. For at least this reason, Applicant maintains that claims 53-54 meet the test for written description under 35 U.S.C. § 112, first paragraph, and reasonably conveys to

those skilled in the art that the inventors had possession of the claimed subject matter as of the filing date.

In summary, based at least on the disclosure cited above, the present application meets the test for written description under 35 U.S.C. § 112, first paragraph, and reasonably conveys to those skilled in the art that the inventors had possession of the claimed subject matter as of the filing date

Claims 31-58 stand rejected under 35 U.S.C. 112 (pre-AIA), second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention. Without conceding the appropriateness of the rejection, and solely in the interested of advancing prosecution, Applicant has amended the claims to obviate the rejection. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 102

Claims 31, 33-36, 38 and 40 are rejected under pre-AIA 35 U.S.C. § 102(b) as being anticipated by Tong et al. ("Blood Composition of Different Beef Breed Types," Can. J. Anim. Sci, 66, Dec. 1986, pp. 915-924)("Tong") as evidenced by Shimbayashi et al. ("Free Amino Acids and Phsphorylethanolamine in Milk Whey of Cow," Agr. Biol. Chem, Vol. 29, No. 1, 1965, pp. 13-19)("Shimbayashi"). To the extent that the rejection may be applied to the amended claims, Applicants traverse.

Under Federal Circuit law, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Also, "unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102." *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008).

Tong was cited for disclosing that blood from cattle comprise hemoglobin, glucose, protein, and albumin. Shimbayashi was cited as evidence that blood from cattle was known to comprise free amino acids including methionine, taurine, threonine, serine, glutamic acid, proline, glycine, alanine, valine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, and arginine. Neither Tong, nor Shimbayashi, disclose a food flavor additive composition that is packaged and in the form of a bouillon as presently claimed.

For at least the reasons above, Tong does not anticipate the pending claims. Reconsideration and withdrawal of the rejection under 35 U.S.C. 102(b) of claims 31, 33-36, 38 and 40 is requested.

Claims 31-36 and 38 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Koutsidis et al. ("Water-soluble precursors of beef flavor: I. Effect of diet and breed," Meat Science, 79, 2008, pp. 124-130)("Koutisids") as evidenced by Field et al. ("Heme Pigment Content of Bovine Hemopoietic Marrow and Muscle," J. Food Sci., Volume 45, 1980, pp. 1109-1112)("Field"). To the extent that the rejection may be applied to the amended claims, Applicants traverse.

Koutsidis was cited for disclosing that beef comprises sugars and free amino acids. Field was cited as evidence that "beef muscle is known to comprise about 0.06 % by weight hemoglobin." Neither Koutsidis, nor Field, disclose a food flavor additive composition that is packaged and in the form of a bouillon as presently claimed.

For at least the reasons above, Koutsidis, as evidenced by Field or otherwise, does not anticipate the pending claims. Reconsideration and withdrawal of the rejection under 35 U.S.C. 102(b) of claims 31-36 and 38 is requested.

Claims 31, 33-36, 38, 39-45, 50, 51 and 58 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Jamieson ("Iroquois Stew With Beef, Chicken and Pork," Bon Appetit, November 1995, http://www.epicurious.conilrecipesifoodiviewsiiroquois-stewwith-beef-chicken-and-pork-865) as evidenced by Koutsidis, Field and Griffiths ("XCIII. The Action of Gastric Juice on Beef Muscle-Globulin, With Reference to Anaemia," Biochemistry Journal, Vol. 28, 1934, pp. 671-675)("Griffiths").

According to the Examiner, Jamieson discloses Iroquois stew with beef and method for making the stew comprising adding beef to a composition of pork, chicken, flour, vegetable oil, onion, chicken broth, carrots, bay leaves, all spice and potatoes." Koutsidis and Field were cited for the reasons outlined above. Griffiths was cited for teaching that "beef is known to comprise globulin."

Jamieson does not disclose a food flavor additive composition that "contains no animal meat" as presently claimed. Nor does Jamieson teach or suggest a food flavor additive composition that is packaged and in the form of a bouillon. Thus, Jamieson fails to teach all elements of the claims. Koutsidis, Field and Griffiths were not cited for, nor do they teach, the deficiencies of Jamieson discussed above.

For at least the reasons above, Jamieson, as evidenced by Koutsidis, Field and Griffiths, or otherwise, does not anticipate the pending claims. Reconsideration and withdrawal of the rejection under 35 U.S.C. 102(b) of claims 31-36 and 38 is requested.

*The Effect of a Heme-containing Protein on Flavor Generation*

Enclosed herewith is a Declaration under 37 CFR § 1.132 by 132 by Dr. Celeste Holz-Schietinger (the "Holz-Schietinger Declaration"), attached as **Exhibit 1**; a Declaration under 37 CFR § 1.132 by Dr. Keith R. Cadwallader ("the Cadwallader Declaration"), attached as **Exhibit 2**; and a Declaration under 37 CFR § 1.132 by Dr. Devin Grant Peterson ("the Peterson Declaration"), attached as **Exhibit 3**. The Holz-Schietinger Declaration describes flavor reactions mixtures (1) containing only Leghemoglobin (LegH-only); (2) containing Ribose and Cysteine (Ribose + Cysteine); and (3) containing Leghemoglobin with Ribose and Cysteine (LegH + Ribose + Cysteine) that have been cooked and then analyzed using GC-MS. Many different volatile compounds were produced, but the Holz-Schietinger Declaration focuses on those volatile compounds that have been associated in the art with a beef (or meat) aroma. Significantly, described in the Holz-Schietinger Declaration, there were twenty-eight (28) different volatile compounds that were produced in the Ribose + Cysteine sample only when LegH was present. 28 volatile compounds whose generation is attributable to the presence of the heme-containing protein have been associated in the art, directly or indirectly, with a beef (or meat) aroma.

The Cadwallader Declaration and the Peterson Declaration confirm that the GC-MS experiments performed in the Holz-Schietinger Declaration are art-recognized methods that support a correlation between the volatile compound profile produced in an aqueous thermal reaction sample and that produced in a food matrix in the presence of the same substrates and the heme-containing protein. The Cadwallader Declaration and the Peterson Declaration also discuss the surprisingly and unexpectedly improved organoleptic properties, including, in particular, the beef-associated aroma profile, resulting for the addition of a heme-containing protein to a food product (e.g., a food flavor additive).

*Heme-containing protein*

Enclosed herewith is a Declaration under 37 CFR § 1.132 by Dr. David J. Lipman ("the Lipman Declaration"), attached as **Exhibit 4**. As explained in the Lipman Declaration, an alignment of 27 heme-containing proteins from a diverse range of organisms was performed. Despite adopting a highly conservative approach to align such sequences, heme-containing proteins are highly diverse and share very little sequence similarity. Paragraph 10 of the Lipman Declaration.

The Lipman Declaration refers to data presented in the present application, in which the production of volatile compounds was evaluated, including those associated with a meaty aroma, during cooking of aqueous flavor reaction mixtures containing four distinct globin heme-containing proteins, as well as reaction mixtures containing myoglobin free in solution or hemin (heme unbound to protein) coupled to a solid support (paragraphs 11 and 15 of the Lipman Declaration). According to the Lipman Declaration, the ability of five very distinct members of heme-containing proteins to generate meat-associated volatile aroma compounds upon heating, coupled with the experimental data demonstrating that even heme unbound to protein (i.e., hemin) shared such meat aroma and flavor production properties when heated in a reaction mixture, make it likely that these functional properties are not based on protein sequence similarity, but are instead based on the commonality among the proteins and hemin, namely, the inclusion of the heme co-factor (paragraph 18 of the Lipman Declaration).

## CONCLUSION

Applicants respectfully request that claims 30-58 be allowed. If any issues remain, the Examiner is asked to telephone the undersigned to arrange a time for an interview.

Applicants do not concede any positions of the Office that are not expressly addressed above, nor do Applicants concede that there are no other good reasons for patentability of the presented claims or other claims.

Apply any fees and any other necessary charges or credits to Deposit Account 06 1050, referencing the above attorney docket number.

Respectfully submitted,

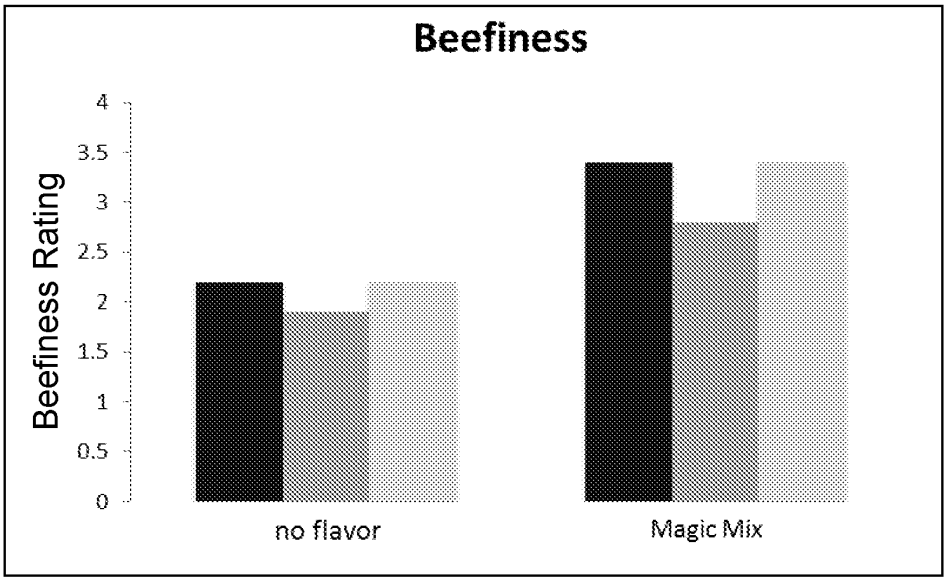
Date: July 14, 2017

/Ian J.S. Lodovice, Reg. No. 59,749/
Ian J.S. Lodovice,
Reg. No. 59,749

Customer Number 26161
Fish & Richardson P.C.
Telephone: (617) 956-5972
Facsimile: (877) 769-7945

61492929.doc

FIG. 2


Beefiness
Beefiness Rating
4
3.5
3
2.5
2
1.5
1
0.5
0
no flavor
Magic Mix

Attorney's Docket No.: 38767-0015001 / M3CON-Track 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | 1791 |
| Serial No. | : | 14/797,006 | Examiner | : | Elizabeth A. Gwartney |
| Filed | : | July 10, 2015 | | | |
| | | | Conf. No. | : | 8496 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR §1.132

I, Celeste Holz-Schietinger, Ph.D., hereby declare as follows:

1. I am currently a Principal Scientist at Impossible Foods in Redwood City, California. I have held this position since 2015, and I am responsible for leading the Flavor Department. In this role, I direct flavor technology research as well as flavor product integration. I began working for Impossible Foods in 2012 as a Scientist, and I was elevated to a Senior Scientist in 2013. While at Impossible Foods, I have been the lead chemist on the identification, characterization and manipulation of biological flavor catalysis and potentiation, including through the use of heme-containing proteins.

2. I received my Bachelors of Science (B.S.) degree in Molecular Biology and Evolution, with a minor in Chemistry, in 2005 from The Evergreen State College in Olympia, Washington, and I received my Doctor of Philosophy (Ph.D.) degree in Biochemistry from the University of California at Santa Barbara in 2012. I was an Enzymology Research Associate at the University of California at Santa Barbara from 2007 to 2012, and I also was a Biochemistry Visiting Associate at Stanford University in 2009.

3. A copy of my curriculum vitae is attached as **Exhibit A**.

4. I am a named inventor on the above-referenced patent application.

5. I have read U.S. Application No. 14/797,006 ("the '006 application") as well as the Office Action mailed June 6, 2016, in which the claims were rejected as being anticipated by Proulx et al. (2006, *J. Agric. Food Chem.*, 54:1518-22) and obvious over Hseih et al. (US 2012/0093994) in view of Proulx et al.

6. Gas Chromatography-Mass Spectroscopy (GCMS) and Gas Chromatography-Olfactory (GCO) methods were used to evaluate the production of volatile compounds during cooking of three flavor reaction mixtures, and in particular, to evaluate the production of volatile compounds that are associated with meaty aroma. The first flavor reaction mixture contained 1% (10 mg/ml) Leghemoglobin (LegH-only); the second contained 50 mM Ribose with 50 mM Cysteine (Ribose + Cysteine); and the third contained 1% Leghemoglobin with 50 mM Ribose and 50 mM Cysteine (LegH + Ribose + Cysteine). All flavor reaction mixtures were adjusted to pH 6.5 using 50 mM of potassium phosphate buffer and 100 mM of sodium chloride buffer. Two mls of each flavor reaction mixture were prepared in 10 ml GCMS glass vials (referred to as "flavor reaction mixture samples" or "samples" hereinafter). Each sample was analyzed in duplicate.

7. An Agilent 7890A GC system coupled with a Leco TruTOF HT system was used along with a Gerstel MultiPurpose Sampler for auto-sampling. The Gerstel auto-sample was used to cook, cool, and perform HS-SPME on each of the samples. Each sample was heated to 150°C for 3 minutes with 750 rpm of agitation to "cook" the material. This was followed by a two-phase active cooling step that decreased the agitator temperature from 150°C to 50°C. The sample was extracted for 20 minutes at 50°C with 500 rpm of agitation using a 50/30 μm Divinylbenzene / Carboxen / Polydimethylsiloxane (DVB/CAR/PDMS), Stable flex, 23 Ga, Autosampler (Supleco, Cat# 57298-U) fiber.

8. Extracted samples were run on the GCMS by desorbing the SPME fiber in the Gerstel controlled CIS inlet for 6 minutes at 240°C. The desorbed sample was separated on a 60-meter wax column (Agilent, VF-Waxms 60 m x 0.25 mm x 0.25 mm, Part# CP9207) using a 35 minutes GCMS method (35°C for 2 minutes, ramp of 5C°/min until 172°C, ramp of 60C°/min until 255°C, 255°C for 4 minutes) and 1.75 mL/min Helium flow rate and splitless mode. Separated compounds were analyzed by the mass spectrometer, and all data was collected over a 14-500 μ mass range, with an acquisition rate of 10 spectra/sec, and a detector voltage off-set of 100.

9. Samples were then analyzed using Leco ChromaTOF optimized for TruTOF HT (Version 4.51.6.0) coupled with the NIST MS Search 2.2. The identity of each peak in each sample was identified in a two-step process. First, the mass spectrum of each peak with a signal

to noise greater than 50 was matched to a mass spectrum in the NIST library using a match similarity score of 650, which in my experience is a conservative match similarity score. Additionally, an internally developed calibration method was applied to the data set to confirm the identity of the compounds of interest. In the second step, the Statistical Compare function of ChromaTOF was used to align the named analytes across all samples in a set. The criteria for aligning a single peak across all samples were a similarity score (similarity between the peak spectra across all samples) of 700, a maximum retention time difference of 3 secs, and the peak must have been present in at least two samples.

10. The amount of each volatile compound was determined by averaging the signal intensities from the duplicate experiments. The amount of each volatile compound that can be attributed to Leghemoglobin (LegH)[1] was determined by using the average signal intensity for each volatile compound produced in the LegH-only sample as a baseline to standardize the average signal intensity for the same volatile compound produced in the LegH + Ribose + Cysteine sample. The fold-change in each volatile compound was determined by dividing the signal intensity produced in the presence of LegH (i.e., in the LegH + Ribose + Cysteine sample) by the signal intensity produced in the absence of LegH (i.e., the Ribose + Cysteine sample). If the signal intensity in the absence of LegH (i.e., the Ribose + Cysteine sample) was not detectable, the volatile compound produced in the presence of LegH (i.e., in the LegH + Ribose + Cysteine sample) was indicated as "novel," meaning that the volatile compound was newly produced (within the limits of detection of the technique) in the LegH + Ribose + Cysteine sample.

11. The results of the above-described experiments are shown in **Exhibit B**. The first column shows a list of volatile compounds, grouped into eight (8) different classes of chemicals. The next three columns show the amount of each volatile compound, calculated as described above, for each of the samples (LegH only, Ribose + Cysteine, and LegH + Ribose + Cysteine) followed by a column indicating the fold-change, calculated as described above, or indicating that the volatile compound is novel as described above. The next column provides, where

[1] Volatile compounds that can be attributed to LegH refer to compounds that are, independently, either not detectably produced or produced in a detectably smaller amount upon cooking compared with the control samples (e.g., LegH-alone or Ribose + Cysteine in the absence of LegH).

available, one or more peer-reviewed publications in which that particular volatile compound is associated with meaty aroma.

12. The presence of LegH resulted in the production of **twenty-eight (28)** novel volatile compounds that were not produced in the absence of LegH. The 28 novel volatile compounds can be divided into eight (8) different classes of compounds as follows. Representative volatile compounds in each class are shown below; the full list can be found in **Exhibit B**.

- *Oxygen (O)- and/or Nitrogen (N)-containing heterocyclic*: six (6) novel O- and/or N-containing heterocyclic compounds were produced (i.e., 2-methyl furan; 2-pentyl furan; bis(2-methyl-3-furyl) disulfide; 2,5-dimethyl-pyrazine; methyl-pyrazine; and 2-ethyl-5-methyl-pyrazine);
- *Sulfur (S)-containing heterocyclic*: nine (9) novel S-containing heterocyclic compounds were produced (e.g., 2-methyl-3-furanthiol; 3-thiophenemethanol; and 2-methyl-thiazole);
- *sulfides*: one (1) novel sulfide compound was produced (i.e., dimethyl sulfide);
- *aldehydes*: four (4) novel aldehydes were produced (e.g., (E,E)-2,4-hexadienal; and decanal);
- *lactones*: two (2) novel lactones were produced (i.e., 5-ethyldihydro-2(3H)-furanone; and dihydro-5-pentyl-2(3H)-furanone);
- *ketones*: three (3) novel ketones were produced (e.g., 2-octanone; and 3-nonanone);
- *alcohols*: one (1) novel alcohol was produced (i.e., p-cresol); and
- *carboxylic acids*: two (2) novel carboxylic acids were produced (i.e., hexanoic acid; and hexadecanoic acid).

Significantly, each of the 28 different novel volatile compounds have been associated, directly or indirectly, with a meaty aroma; see, for example, the references provided in **Exhibit B**. Of further significance, the presence of LegH in the flavor reaction mixture with Cysteine and Ribose resulted in the generation of two (2) novel volatile compounds upon heating: **2-methyl-3-furanthiol** and **bis(2-methyl-3-furyl)disulfide**. As noted in the Cadwallader

Declaration, which I have reviewed, both compounds are important aroma compounds in cooked meat and have extremely low odor detection thresholds of 0.7 parts-per-trillion (pptr) and 0.02 pptr, respectively (Belitz et al., 2006, Food Chemistry, Springer-Verlag, Berlin, p. 368). Both compounds usually are only present in low abundance (pptr range) in cooked meat (Tang et al., 2013, J. Sulfur Chem., 34:38-47). Despite their low abundance in meat, they are still among the most impactful aroma compounds because of their extremely low odor detection thresholds.

13. The presence of LegH in the flavor reaction mixture with Cysteine and Ribose also resulted in a synergistic and dramatic increase in the amount of **two (2)** volatile compounds produced upon heating compared to the amount of the same volatile compounds produced upon heating in the absence of LegH (i.e., in the Ribose + Cysteine sample) or in the LegH-only sample. In the presence of LegH, the amount of:

- 2-acetylthiazole was increased **2,851-fold**; and
- thiophene was increased **89-fold**.

Significantly, 2-acetylthiazole and thiophene have been associated with a meaty aroma. See, for example, the references cited in **Exhibit B**.

14. In sum, the presence of LegH with Cysteine and Ribose dramatically increased the number and amount of aroma compounds associated with meat upon cooking.

15. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: Dec 2nd 2016

Celeste Holz-Schietinger, Ph.D.

EXHIBIT A

# Celeste Holz-Schietinger, PhD

## Principal Scientist, Impossible Foods

Redwood City, CA
celeste.holz@impossiblefoods.com

Innovative R&D Scientist and Product Developer responsible for leading the Flavor Department at Impossible Foods. Technical skills include enzymology, flavor chemistry, sensory science, lipid and protein biochemistry, protein purification, analytical chemistry, metabolic pathways and small molecule identification.

## Education

Ph.D. Biochemistry, **University of California** at Santa Barbara *2007-2012*
from the Biomolecular Science and Engineering Program

B.S. Molecular Biology & Evolution, minor in Chemistry, *2001- 2005*
**The Evergreen State College**, Olympia, WA

## Research

Principal Scientist, *Impossible Foods, Dr. Pat Brown* *2015- Current*

Senior Scientist, *Impossible Foods, Dr. Peg Scott, Dr. Chris Davis* *2013- 2015*

Scientist, *Impossible Foods, Dr. Chris Davis* *2012-2013*

- R&D scientist and flavor department leader at Impossible Foods, directing flavor technology research and flavor product integration.
- Manage a team of scientists to understand the fundamental biology and chemistry of flavor perception and flavor creation. We identify the catalysis and precursors that create aroma compounds, determine how aroma compounds create particular flavors profiles, and then how to recreate these flavors in products.
- Lead chemist on the identification, characterization and manipulation of biological flavor catalysis, including heme-proteins, microbes, and enzymes.
- Support off flavor identification and removal in products and feedstock with product developers, protein biochemist and process engineers.
- Flavor product integration, leading efforts for creating meat replicas from plants that taste and smell like animal based meats, working closely with manufacturing to scale the process, and marketing to meet consumers desires.
- Previous roles also included but not limited to sensory panel leader, lipid group leader, and product developer creating nut-base cheese (Kite Hill Cheese).

**Enzymology Research Associate**, *UC Santa Barbara, Dr. Norbert Reich* *2007 –2012*

- Researched the underlying chemical mechanisms that regulate how the genetic code is translated to creates phenotypic variation in human cells; particularly, understanding the developmental enzymes (DNMT3B and DNMT3A) and their modulators.
- Identified the mechanisms and structural changes that occurred with mutated forms of DNMT3A, highly associated with diseased states that change gene expression.

- Particular specialty was the development and execution of kinetic and biophysical assays to characterize the enzymology and regulation of the *de novo* DNA methyltransferase (DNMT3A).
- Mentored and lead 6 undergraduate researchers.

**Biochemistry Visiting Associate,** *Stanford University, Dr. Pat Brown (collaboration 2008-2010) 06-11/2009*

- Global identification of RNA associated with developmental enzymes (DNMT3B and DNMT3A) through cellular differentiation and correlated to gene expression and DNA methylation patterns. Developed RNA library construction protocols for next generation sequencing, and became skilled in microarray, hES cell culture, and fluorescence microscopy.

**Scientist in Endocrinology,** *U.S. Geological Survey* *05-09/2006*

- Conducted research on the stress response of translocation on the desert tortoise, though ELISA-based assays, leading team of 5 interns.

**Molecular Biology NSF Fellow,** *University of Georgia, Dr. Travis Glenn* *05-09/2005*

- Conducted independent research on pair bonding in alligators and determining mutation rates by carrying out ABI Prism sequencing for SNP and microsatellites, multiplexed PCR, and sequence analyzes for genotyping.

**Genetics Research Assistant,** *Evergreen State College, Dr. Erik Thusen* *2004–2005*

- Independent research on the population genetics of moon jellies, gaining experience in genomic DNA purification, PCR for species identification, and phylogenetic analyzes.

**Developmental Biology Research Assistant,** *Evergreen State College, Dr. Donald Morisato* *2003–2004*

- Investigated the molecular mechanisms of generating the anterior-posterior axis in *Drosophila*, by carrying out *lac z* staining, *in situ* hybridization, and genetic crosses.

**Environmental Science Research Assistant,** *Pacific Crest Community School, Dr. Tigerin Peare* *2000–2001*

- Independent research on the *E. coli* levels in the Willamette River, Portland, OR. Data collected results in new city testing and regulations on the city water treatment facilities.

## Teaching/Mentoring Experience

**Research Mentor for Undergraduate Students,** *UC Santa Barbara* *2008-2011*

- Lead undergraduate students in research projects; taught techniques and guided experiments.

**Teaching Assistant for epigenetics, developmental & biology laboratory,** *UCSB, intermittently 2007-2010*

- Prepared lectures, gave lectures, and instructed laboratory sections.

**Teaching Assistant,** *Santa Barbara City College,* *2006 - 2007*

- Molecular biology, botany and general biology laboratories.

**Scientific Computing Specialist,** *Evergreen State College* *2003 –2006*

- Taught and helped students with science software - including biological modeling, statistics, phylogenetic, mathematical, and graphical programs.

EXHIBIT B

| Compound | Signal intensity (ND = Not detected (signal to noise of 50, ~ signal of > 20,000)) | | | Fold Increase or Novel ((LegH + Ribose + Cysteine) - (LegH))/ (Ribose + Cysteine) | References |
|---|---|---|---|---|---|
| | LegH | Ribose + Cysteine | LegH + Ribose + Cysteine | | |
| **O- and N-Heterocyclic compounds** | | | | | |
| Furan, 2-methyl- | ND | ND | 162,329 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24); Kerth et al. (2013, White Paper: Product Quality, Texas A&M University Dept of Animal Sciences); Moon et al. (2006, Food Res. Int., 39:294-308); www.thegoodscentscompany.com |
| Furan, 2-pentyl- | ND | ND | 3,574,602 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24); Moon et al. (2006, Food Res. Int., 39:294-308); Brewer (2006, "The Chemistry of Beef Flavor -- Executive Summary," National Cattlemen's Beef Association, #12814); Karahadian & Lindsay (1989, J. Amer. Oil Chem. Soc., 66:1302-8); Leduc et al. (2012, J. Sci. Food Agric., 92:2560-8); www.thegoodscentscompany.com |
| bis(2-methyl-3-furyl) disulfide* | ND | ND | 1,215,514 | Novel | Mottram (1998, Food Chem., 62:415-24); Macleod (1994, The flavour of beef in "The falvour of Meat and Meat Products," ed Shahidi); Moon et al. (2006, Food Res. Int., 39:294-308); Song et al. (2012, J. Chromatog. A, 1254:115-24); www.thegoodscentscompany.com |
| Pyrazine, 2,5-dimethyl- | ND | ND | 224,117 | Novel | Brewer (2006, "The Chemistry of Beef Flavor – Executive Summary," National Cattlemen's Beef Association, #12814); Morita et al. (2003, J. Sci. Food Agric., 83:289-97); www.thegoodscentscompany.com |
| Pyrazine, methyl- | 1049328 | ND | 12,559,346 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24); Brewer (2006, "The Chemistry of Beef Flavor -- Executive Summary," National Cattlemen's Beef Association, #12814); Morita et al. (2003, J. Sci. Food Agric., 83:289-97) |
| Pyrazine, 2-ethyl-5-methyl- | 40894 | ND | 87,684 | Novel | Van Ba et al. (2012, "Principle of meat aroma flavors and future prospect," Ch 7 in Latest Research into Quality Control, InTech Open Access Publisher) |
| **S-Heterocyclic compounds** | | | | | |
| 2-Methyl-3-furanthiol | ND | ND | 793,456 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24); Mottram (1998, Food Chem., 62:415-24); Moon et al. (2006, Food Res. Int., 39:294-308); www.thegoodscentscompany.com; |
| 2-Acetylthiazole | ND | 153,183 | 436,716,305 | 2851 | Song et al. (2012, J. Chromatog. A, 1254:115-24); McGorrin et al. (2001, Special Publication - Royal Soc. Chem., 274:67-84); Kerth et al. (2013, White Paper: Product Quality, Texas A&M University Dept of Animal Sciences); Karahadian & Lindsay (1989, J. Amer. Oil Chem. Soc., 66:1302-8); www.thegoodscentscompany.com; |
| Dihydro-3-(2H)-thiophenone | ND | ND | 1,168,594 | Novel | www.thegoodscentscompany.com; |
| Thiophene, 3-methyl- | ND | 1,127,036 | 2,650,365 | 2 | Shibamoto (1980, J. Agric. Food Chem., 28:237-43) |

| | | | | | |
|---|---|---|---|---|---|
| 3-Thiophenemethanol | ND | ND | 430,476 | Novel | Chen et al. (2000, J. Agric. and Food Chem., 48:3512-6) |
| Thiophene, 2,3-dihydro-5-methyl- | ND | ND | 11,799,570 | Novel | Elmore et al. (1999, J. Agric. Food Chem., 47:1619-25) |
| Thiophene | ND | 2,422,423 | 216,296,040 | 89 | Shibamoto (1980, J. Agric. Food Chem., 28:237-43); Macleod (1994, The flavour of beef in "The falvour of Meat and Meat products" ed Shahidi); www.thegoodscentscompany.com |
| 3(2H)-Thiophenone, dihydro-2-methyl- | ND | ND | 204,409 | Novel | www.thegoodscentscompany.com |
| 5-Methyl-2-thiophenecarboxaldehyde | ND | ND | 3,046,036 | Novel | Shibamoto (1980, J. Agric. Food Chem., 28:237-43); www.thegoodscentscompany.com; |
| 3-Methyl-2-thiophenecarboxaldehyde | ND | ND | 657,464 | Novel | Shibamoto (1980, J. Agric. Food Chem., 28:237-43); www.thegoodscentscompany.com |
| Ethanone, 1-(4,5-dihydro-2-thiazolyl)- | ND | ND | 1,304,816 | Novel | www.thegoodscentscompany.com; |
| Thiazole, 2-methyl- | ND | ND | 18,835,504 | Novel | Shibamoto (1980, J. Agric. Food Chem., 28:237-43) |
| **Sulfides** | | | | | |
| Dimethyl sulfide | ND | ND | 1,601,935 | Novel | Van Ba et al. (2012, "Principle of meat aroma flavors and future prospect," Ch 7 in Latest Research into Quality Control, InTech Open Access Publisher); Kerth et al. (2013, White Paper: Product Quality, Texas A&M University Dept of Animal Sciences); Grigorakis et al. (2003, Aquaculture, 225:109-19); Leduc et al. (2012, J. Sci. Food Agric., 92:2560-8); www.thegoodscentscompany.com |
| **Aldehydes** | | | | | |
| 2,4-Hexadienal, (E,E)- | ND | ND | 9,495,304 | Novel | Rochet & Chaintreau (2005, J. Agric. Food Chem., 53:9578-85); Karahadian & Lindsay (1989, J. Amer. Oil Chem. Soc., 66:1302-8); Grigorakis et al. (2003, Aquaculture, 225:109-19); www.thegoodscentscompany.com; |
| Benzaldehyde, 4-ethyl- | ND | ND | 24,320,418 | Novel | Morita et al. (2003, J. Sci. Food Agric., 83:289-97); www.thegoodscentscompany.com |
| Decanal | ND | ND | 26,163 | Novel | Van Ba et al. (2012, "Principle of meat aroma flavors and future prospect," Ch 7 in Latest Research into Quality Control, InTech Open Access Publisher); Morita et al. (2003, J. Sci. Food Agric., 83:289-97); Moon et al. (2006, Food Res. Int., 39:294-308); Song et al. (2012, J. Chromatog. A, 1254:115-24); Leduc et al. (2012, J. Sci. Food Agric., 92:2560-8); www.thegoodscentscompany.com |
| Undecanal | ND | ND | 813,152 | Novel | Moon et al. (2006, Food Res. Int., 39:294-308); Rochet & Chaintreau (2005, J. Agric. Food Chem., 53:9578-85); Van Ba et al. (2012, "Principle of meat aroma flavors and future prospect," Ch 7 in Latest Research into Quality Control, InTech Open Access Publisher); Morita et al. (2003, J. Sci. Food Agric., 83:289-97) |
| **Lactones** | | | | | |
| 2(3H)-Furanone, 5-ethyldihydro- | ND | ND | 72,377,175 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24) |
| 2(3H)-Furanone, dihydro-5-pentyl- | ND | ND | 31,360,192 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24) |
| **Ketones** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 2-Octanone | ND | ND | 1,242,778 | Novel | Moon et al. (2006, Food Res. Int., 39:294-308); Song et al. (2012, J. Chromatog. A, 1254:115-24); Van Ba et al. (2012, "Principle of meat aroma flavors and future prospect," Ch 7 in Latest Research into Quality Control, InTech Open Access Publisher); Karahadian & Lindsay (1989, J. Amer. Oil Chem. Soc., 66:1302-8); Grigorakis et al. (2003, Aquaculture, 225:109-19) |
| 3-Nonanone | ND | ND | 650,546 | Novel | Leduc et al. (2012, J. Sci. Food Agric., 92:2560-8); www.thegoodscentscompany.com |
| 3,5-Octadien-2-one, (E,E)- | ND | ND | 537,770 | Novel | Karahadian & Lindsay (1989, J. Amer. Oil Chem. Soc., 66:1302-8); Grigorakis et al. (2003, Aquaculture, 225:109-19); Leduc et al. (2012, J. Sci. Food Agric., 92:2560-8); www.thegoodscentscompany.com; |
| **Alcohols** | | | | | |
| p-Cresol | ND | ND | 536,008 | Novel | Kerth et al. (2013, White Paper: Product Quality, Texas A&M University Dept of Animal Sciences) |
| **Carboxylic Acids** | | | | | |
| Hexanoic acid | ND | ND | 14,935 | Novel | Moon et al. (2006, Food Res. Int., 39:294-308); Song et al. (2012, J. Chromatog. A, 1254:115-24); Brewer (2006, "The Chemistry of Beef Flavor – Executive Summary," National Cattlemen's Beef Association, #12814); Karahadian & Lindsay (1989, J. Amer. Oil Chem. Soc., 66:1302-8); Selli et al. (2009, Food Chem., 114:317-22) |
| Hexadecanoic acid | ND | ND | 1,959,921 | Novel | Song et al. (2012, J. Chromatog. A, 1254:115-24); www.thegoodscentscompany.com; |
| * in addition to being categorized as an O- and N-containing heterocyclic, bis(2-methyl-3-furyl) disulfide also can be categorized as a sulfide and as a S-containing heterocyclic compound. | | | | | |

Attorney's Docket No.: 38767-0015001 / M3CON-Track 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | 1791 |
| Serial No. | : | 14/797,006 | Examiner | : | Elizabeth A. Gwartney |
| Filed | : | July 10, 2015 | | | |
| | | | Conf. No. | : | 8496 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 35 U.S.C. § 1.132

I, Keith R. Cadwallader, Ph.D., hereby declare as follows:

1. I am currently a Professor of Food Chemistry in the Department of Food Science and Human Nutrition at the University of Illinois in Urbana, Illinois. I have held this position since 2007. I have worked and taught in the fields of Food Science, Food Chemistry and Flavor Science since 1985. Prior to my current position, I held Assistant/Associate Professor positions in Food Chemistry at Louisiana State University and Mississippi State University and was an Associate Professor at the University of Illinois.

2. I received my B.S. degree in Food Science from the University of Georgia in 1985, my M.S. degree in Food Science from the University of Florida in 1987, and my Ph.D. degree in Food Science (minor in Chemistry) from the University of Florida in 1990.

3. A copy of my curriculum vitae is attached as **Exhibit A**.

4. My research includes: chemistry and analysis of food and beverage flavors, flavor (aroma) characterization and flavor quality determination, instrumental and sensory identification and quantification of character-impact flavor compounds in foods/beverages and agricultural/ industrial materials, process flavor development, recovery of flavor constituents

from food processing by-products, development of methods to stabilize labile flavors, occurrence and mechanisms of flavor formulation in foods and beverages, technology for production of food and beverage flavors, and physical chemistry of food/beverage matrix-flavor binding, flavor release and flavor-packaging interactions. I have taught courses relating to food analysis, flavor chemistry, food products analysis, applied food chemistry, flavor and food acceptance, food composition, and flavor/color of foods.

5. I am a nationally and internationally recognized expert and scholar in the field of flavor science. I have co-edited five books and published 57 refereed book chapters and 96 refereed journal articles in the area of food flavor chemistry and analysis. My research has been published in well-respected journals in the field of flavor chemistry, including the *Journal of Agricultural and Food Chemistry*, *Food Chemistry*, *Journal of Food Science*, *Analytical Chemistry*, *Journal of Sensory Studies*, *Journal of the American Oil Chemists Society*, *Cereal Chemistry*, *Journal of Dairy Science*, *Flavour and Fragrance Journal* and others. I have presented more than 50 invited symposium talks and over 115 scientific papers at national and international scientific meetings. I am co-inventor of an invention described in a U.S. patent application related to stabilized compositions and methods of manufacture (Publication No. US 2014/0275543 A1).

6. Through my research and teaching, I have made both fundamental and applied contributions to the current understanding of flavor chemistry and analysis. In 2016, I received the University of Illinois, College of Agriculture, Consumer and Environmental Sciences, *Senior Faculty Award for Excellence in Research.* I was awarded the *2007 Stephen S. Chang Award for Excellence in Lipid or Flavor Science* from the Institute of Food Technologists. In 2010, I was

elected a *Fellow in the Agricultural and Food Chemistry Division of the American Chemical Society* in recognition of my scientific contributions to the field of agricultural and food chemistry, specifically in the area of flavor science.

7. I am a professional member of the Institute of Food Technologists and the American Chemical Society (Agricultural and Food Chemistry Division). From 2003-2005, I was the Chair and Program Chair of the Agricultural and Food Chemistry Division of the American Chemical Society. I currently serve on the editorial board of the *Flavour and Fragrance Journal* and as an associate editor of the *Journal of Food Science*.

8. In the preparation of my declaration, I have reviewed the U.S. Application Serial No. 14/797,006 ("the '006 application"), as well as the Office Action mailed June 6, 2016, in which the claims of the '006 application were rejected as being anticipated by Proulx et al. (2006, J. Agric. Food Chem., 54:1518-22) ("Proulx") and as being obvious considering Hsieh et al. (US 2012/0093994) ("the '994 application") in view of Proulx. I have also considered additional materials listed in **Exhibit B**.

9. Flavor is the integrated response to the simultaneous perception (total or combined sensation) of the taste, aroma and somatosensory (nerve response) characteristics of substances naturally present in foods. Although the peripheral sensory organs for detection of taste and smell stimuli are quite distinct, their signals are integrated in the orbitofrontal and other areas of the cerebral cortex of the brain to generate the perception of "flavor" and to mediate food recognition and overall acceptance (Chaudhari and Roper, 2010). It is generally accepted by most researchers that olfaction (aroma) plays the dominant role in the flavor of food (Spence, 2015), and aroma has been regarded as the single most important factor contributing to the

characteristic flavor of meat (Shahidi et al., 1986).

10. Gas chromatography-mass spectrometry (GC-MS) has been the method of choice for the analysis of aroma components of meat for over five decades (Cadwallader and MacLeod, 1998). Before GC-MS can be conducted, the volatile components of the product must first be isolated from the sample and then transferred to the instrument for subsequent analysis. Headspace solid phase microextraction (HS-SPME) combined with GC-MS has been widely and successfully used for analysis of aroma components of meat (Rochat et al., 2007) and "meat aroma" reaction mixtures (Jublot et al., 2010). During analysis, the GC-MS system separates the individual volatile compounds in the mixture and then the mass-spectrometer detects and characterizes each component individually, enabling both qualitative (compound identification) and quantitative (compound concentration) analyses to be performed.

11. In my opinion, Applicants discovered a "ground beef-like food product" containing no animal products and including:

0.01%-5% by weight of a heme-containing protein comprising an amino acid sequence having at least 80% sequence identity to the polypeptide set forth in SEQ ID NO:4;

a sugar, sugar alcohol, sugar acid, or sugar derivative selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, and galactose, and mixtures of two or more thereof; and

at least 10 mM of a compound selected from cysteine, cystine, selenocysteine, thiamine, methionine, and mixtures of two or more thereof; and

at least 10% or more by weight one or more plant proteins,

which has the surprising capability of promoting, upon heating, the efficient conversion of

nonvolatile flavor precursors into desirable meaty aroma compounds. This is a significant discovery since a person having ordinary skill in the art would not have anticipated that the inclusion of a heme protein would have any beneficial effect on flavor. In fact, iron, and specifically heme iron, has been most often associated with causing deleterious off-odor consequences in foods and especially meat products (Calkins, 2007). As a flavor scientist who has worked in the field for over 30 years, I consider Applicants' discovery to be completely unexpected.

12. In forming my opinion, I reviewed and considered Applicants' experiments related to their discovery and demonstration that the addition of heme protein (in some cases as leghemoglobin or LegH) is required or essential for the development of meaty aroma in a "ground beef-like food product" comprising no animal products. These experiments are described in the '006 application. In addition, I reviewed the experiments in the Declaration Under 37 CFR §1.132 of Dr. Celeste Holz-Schietinger, Ph.D. ("Holz-Schietinger Declaration").

13. The Hotz-Schietinger Declaration describes the application of state-of-the-art instrumental aroma analysis methods, specifically the aforementioned HS-SPME combined with GC-MS, to monitor the effect of LegH addition on the formation of volatile compounds, specifically those with meaty aroma characteristics, during heating (i.e., cooking). The objective was to demonstrate that LegH was capable of promoting or catalyzing the formation of meaty aroma compounds via the Maillard reaction and other thermal reactions between ribose and cysteine. Three flavor reaction systems were compared, consisting of: 1) 1% (10 mg/mL) LegH alone (**LegH control**), 2) 50 mM ribose + 50 mM cysteine alone (**Rib + Cyst**) and 3) 1% (10 mg/mL) LegH + 50 mM ribose + 50 mM cysteine (**LegH + Rib + Cyst**). The above reaction

mixtures were diluted in a buffer (50 mM potassium phosphate and 100 mM sodium chloride) and adjusted to pH 6.5, which is near the physiological pH of ground beef. A 2 mL aliquot of each reaction mixture was transferred to sample vials (sealed) which were subsequently heated (150C for 3 min) and then analyzed by HS-SPME-GC-MS.

14. It is my opinion that the above experimental approach and subsequent data analyses techniques used by Dr Celeste Holz-Schietinger are appropriate and acceptable for the purpose of evaluating and comparing aroma compound formation in the three reaction systems under heating conditions. It is also my opinion that these conditions which would simulate the cooking of a "ground beef-like food product" containing no animal products as described in the '006 application, and that the data obtained from the experimental approach would be reasonably predictive of the expected aroma compound formation from a "ground beef-like food product" containing no animal products and including the flavor reaction system components LegH, ribose, and cysteine.

15. In my opinion, Applicants' experiments in the '006 application clearly demonstrate that inclusion of LegH in the reaction mixture has the surprising result of greatly enhancing the reaction of ribose and cysteine to form a variety of volatile compounds possessing meaty aromas. Moreover, it is my opinion that Dr. Celeste Holz-Schietinger's experiments confirm these surprising results. Among the 28 compounds identified in her experiments, two in particular are well-known to possess meaty sensory characteristics and to be important and potent odorants in cooked meat. Specifically, 2-methyl-3-furanthiol (MFT) and its dimerized form bis(2-methyl-3-furyl)disulfide (MFT-MFT) are important aroma compounds in cooked meat (Tang et al., 2013). Both compounds have extremely low odor detection thresholds of 0.7

parts-per-trillion (pptr) and 0.02 pptr, respectively (Belitz et al. 2006), and are usually only present in low abundance (pptr range) in cooked meat (Tang et al., 2013). Despite their low abundance in meat they are still among the most impactful aroma compounds because of their extremely low odor detection thresholds.

16. On the basis of my considerable knowledge and experience in the field of flavor science, it is my opinion that Applicants have indeed discovered and demonstrated the unique ability of heme-protein, including LegH, to serve as an efficient catalyst or promoter of the Maillard reaction and/or other relevant thermal reactions (e.g. thiamine degradation) which can form meaty aroma compounds in a "ground beef-like food product" containing no animal products.

17. It is also my opinion that a person having ordinary skill in the art would not have anticipated or expected this discovery based on the prior art cited. My opinion takes into consideration the Proulx et al. (2006) study, which did not disclose, mention or otherwise anticipate the potential for a heme-protein to influence or promote the formation of desirable meaty aroma compounds. Furthermore, Applicants' unique flavor precursor system, in which a heme-protein is intentionally added to act as an essential promotor of meat flavor generation during cooking, was not disclosed, mentioned or otherwise anticipated in the '994 application. My opinion also takes into consideration the common understanding of those in the field that the inclusion of iron, including heme iron, has been most often associated with causing deleterious off-odor consequences in foods and especially meat products.

18. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: December 3, 2016

Keith Cadwallader

EXHIBIT A

# Keith R. Cadwallader

*Office/Laboratory:*
Department of Food Science
and Human Nutrition
University of Illinois at Urbana-Champaign
102 Agricultural Bioprocess Laboratory
1302 West Pennsylvania Avenue, Urbana, IL
Phone: 217-333-5803; e-mail: cadwlldr@illinois.edu

*Home:*
4005 Turnberry Dr.
Champaign, IL 61822

*Campus:*
102 ABL, MC-640

## Education

| | | |
|---|---|---|
| University of Florida, Gainesville, FL | Fall, 1990 | Ph.D. Food Science (Chem. minor) |
| University of Florida | Summer. 1987 | M.S. Food Science |
| University of Georgia, Athens, GA | Spring, 1985 | B.S. Food Science |

## Professional Experience

**2007-present.** Professor of Food Chemistry, Department of Food Science & Human Nutrition, University of Illinois. **Research Interests:** Chemistry and analysis of food flavor. Food flavor (aroma) characterization and flavor quality determination. Use of instrumental and sensory methods to identify and quantify character-impact flavor compounds in foods/agricultural/industrial materials. Development of process flavors. Recovery of flavor constituents from food processing by-products. Measurement and prediction of flavor diffusion, release and binding. Development of methods to stabilize labile flavors.
**1999-2007.** Associate Professor of Food Chemistry, University of Illinois.
**1996-1999.** Associate Professor of Food Science, Food Science & Technology, Mississippi State Univ.
**1994-1996.** Assistant Professor of Food Science, Mississippi State University
**1991-1994.** Assistant Professor of Food Science, Dept. Food Science, Louisiana State University.
**1985-1990.** Pre-doctoral Research Fellow, Dept. Food Science & Human Nutrition, Univ. Florida.

## Current Appointment (UIUC)

Research – 60%; Teaching – 40%

## Awards/Honors

- 2016 College of ACES Senior Faculty Award for Excellence in Research, University of Illinois,
- 2010 Elected Fellow, Agricultural and Food Chemistry Division of the American Chemical Society.
- Co-recipient, 2008 Donald A. Holt Achievement Award, Illinois Council on Food and Agricultural Research, presented to the Illinois Center for Soy Foods leadership team.
- 2007 Stephen S. Chang Award for Excellence in Lipid or Flavor Science, Institute of Food Technologists.
- Co-recipient, 2007 College of ACES Team Award for Excellence, University of Illinois, presented to the Illinois Center for Soy Foods leadership team
- Co-recipient, 2005 Bor S. Luh International Award, Institute of Food Technologists
- UIUC Incomplete list of teachers rated as excellent (Spr00, Fall00, Fall01, Spr03, Spr04, Spr05, Fall05; Spr06; Spr08; Spr10; Fall12; Fall14)
- 1996 Alpha Zeta Outstanding Teaching Award
- 1985-1990 FMC Corp. Research Fellowship Recipient
- 1984 U. Georgia Food Science Department Faculty Scholarship Recipient

## Professional Memberships

Institute of Food Technologists & IFT, Chicago Section
American Chemical Society & ACS, Division of Agricultural and Food Chemistry

**Teaching Interests and Experience**

Teaching interests include food analysis, food chemistry, flavor chemistry and analysis, and sensory evaluation of foods. Courses taught are listed below.

***University of Illinois***

FSHN 418, *Food Analysis*: *2 h lecture: 6 h lab.* Principles and application of the chemical, physical, and instrumental methods used to determine the constituents of foods; special considerations applicable to the analysis of certain foods.

FSHN 519, Flavor Chemistry and Analysis: *2 h lecture: 6 h lab.* a graduate level course that involves the discussion/demonstration of the chemistry, manufacture/delivery and analysis (sensory, instrumental, and physical) of food flavor.

***Mississippi State University***

FST 4114/6114 *Analysis of Food Products*: *2 h. lecture; 6 h lab.* Principles, methods and techniques for quantitative, physical, chemical, and/or biological analysis of food products and ingredients.

FST 4241/6241 *Applied Food Chemistry*: *2 h lab.* Basic laboratory experiments to provide understanding of the function and interactions of chemical components of food.

FST 8163 *Flavor and Food Acceptance*: *2 h lecture; 1 h demonstration.* Theory and application of sensory evaluation and analytical chemistry techniques for the analysis of food flavor.

***Louisiana State University***

FDSC 4050 *Food Composition and Analysis*: *2 h. lecture; 6 h lab.* Principles, methods and techniques for quantitative, physical, chemical, and/or biological analysis of food products and ingredients.

FDSC 7040 *Flavor and Colors of Foods*: *2 h lecture; 3 lab.* Methods of chemical, physical, and instrumental analysis of food colors and flavors; natural and synthetic flavorings and colorants.

**Research Publications**

***Books Edited (5)***

Cadwallader, K.R. and Chang, S.K.C. (Eds.). 2010. *Chemistry, Texture and Flavor of Soy.* ACS Symposium Series 1059, American Chemical Society, Washington, DC.

Cadwallader, K.R., Drake, M.A. and McGorrin, R.J. (Eds.) 2007. *Flavor of Dairy Products.* ACS Symposium Series 971, American Chemical Society, Washington, DC.

Cadwallader, K.R. and Weenen, H. (Eds.). 2003. *Freshness and Shelf Life of Foods.* ACS Symposium Series 836, American Chemical Society, Washington, DC.

Rouseff, R.L. and Cadwallader, K.R. (Eds.). 2001. *Headspace Analysis of Foods and Flavor: Theory and Practice.* Kluwer Academic/Plennum Publishers, New York.

Shahidi, F. and Cadwallader, K.R. (Eds.). 1997. *Flavor and Lipid Chemistry of Seafoods.* ACS Symposium Series 674. American Chemical Society, Washington, DC.

***Patent Applications (1)***

Cadwallader, K.R. and Fang, M.-C. 2014. Stabilized compositions and methods of manufacture. US Patent Application US 2014/0275543 A1.

***Book Chapters (57)***

Cadwallader, K.R. 2016. Flavor challenges in functional beverages. Chapter 3. In *Handbook of Functional Beverages and Human Health*. Alasalvar, C. and Shahidi, F. (Eds.), CRC Press, pp. 27-34.

Yin, Y., Cadwallader, K.R. and Fang, M.-C. 2015. A novel method for the stabilization of the potent odorant 2-acety-1-pyrroline. In *Flavour Science: Proceedings of the XIV Weurman Flavour Research Symposium*, Taylor, A.J. and Mottram, D.S (Eds.), Context Products Ltd, Leicestershire, UK, pp. 571-574.

Burnside, E. and Cadwallader, K.R. 2014. Aroma components of commercial and self-prepared rum ethers. In *Current Topics in Flavor Chemistry and Biology: Proceedings of the 9th Wartburg Symposium on Flavor Chemistry & Biology*, T. Hofmann, W. Krautwurst, D., and Schieberle, P. (Eds.), Eigenverlag Deutsche Forschungsanstalt für Lebensmittelchemie, Freising, Germany, pp. 244-249.

Moran, L., Yin, Y. Cadwallader, K.R. and Padua, G.W. 2014. Testing tools and physical, chemical, and microbiological characterization of microencapsulated systems. In *Microencapsulation in the Food Industry: A Practical Implementation Guide*. Gaonkar, A., Vasisht, N, Khare, A. and Sobel, R. (Eds.). Academic Press/Elsevier Inc., Oxford, UK, pp. 323-352.

Lorjaroenphon, Y., Hausch, B.J. and Cadwallader, K.R. 2014. Formation and stability of 2,3-dehydro-1,8-cineol in a model carbonated beverage system. In *Flavor Science: Proceedings from the XIII Weurman Flavour Research Symposium*, Elsevier, Inc. Oxford, UK.

Fang, M. and Cadwallader, K.R. 2012. Improved synthesis of deuterium-labeled alkyl pyrazines for use in stable isotope dilution analysis. In *Recent Advances in the Analysis of Foods and Flavor*. Mussinan, C. et al. (Eds.). ACS Symposium Series 1098, American Chemical Society, Washington, DC, pp. 57-69.

Lahne, J. and Cadwallader, K.R. 2012. Streamlined analysis of potent odorants in distilled alcoholic beverages. In *Chemistry and Flavor of Alcoholic Beverages.* Qian, M. et al., (Eds.). ACS Symposium Series 1104, American Chemical Society, Washington, DC, pp. 37-53.

Cadwallader, K.R., Potts, D., Brisske-BeVier, L. and Mirarefi, S. 2011. Contribution of volatile sulfur compounds to the characteristic aroma of roasted garlic. In *Volatile Sulfur Compounds in Food.* Qian, M.C., Fan, X. and Mahattanatawee, K. (Eds.). ACS Symposium Series 1068, American Chemical Society, Washington, DC, pp. 137-151.

Genthner, L.R. and Cadwallader, K.R. 2011. Structure-odor relationships of selected esters with (Z,Z)-3,6-nonadiene backbone structures. In *Advances and Challenges in Flavor Chemistry & Biology: Proceedings of the 9th Wartburg Symposium on Flavor Chemistry & Biology*, T. Hofmann, W. Meyerhof, P. Schieberle, Eds., Eigenverlag Deutsche Forschungsanstalt für Lebensmittelchemie, Garching, Germany, pp. 123-128.

Kim, H.K. and Cadwallader, K.R. 2011. Instrumental analysis of seafood flavor. In *Handbook of Seafood Quality, Safety and Health Applications.* Alasalvar, C., Shahidi, F., Miyashita, K. and Wanasundara, U. (Eds.). Blackwell Publishing Ltd., UK, pp. 50-67.

Cadwallader, K.R., Moore, J.J., Zhang, Z. and Schmidt, S.J. 2010. Comparison of spray drying and Refractance Window™ drying technologies for the encapsulation of orange oil. In *Recent Advances in Food and Flavor Chemistry: Food Flavors and Encapsulation, Health Benefits, Analytical Methods, and Molecular Biology of Functional Foods.* Ho C.-T., Mussinan, C.J., Shahidi, F. and Tratras Contis, E. (Eds.). The Royal Society of Chemistry, Cambridge, UK, pp. 246-254.

Sun, C., Cadwallader, K.R. and Kim, H. 2010. Comparison of key aroma components between soymilks prepared by cold and hot grinding methods. In *Chemistry, Texture and Flavor of Soy.* Cadwallader, K.R. and Chang, S.K.C. (Eds.). ACS Symposium Series 1059, American Chemical Society, Washington, DC, pp. 361-373.

Suppavorasatit, I. and Cadwallader, K.R. 2010. Flavor-soy protein interactions. In *Chemistry, Texture and Flavor of Soy.* Cadwallader, K.R. and Chang, S.K.C. (Eds.). ACS Symposium Series 1059, American Chemical Society, Washington, DC, pp. 339-359.

Cadwallader, K.R., Tamamoto, L.C. and Sajuti, S.C. 2010. Aroma components of fresh and stored pomegranate (*Punica granatum* L.) juice. In *Flavors in Noncarbonated Beverages.* Da Costa, N.C. and Cannon, R.J. (Eds.). ACS Symposium Series 1036. American Chemical Society, Washington, DC, pp. 93-101.

Liu, G.-L. and Cadwallader, K.R. 2010. Aroma-impact components of "Carlos" muscadine grape juice. In *Flavor and Health Benefits of Small Fruits.* Qian, M.C. and Rimando, A.M. (Eds.). ACS Symposium Series 1035, American Chemical Society, Washington, DC, pp. 63-77.

Cadwallader, K.R. and Singh, T. 2009. Flavours and off-flavours in milk and dairy products. In *Advanced Dairy Chemistry-Volume 3. Lactose, Water, Salts and Minor Constituents.* McSweeny, P.L.H. and Fox, P.F. (Eds). Springer Science+Business Media, LLC, New York, pp. 631-690.

Cadwallader, K.R. and Puangpraphant, S. 2008. Volatile compounds in tree nuts. In Tree Nut s: Composition, Phytochemicals, and Health Effects. Alasalvar, C. and Shahidi, F. (Eds.) Taylor and Francis, LLC, Boca Raton, FL, pp. 109-125.

Singh, T. and Cadwallader, K.R. 2008. Cheese. In *Dairy Processing and Quality Assurance.* Chandan, R.C., Kilara, A. and Shah, N. (Eds.), Wiley-Blackwell, Danvers, MA, pp. 273-308.

Lorjaroenphon, Y., Cadwallader, K.R., Kim, H. and Lee, S-Y. 2008. Evaluation of key odorants in chipotle pepper by quantitative analysis, calculation of odor activity values and omission studies. In *Recent Highlights in Flavor Chemistry and Biology: Proceedings of the 8th Warburg Symposium on Flavor Chemistry & Biology,* Hofmann, T., Meyerhof, W. and Schieberle, P. (Eds.). Deutche Forschungsanstalt für Lebensmittelchemie, Garching, Germany, pp. 191-200.

Zhou, Q. and Cadwallader, K.R. 2008. Measurement of flavor-soy protein interactions in low-moisture solid food systems by inverse gas chromatography. Ch. 4. In *Food Flavor: Chemistry, Sensory Evaluation and Biological Activity.* Tamura, H., Ebeler, S.E., Kubota, K. and Takeoka, G.R. (Eds.). ACS Symposium Series 988. American Chemical Society, Washington, DC., pp. 45-54.

Cadwallader, K.R. 2007. Wood smoke flavor. In *Handbook of Meat, Poultry & Seafood Quality.* Nollet, L.M.L. (Ed.) and Boylsten, T., Chen, F. Coggins, P.C., Gloria, M.B., Hyldig, G., Kerth, C.R., McKee, L.H., Hui, Y.H. (Assoc. Eds.), Blackwell Publishing, Inc., Lancaster, PA, pp. 201-210.

Cadwallader, K.R. 2007. Measuring cheese flavour. In *Improving the Flavour of Cheese.* Weimer, B. (Ed.), Woodhead Publishing Ltd., Cambridge, UK, pp. 401-412.

Cadwallader, K.R., Singh, T.K. and Jerrell, J.P. 2007. Streamlined analysis of short-, medium- and long-chain free fatty acids in Dairy Products. In *Flavor of Dairy Products.* Cadwallader, K.R., Drake, M.A. and McGorrin, R.J. (Eds.). ACS Symposium Series 971, American Chemical Society, Washington, DC. pp. 111-122.

Drake, M.A., Cadwallader, K.R., Carunchia Whetstine, M.E. 2007. Establishing links between sensory and instrumental analyses of dairy flavors: Example Cheddar cheese. In *Flavor of Dairy Products.* Cadwallader, K.R., Drake, M.A. and McGorrin, R.J. (Eds.). ACS Symposium Series, American Chemical Society, Washington, DC., pp. 51-77.

Singh, T.K., Cadwallader, K.R. and Drake, M.A. 2007. Flavor of dairy products. In *Handbook of Food Products Manufacturing: Health, Meat, Milk, Poultry, Seafood, and Vegetables.* Hui, Y.H. (Ed.), John Wiley & Sons, Inc., Hoboken, NJ, pp. 715-748.

Drake, M.A., Miracle, R.E., Caudle, A.D. and Cadwallader, K.R. 2007. Relating sensory and instrumental analyses. In *Sensory-Directed Flavor Analysis.* Marsili, R. (Ed.), CRC Press/Taylor & Francis Group, LLC, Boca Raton, FL, pp. 23-54.

Cadwallader, K.R., Gnadt, T.A. and Jasso, L. 2007. Aroma components of chipotle peppers. In *Chemistry and Flavor of Hispanic Foods.* Tunick, M. and Gonzales de Mejia, E. (Eds), ACS Symposium Series 946, American Chemical Society, Washington, DC, pp. 57-66.

Lecona-Uribe, S., Loarca-Piña, G., Arcila-Lozano, C. and Cadwallader, K.R. 2007. Chemical characterization of *Lippa graveolens* Kunth and its comparison to *Origanum vulgare* and *Origanum laevigatum herrenhausen.* In *Chemistry and Flavor of Hispanic Foods.* Tunick, M. and Gonzales de Mejia, E. (Eds), ACS Symposium Series 946, American Chemical Society, Washington, DC, pp. 45-56.

Lozano, P.R., Cadwallader, K.R. and Gonzales de Mejia, E. 2007. Identification of characteristic aroma components of Mate (*Ilex paraguariensis*) tea. In *Chemistry and Flavor of Hispanic Foods.* Tunick, M. and Gonzales de Mejia, E. (Eds), ACS Symposium Series 946, American Chemical Society, Washington, DC, 143-152.

Cadwallader, K.R., Drake, M.A., Carunchia-Whetstine, M.E. and Singh, T.J. 2006. Characterisation of Cheddar cheese flavour by sensory directed instrumental analysis and model studies. In *Flavour Science: Recent Trends.* Bredie, W.P. and Peterson, M.A. (Eds.), Developments in Food Science 43, Elsevier, New York, pp. 157-160.

Jarunrattanasri, A., Cadwallader, K.R., Theerakulkait, C. 2005. Aroma and amino acid composition of hydrolyzed vegetable protein from rice bran. In *Process and Reaction Flavors*, Weerasinghe, D.K. (Ed.), ACS Symposium Series 905, American Chemical Society, Washington, DC, pp. 83-97.

Cadwallader, K.R., Benitez, D., Pojjanapimol, S., Syriyaphan, O. and Singh, T. 2005. Characteristic aroma components of the cilantro mimics. In. *Natural Flavors and Fragrances*, Frey, C. and Rouseff, R. (Eds.), ACS Symposium Series 908, American Chemical Society, Washington, DC, pp. 117-128.

Cadwallader, K.R. 2005. Flavor and volatile metabolism in produce. Chapter 6. In *Produce Degradation: Pathways and Prevention,* Lamikanra, O., Imam, S.H. and Ukuku, D.O. (Eds.), CRC Press LLC, Boca Raton, FL, pp 155-189.

Pojjanapimol, S., Chaiseri, S. and Cadwallader, K. 2004. Heat-induced changes in aroma components of holy basil (*Ocimum sanctum* L.). Ch. 15. In *Handbook of Flavor Characterization: Sensory analysis, chemistry, and physiology*, Diebler, K.D. and Delwiche, J. (Eds.), Marcel Dekker, Inc., New York, pp. 217-230.

Singh, T.K. and Cadwallader, K.R. 2004. Ways of measuring shelf-life and spoilage. Ch. 9. In *Understanding and Measuring the Shelf-life of Food*, Steele, R. (Ed.). CRC Press LLC, Boca Raton, FL, pp. 165-183.

Cadwallader, K.R., Lopez, J.R., Menke, S.D. and Surakarnkul, R. 2003. Aroma components of wines from Chardonel - A French-American hybrid grape. In *Nutraceutical Beverages. Chemistry, Nutrition, and Health Effects*, Shahidi, F. and Weerasinghe, D.K. (Eds.), ACS Symposium Series 871. American Chemical Society, Washington, DC, Chapter 27.

Karagül-Yüceer, Y., Drake, M.A. and Cadwallader, K.R. 2002. Aroma characterization of fresh and stored nonfat dry milk. In *Freshness and Shelf Life of Foods.* Cadwallader, K.R. and Weenen, H. (Eds.), ACS Symposium Series 836, American Chemical Society, Washington, DC, pp. 108-123.

Singh, T.K. and Cadwallader, K.R. 2002. The shelf life of foods: An overview. In *Freshness and Shelf Life of Foods.* Cadwallader, K.R. and Weenen, H. (Eds.), ACS Symposium Series 836. American Chemical Society, Washington, DC, pp. 2-21.

Cadwallader, K.R. 2001. Flavor chemistry of saffron. In *Carotenoid-derived Aroma Compounds.* Winterhalter, P. and Rouseff, R.L. (Eds.). ACS Symposium Series 802, American Chemical Society, Washington, DC, pp. 220-239.

Cadwallader, K.R. and Heo, J. 2001. Aroma of roasted sesame oil: Characterization by direct thermal desorption-gas chromatography-olfactometry and sample dilution analysis. In *Gas Chromatography-Olfactometry: The State of the Art.* Leland, J.V.; Schieberle, P.; Buettner, A.; Acree, T.E. (Eds.). ACS Symposium Series 782; American Chemical Society, Washington, DC, pp. 187-202.

Cadwallader, K.R. and Shahidi, F. 2001. Identification of potent odorants in seal blubber oil by direct thermal desorption-gas chromatography-olfactometry. In *Omega-3 Fatty Acids: Chemistry, Nutrition, and Health Effects.* Shahidi, F. and Finley, J.W. (Eds.) ACS Symposium Series 788; American Chemical Society, Washington, DC, pp. 221-234.

Rouseff, R. and Cadwallader K. 2001. Headspace techniques in foods, fragrances and flavors. In *Headspace Analysis of Foods and Flavor: Theory and Practice.* Rouseff, R.L. and Cadwallader, K.R., (Eds.). Advances in Experimental Medicine and Biology, Volume 488, Kluwer Academic/Plennum Publishers, New York, pp. 1-8.

Webb, T.E. and Cadwallader, K.R. 2001. Aroma components of an oil-based grill flavoring by direct thermal desorption-gas chromatography-olfactometry and sample dilution analysis. In *Headspace Analysis of Foods and Flavor: Theory and Practice.* Rouseff, R.L. and Cadwallader, K.R., (Eds.). Kluwer Academic/Plennum Publishers, New York, pp. 143-150.

Cadwallader, K.R. 2000. Flavor recovery from crustacean processing by-products. In *Seafood in Health and Nutrition. Transformation in Fisheries and Aquaculture: Global Perspectives.* Shahidi, F. (Ed.). ScienceTech Publishing Co., St. John`s, Canada, Ch. 12, pp. 159-168.

Cadwallader, K.R. 2000. Enzymes and flavor biogenesis in fish. In *Seafood Enzymes.* Haard, N.F. and Simpson, B.K. (Eds.). Marcel Dekker, Inc., New York, pp. 365-383.

Cadwallader, K.R., Surakarnkul, R., Yang, S.-P., and Webb, T. 1999. Character-impact aroma components of coriander (*Coriandrum sativum*) herb. In *Flavor and Chemistry of Ethnic Foods.* Shahidi, F. and Ho, C.-T. (Eds.). Plenum Publishing Corporation, New York.

Cadwallader, K.R. and Baek, H.H. 1998. Aroma-impact components in cooked tailmeat of freshwater crayfish (*Procambarus clarkii*). In *Food Flavors: Formation, Analysis and Packaging Influences.* Contis, E.T., Ho, C.T.; Mussinan, C.J., Parliment, T.H., Shahidi, F., Spanier, A.M. (Eds.), Elsevier Science B.V., Amsterdam.

Cadwallader, K.R. and Howard, C.L. 1998. Analysis of aroma-components of light-activated milk. In *Flavor Analysis: Developments in Isolation and Characterization.* Mussinan, C.J. and Morello, M.J. (Eds.). ACS Symposium Series 705. American Chemical Society, Washington, DC, pp. 343-358.

Cadwallader, K.R. and MacLeod, A.J. 1998. Instrumental methods for analyzing the flavor of muscle foods. Ch. 16. In *Flavor of Meat, Meat Products, and Seafoods, 2nd Ed.* Shahidi, F. (Ed.). Blackie Academic & Professional, New York.

Baek, H.H. and Cadwallader, K.R. 1997. Character-impact aroma components of crustaceans. In *Flavor and Lipid Chemistry of Seafoods,* Shahidi, F. and Cadwallader, K.R. (Eds.). ACS Symposium Series. 674. American Chemical Society, Washington, DC, pp. 85-94.

Weng, H.-J., Cadwallader, K.R., Baek, H.H., D'Abramo, L.R.D., and Sullivan, J.A. 1997. Manipulating the flavor of freshwater crustacea using postharvest seawater acclimation. In *Flavor and Lipid Chemistry of Seafoods,* Shahidi, F. and Cadwallader, K.R. (Eds.). ACS Symposium Series. 674. American Chemical Society, Washington, DC, pp. 120-130.

Cha, Y.J., Lee, G.H., Cadwallader, K.R. 1997. Aroma-active compounds in salt-fermented anchovy. In *Flavor and Lipid Chemistry of Seafoods,* Shahidi, F. and Cadwallader, K.R. (Eds.). ACS Symposium Series. 674. American Chemical Society, Washington, DC, pp. 131-147.

Shahidi, F. and Cadwallader, K.R. 1997. Flavor and lipid chemistry of seafoods: An overview. In *Flavor and Lipid Chemistry of Seafoods,* Shahidi, F. and Cadwallader, K.R. (Eds.). ACS Symposium Series 674. American Chemical Society, Washington, DC, pp. 1-8.

Cadwallader, K.R., Baek, H.H., and Cai, M. 1997. Characterization of saffron flavor by aroma extract dilution analysis. In *Spices: Flavor Chemistry and Antioxidant Properties.*, Risch, S.J. and Ho, C.-T. (Eds.). ACS Symposium Series 660. American Chemical Society, Washington, DC, pp. 66-79.

Braddock, R.J. and Cadwallader, K.R. 1995. Bioconversion of citrus d-limonene. In *Fruit Flavors: Biogenesis, Characterization, and Authentication,* Rouseff, R.L. and Leahy, M.M. (Eds.). ACS Symposium Series 596. American Chemical Society, Washington, DC, pp. 142-147.

Cadwallader, K.R., Baek, H.H., Chung, H.Y., and Moody, M.W. 1994. Contribution of lipid-derived components to the flavor of alligator meat. In *Lipids in Food Flavors*, Ho, C.T. and Hartman, T.G. (Eds.) ACS Symposium Series No. 558. American Chemical Society, Washington, DC, pp. 186-195.

Cadwallader, K.R. and Braddock, R.J. 1992. Enzymatic hydration of (4R)-(+)-limonene to (4R)-(+)-α-terpineol. In *Developments in Food Science: Food Science and Human Nutrition*, Volume 29, Charalambous, G. (Ed.) Elsevier, New York, pp. 571-584.

***Journal Articles (96)***

Erten, E.S and Cadwallader, K.R. 2017. Identification of predominant aroma components of raw, dry roasted and oil roasted almonds. Food Chem. 217:244-253.

Kelly, L. and Cadwallader, K.R. 2016. Identification and quantitation of potent odorants in spearmint oil. J. Agric. Food Chem. (ubmitted).

Donovan J, Cadwallader K, Lee Y, 2016. Volatile retention and morphological properties of microencapsulated tributyrin varied by wall material and drying method. J. Food Sci. 81: E643-E650.

Suteebut, N., Chanthachum, S., Intarapichet, K., Cadwallader, K.R. and Miller, M.J. 2016. Factors affecting conjugated linoleic acid production by *Lactobacillus plantarum* GSI 303. Intern. Food Res. J. 23: 1739-1746.

Erten, E.S and Cadwallader, K.R. 2017. Identification of predominant aroma components of raw, dry roasted and oil roasted almonds. Food Chem. 217:244-253.

Lapsongphon, N., Yongsawatdigul, J. and Cadwallader, K.R. 2015. Identification and characterization of the aroma-impact components of Thai fish sauce J. Agric. Food Chem. 65: 2628-2638.

Thompson-Witrick, K.A., Rouseff, R.L., Cadwallader, K.R., Duncan, S.E., Eigel, W.N., Tanko, J.M. and O'Keefe, S.F. 2015. Comparison of two extraction techniques, solid-phase microextraction versus continuous liquid-liquid extraction/solvent-assisted flavor evaporation, for the analysis of flavor compounds in gueuze lambic beer. J. Food Sci. 80: C571-C576.

Tinchan, P., Lorjaroenphon, Y., Cadwallader, K.R. and Chaiseri, S. 2015. Changes in the profile of volatiles of canned coconut milk during storage. J. Food Sci. 80: C49-C54.

Lorjaroenphon, Y. and Cadwallader, K.R. 2015. Typical odorants of cola-flavored carbonated beverages - Part I. Identification of potent odorants by aroma extract dilution analysis. J. Agric. Food Chem. 63: 769-775.

Lorjaroenphon, Y. and Cadwallader, K.R. 2015 Typical odorants of cola-flavored carbonated beverages - Part II. Characterization of potent odorants by quantitative analysis and sensory studies of aroma reconstitution and omission models. J. Agric. Food Chem. 63: 776-786

Hausch, B.H., Lorjaroenphon, Y. and Cadwallader, K.R. 2015. Flavor chemistry of lemon-lime carbonated beverages. J. Agric. Food Chem. 63: 112-119.

Kiatbenjakul, P., Intarapichet, K-O. and Cadwallader, K.R. 2015 Characterization of potent odorants in male giant water bug (*Lethocerus indicus* Lep. and Serv.), an important edible insect of Southeast Asia. Food Chem. 168: 639-647

Buttara, M., Intarapichet, K.-O. and Cadwallader, K.R. 2014. Characterization of potent odorants in Thai chempedak fruit (*Artocarpus integer* Merr.), an exotic fruit of Southeast Asia. Food Research International 66: 388-395.

Fang, M. and Cadwallader, K.R. 2014. Stabilization of the potent odorant 2-acetyl-1-pyrroline and structural analogs by complexation with zinc halides. J. Agric. Food Chem. 62: 8808-8813.

Yang, X., Lorjaroenphon, Y., Cadwallader, K.R., Wang, X., Zhang, Y., Lee, J. 2014. Analysis of particle-borne odorants emitted from concentrated animal feeding operations. Sci. Total Environment 490, 322-333.

Kiatbenjakul, P., Intarapichet, K.-O. and Cadwallader, K.R. 2014. Indentification of potent sulfur-containing odorants in scent glands of edible giant water bug, Lethcerus indicus (Lep. and Serv.). Flavour Frangrance J. 29(2): 107-113.

Fang, M. and Cadwallader, K.R. 2013. Convenient synthesis of stable deuterium labeled alkyl pyrazines for use in stable isotope dilution assays. J. Agric. Food Chem. 61: 3580-3588.

Kim, H., Cadwallader, K.R., Kido, H, Watanabe, Y. 2013. Effect of addition of commercial rosemary extracts on potent odorants in cooked beef. Meat Sci. 94: 170-176.

Lee, H., Kim, H., Cadwallader, K.R., Feng, H. and Martin, S.E. 2013. Sonication in combination with heat and low pressure as an alternative pasteurization treatment – Effect on Escherichia coli K12 inactivation and quality of apple cider. Ultrasonics Sonochemistry 20(4): 1131-1138.

Lapsongphon, N., Cadwallader, K.R., Rodtong, S., and Yongsawatdigul, J. 2013. Characterization of protein hydrolysis and odor-active compounds of fish sauce inoculated with *Virgibacillus* sp. SK37 under reduced salt content. J. Agric. Food Chem. 61: 6604-6613.

Suppavorasatit, I., Lee, S.-Y. and Cadwallader, K.R. 2013. Effect of enzymatic protein deamidation on protein solubility and flavor binding properties of soymilk. J. Food Sci. 78: C1-C7.

Suppavorasatit, I. and Cadwallader, K.R. 2012. Effect of enzymatic deamidation of soy protein by potein-glutaminase on the flavor-binding properties of the protein under aqueous conditions. J. Agric. Food Chem. 60: 7817-7823.

Kaewka, K., Theerakulkait, C. and Cadwallader, K.R. 2011.Effect of drying and proline addition on aroma volatile compounds of acid-hydrolyzed rice bran protein concentration. International J. Food Sci. Technol. 46: 1654-1660.

LaFond, S., Jerrell, J.P., Artz, W.E. and Cadwallader, K.R. 2011. Formation of 4-hydroxy-2-(*E*)-nonenal in a corn-soy oil blend: A controlled heating study using a French fried potato model. J. Am. Oil Chem. Soc. 88: 763-772.

Suppavorasatit, I., Gonzales de Mejia, E. and Cadwallader, K.R. 2011. Optimization of the enzymatic deamidation of soy protein by protein-glutaminase and its effect on the functional properties of the protein. J. Agric. Food Chem. 59: 11621-11628.

Lee, J.-W., Thomas, L.C., Jerrell, J., Feng, H., Cadwallader, K.R. and Schmidt, S.J 2010. Investigation of thermal decomposition as the kinetic process that causes the loss of crystalline structure in sucrose using a chemical analysis approach (Part II). J. Agric. Food Chem. 59: 702-712.

Kaewka, K., Theerakulkait, C. and Cadwallader, K.R. 2009. Effect of preparation conditions on composition and sensory aroma characteristics of acid hydrolyzed rice bran protein concentrate. J. Cereal Sci. 50: 56-60.

Kim, H., Cadwallader, K.R., Jeong, E.-J. and Cha, Y.-J. 2009. Effect of refrigerated and thermal storage on the volatile profile of commercial aseptic Korean soymilk. J. Food Sci. Nutr. 14: 76-85.

Watcharananun, W, Cadwallader, K.R., Huangrak, K. Kim, H. and Lorjaroenphon, Y. 2009. Identification of predominant odorants in Thai desserts flavored by smoking with "tian op", a traditional Thai scented candle. J. Agric. Food Chem. 57: 996-1005.

Radadia, A., Masel, R.I., Shannon, M.A., Jerrell, J.P. and Cadwallader, K.R. 2008. Micromachined GC columns for fast separation of organophosphonate and organosulfur compounds. Anal. Chem. 80: 4087-4094.

Song, H., Cadwallader, K.R., and Singh, T.K. 2008. Odour-active compounds in Jinhua ham. Flavour Fragr. J. 23: 1-6.

Stetzer, A.J., Cadwallader, K., Singh, T.K., McKeith, F.K. and Brewer, M.S. 2008. Effect of enhancement and ageing on flavor and volatile compounds in various beef muscles.J. Meat Sci. 79: 13-19.

Rotsatchakul, P., Chaiseri, S. and Cadwallader, K.R. 2008. Identification of characteristic aroma components of Thai fried chili paste. J. Agric. Food Chem. 56: 528-536.

Song, H. and Cadwallader, K.R. 2007. Aroma components of American country ham. J. Food Sci. 73: C29-C35.

Lozano, P.R., Miracle, E.R., Krause, A.J., Drake M.A. and Cadwallader, K.R. 2007. Effect of cold storage and packaging material on the major aroma components of sweet cream butter. J. Agric. Food Chem. 55: 7840-7846.

Jarunrattanasri, A., Theerakulkait, C. and Cadwallader, K.R. 2007. Aroma components of acid-hydrolyzed vegetable protein made by partial hydrolysis of rice bran protein. J. Agric. Food Chem. 55: 3044-3050.

Lozano, P.R., Drake, M.A., Benitez, D. and Cadwallader, K.R. 2007. Instrumental and sensory characterization of heat-induced odorants in aseptically packaged soy milk. J. Agric. Food Chem. 55: 3018-3050.

Ni, Z., Jerrell, J.P., Cadwallader, K.R. and Masel, R.I. 2007. Metal-organic frameworks as adsorbents for trapping and preconcentration of organic phosphonates. Anal. Chem. 79: 1290-1293.

Ugarte-Romero, E., Feng, H., Martin, S., Cadwallader, K.R. and Robinson, S. 2006. Inactivation of *Escherichia coli* with power ultrasound in apply cider. J. Food Sci. 71(2): E102-108.

Zhou, Q., Lee, S.-Y. and Cadwallader, K.R. 2006. Inverse gas chromatographic evaluation of the influence of soy protein on the binding of selected butter flavor compounds in a wheat soda cracker system. J. Agric. Food Chem. 54: 5516-5520.

Zhou, Q. and Cadwallader, K.R. 2006. Effect of flavor compound chemical structure and environmental relative humidity on the binding of volatile flavor compounds to dehydrated Soy protein isolates. J. Agric. Food Chem. 54: 1838-1843.

Bohn DM, Cadwallader KR, and Schmidt SJ. 2005. Development and validation of a dynamic vapor sorption-fast gas chromatography-flame ionization detection method for rapid analysis of volatile release from glassy matrices. J. Agric. Food Chem. 53: 3149-3155.

Bohn DM, Cadwallader KR, and Schmidt SJ. 2005. Use of DSC, DVS-DSC, and DVS-fast GC-FID to evaluate the physicochemical changes that occur in artificial cherry Durarome® upon humidification. J Food Sci. 70(2): E109-16.

Carunchia-Whetstine, M.E., Cadwallader, K.R. and Drake, MA. 2005. Characterization of aroma compounds responsible for rosey/floral flavor in Cheddar cheese. J. Agric. Food Chem. 53: 3126-3132.

Singh, T.K., Young, N.D., Drake, K.R. and Cadwallader, K.R. 2005. Production and sensory characterization of a bitter peptide from beta-casein. J. Agric. Food Chem. 53: 1185-1189.

Alasalvar, C., Odabasi, A.Z., Demir, N., Balaban, M.O., Shahidi, F. and Cadwallader, K.R. 2004. Volatiles and flavor of five Turkish hazelnut varieties as evaluated by descriptive sensory analysis, electronic nose, and dynamic headspace analysis/gas chromatography-mass spectrometry. J. Food Sci. 69:99-106.

Avsar, Y.K., Karagul-Yuceer, Y., Drake, M.A., Singh, T.K., Yoon, Y. and Cadwallader, K.R. 2004. Characterization of nutty flavor in Cheddar cheese. J. Dairy Sci. 87:1999-2010.

Brisske, L.K., Lee, S.-Y., Klein, B.P., Cadwallader, K.R. 2004. Development of a prototype high-energy, nutrient dense food product for emergency relief. J. Food Sci. 69(9): S361-S367.

Zhou, Q. and Cadwallader, K.R. 2004. Inverse gas chromatographic method for measurement of interactions between soy protein isolate and selected flavor compounds under controlled relative humidity. J. Agric. Food Chem. 52: 6271-6277.

Zhou, Q., Guthrie, B. and Cadwallader, K.R. 2004. Development of a system for measurement of permeability of aroma compounds through multilayer polymer films by coupling dynamic vapor sorption with purge-and-trap/fast gas chromatography. Packaging Technol. Sci. 17:175-185.

Singh, T.K., Drake, M.A. and Cadwallader, K.R. 2003. Flavor of Cheddar cheese: A chemical and sensory perspective. Comprehensive Reviews in Food Science and Food Safety (CRFSFS) 2: 139-162.

Karagul-Yuceer, Y., Vlahovich, K.N., Drake, MA and Cadwallader, K.R. 2003. Characteristic aroma components of rennet casein. J. Agric. Food Chem. 51: 6797-6801.

Karagul-Yuceer, Y., Drake, M.A. and Cadwallader, K.R. 2004. Evaluation of the character-impact odorants in skim milk powder by sensory studies on model mixtures. J. Sensory Stud. 19:1-14.

Kiatsrichart, S., Brewer, M.S., Cadwallader, K.R. and Artz, W.E. 2003. Pan frying stability of NuSun oil, a mid-oleic sunflower oil. J. Am. Oil. Chem. Soc. 80(5): 479-483.

Alasalvar, C., Shahidi, F. and Cadwallader, K.R. 2003. Comparision of natural and roasted Turkish Tombul hazelnut (*Corylus avellana* L.) volatiles and flavor by DHA/GC/MS and descriptive sensory analysis. J. Agric. Food Chem. 51(17): 5067-5072.

Drake, M.A., Karagul-Yuceer, Y., Cadwallader, K.R., Civille, G.V., and Tong, P.S. 2003. Determination of the sensory attributes of dried milk powders and dairy ingredients. J. Sensory Studies 18(3): 199-216.

Karagul-Yuceer, Y., Drake, M.A. and Cadwallader, K.R. 2003. Aroma-active components of liquid Cheddar whey. J. Food Science 68(4): 1215-1219.

Drake, M.A., Gerard, P.D., Wright, S., Cadwallader, K.R., and Civille, G.V. 2002. Cross validation of a sensory language for Cheddar cheese. J. Sensory Studies 17: 215-227.

Karagul-Yuceer, Y., Cadwallader, K.R. and Drake, M.A. 2002. Volatile flavor components of stored nonfat dry milk. J. Agric. Food Chem. 50(2): 305-312.

Wu, Y.-F.G. and Cadwallader, K.R. 2002. Characterization of the aroma of a meat-like process flavoring from soybean-based enzyme-hydrolyzed vegetable protein. J. Agric. Food Chem. 50(10): 2900-2907.

Zhou, Q., Wintersteen, C.L. and Cadwallader, K.R. 2002. Identification and quantification of aroma-active components that contribute to the distinct malty flavor of buckwheat honey. J. Agric. Food Chem. 50(7): 2016-2021.

Baek, H.H., Kim, C.J., Ahn, B.A., Nam, H.S., Cadwallader, K.R. 2001. Aroma extract dilution analysis of a beeflike process flavor from extruded enzyme-hydrolyzed soybean protein. J. Agric. Food Chem. 49(2): 790-793.

Drake, M.A., McInvale, S.C., Gerard, P.D., Cadwallader, K.R. and Civille, G.V. 2001. Development of a descriptive language for Cheddar cheese. J. Food Sci. 66(9): 1422-1427.

Lee, G.H., Suriyaphan, O., Cadwallader, K.R. 2001. Aroma components of cooked tail meat of American lobster (*Homarus americanus*). J. Agric. Food Chem. 49(9): 4324-4332.

Karagul-Yuceer, Y., Drake, M.A. and Cadwallader, K.R. 2001. Aroma-active components of nonfat dried milk. J. Agric. Food Chem. 49(6): 2948-2953.

Suriyaphan, O., Drake, M.A., Chen, X.Q., Cadwallader, K.R. 2001. Characteristic aroma components of British Farmhouse Cheddar cheese. J. Agric. Food Chem. 49(3): 1382-1387.

Suriyaphan, O., Cadwallader, K.R., Drake, M.A. 2001. Lecithin associated flavors in fermented dairy products. J. Food Sci. 66(4): 517-523.

Suriyaphan, O., Drake, M.A., Cadwallader, K.R. 2001. Lipid oxidation of deoiled soy lecithin by lactic acid bacteria. Lebensm.-Wiss. u.-Technol. 34: 462-468.

Yoo, S.K., Day, D.F., and Cadwallader, K.R. 2001. Bioconversion of α- and β-pinene by *Pseudomonas* sp. strain PIN. Process Biochem. 36: 925-932.

Wu, Y.-F., Baek, H.H. and Cadwallader, K.R. 2000. Development of a meatlike process flavoring from soybean-based enzyme-hydrolyzed vegetable protein. J. Food Sci. 65:1220-1227.

Kim, D.S., Baek, H.H., Ahn, C.B., Byun, D.S., Jung, K.J., Lee, H.G., Cadwallader, K.R., Kim, H.R. 2000. Development and characterization of a flavoring agent from oyster cooker effluent. J. Agric. Food Chem. 48: 4839-4843.

Bergman, C.J., Delgado, J.T., Bryant, R., Grimm, C., Cadwallader, K.R. and Webb, B.D. 2000. A rapid gas chromatographic technique for quantifying 2-acetyl-1-pyrroline and hexanal in rice (*Oryza sativa*, L.). Cereal Chem. 77(4): 454-458.

Baek, H.H. and Cadwallader, K.R. 1999. Contribution of free and glycosidically bound volatile compounds to the aroma of muscadine juice. J. Food Sci. 64: 441-444.

Baek, H.H. and Cadwallader, K.R. 1999. Optimization of the enzymatic hydrolysis of crab processing by-products using Flavourzyme™. Food Sci. Biotechnol. 8: 43-46.

Drake, M.A. Karagül-Yüceer, Chen, X.Q., and Cadwallader, K.R. 1999. Characterization of desirable and undesirable lactobacilli from cheese in fermented milk. Lebensm-Wiss. u.-Technol. 32: 433-439

Suriyaphan, O., Drake, M.A., Cadwallader, K.R. 1999. Identification of volatile off-flavors in reduced-fat Cheddar cheese containing lecithin. Lebensm-Wiss. u.-Technol. 32: 250-254.

Baek, H.H. and Cadwallader, K.R. 1998. Roasted chicory aroma evaluation by gas chromatography/mass spectrometry/olfactometry. J. Food Sci. 63: 234-237.

Cha, Y.J., Kim, H., and Cadwallader, K.R. 1998. Aroma-active compounds in Kimchi during fermentation. J. Agric. Food Chem. 46: 1944-1953.

Cha, Y.J. and Cadwallader, K.R. 1998. Aroma-active compounds in skipjack tuna sauce. J. Agric. Food Chem. 46: 1123-1128.

Tan, Q., Day, D.F., and Cadwallader, K.R. 1998. Bioconversion of (R)-(+)-limonene by *P. digitatum* (NRRL 1202). Process Biochem. 33: 29-37.

Baek, H.H., Cadwallader, K.R., Marroquin, E., and Silva, J.L. 1997. Identification of predominant aroma compounds in muscadine grape juice. J. Food Sci. 62: 249-252.

Baek, H.H. and Cadwallader, K.R. 1997. Aroma volatiles in cooked alligator meat. J. Food Sci. 62: 321-325.

Baek, H.H. and Cadwallader, K.R. 1996. Volatile compounds in flavor concentrates produced from crayfish-processing byproducts with and without protease treatment. J. Agric. Food Chem. 44: 3262-3267.

Andrews, L.S., Cadwallader, K.R., Grodner, R.M., and Chung, H.Y. 1995. Microbial and sensory quality of ground ginger as affected by gamma irradiation. J. Food Sci. 60: 829-832.

Baek, H.H. and Cadwallader, K.R. 1995. Enzymatic hydrolysis of crayfish processing by-products. J. Food Sci. 60: 929-935.

Cadwallader, K.R., Tan, Q., Chen, F., and Meyers, S.P. 1995. Evaluation of the aroma of cooked spiny lobster tail meat by aroma extract dilution analysis. J. Agric. Food Chem. 43: 2432-2437.

Cha, Y.J. and Cadwallader, K.R. 1995. Volatile components in salt-fermented fish and shrimp pastes. J. Food Sci. 60: 19-24.

Chung, H.Y., Chen, F., and Cadwallader, K.R. 1995. Cooked blue crab claw meat aroma compared with lump meat. J. Food Sci. 60: 289-291, 299.

Cadwallader, K.R. and Xu, Y. 1994. Analysis of volatile components in fresh grapefruit juice by purge and trap/gas chromatography. J. Agric. Food Chem. 42: 782-784.

Chung, H.Y. and Cadwallader, K.R. 1994. Aroma extract dilution analysis of blue crab claw meat volatiles. J. Agric. Food Chem. 42: 2867-2870.

Kim, H.R., Baek, H.H., Cadwallader, K.R., Meyers, S.P., and Godber, J.S. 1994. Improved flavor extractibility from crab waste using the hepatopancreatic enzyme of crawfish, *Procambarus clarkii*. J. Food Sci. 59: 91-96.

Cha, Y.J., Cadwallader, K.R., and Baek, H.H. 1993. Volatile flavor components in snow crab cooker effluent and effluent concentrate. J. Food Sci. 58: 525-530.

Chung, H.Y. and Cadwallader, K.R. 1993. Volatile components in blue crab (*Callinectes sapidus*) meat and processing by-product. J. Food Sci. 58: 1203-1207, 1211.

Braddock, R.J. and Cadwallader, K.R. 1992. Citrus by-products manufacture for food use. Food Technol. 46(2): 105-110.

Cadwallader, K.R., Braddock, R.J. and Parish, M.E. 1992. Isolation of α-terpineol dehydratase from *Pseudomonas gladioli*. J. Food Sci. 57: 241-244, 248.

Cadwallader, K.R., Braddock, R.J., Parish, M.E. and Higgins, D.P. 1989. Bioconversion of (+)-limonene by *Pseudomonas gladioli*. J. Food Sci. 54: 1241-1245.

Braddock, R.J., Temelli, F. and Cadwallader, K.R. 1986. Citrus essential oils – a dossier for materials safety data sheets. Food Technol. 40(11): 114-116.

***Other Publications (UIUC, 2000-present)***

Cadwallader, K.R., Hausch, B. and Yin, Y. 2015. Quest for stability of 2-acetyl-1-pyrroline: The key odorant in aromatic rice and pandan. Proceedings: FIAC 2015 "Innovative ASEAN food research towards the world," Bangkok, Thailand, June 18-19, pp. 560-567.

Cadwallader, K.R., Klein, B.P., Khanna, P., Chen, D., Nash, M., Puzey, M. and Sullivan, C.L. 2005. *Around the World with Soy.* Illinois Center for Soy Foods, University of Illinois, University Board of Trustees, Urbana, IL.

Singh, T.K., Cadwallader, K.R., and Drake, M.A. 2005. Cheddar cheese flavour. *Cheeseworks* Volume 9, number 4. (A publication of the Australian Cheese Technology Program.)

Cadwallader, K.R., Klein, B.P., Sullivan, C.L., Nash, M., Khanna, P. and Weingartner, K.E. 2004. *Soy for the Last Minute Chef.* Illinois Center for Soy Foods, University of Illinois, University Board of Trustees, Urbana, IL.

Klein, B.P., Cadwallader, K.R., Chen, D., Khanna, P., Sullivan, C.L. and Weingartner, K.E. 2003. *Baking with Soy.* Illinois Center for Soy Foods, University of Illinois, University Board of Trustees, Urbana, IL.

Klein, B.P., Cadwallader, K.R., Chen, D., Khanna, P., Sullivan, C.L. and Weingartner, K.E. 2002. *Textured Vegetable Protein in the American Kitchen.* Illinois Center for Soy Foods, University of Illinois, University Board of Trustees, Urbana, IL.

Klein, B.P., Cadwallader, K.R., Chen, D., Khanna, P. and Weingartner, K.E. 2002. *Tofu in the American Kitchen.* Illinois Center for Soy Foods, University of Illinois, University Board of Trustees, Urbana, IL.

Miller, G.Y., Robert, M.J., Maghirang, R.G., Riskowski, G.L., Heber, A.J., and Cadwallader, K.R. Characterization of odor and gas emitting potential from mechanically ventilated deep and shallow pit swine finishing buildings in Illinois. In *Livestock Environment VI: Proceedings of the 6th International Symposium* (21-23 May 2001, Louisville, Kentucky, USA), Stowell, R.R., Bucklin, R. and Bottcher, R.W., Eds., May 21, 2001, pp. 664-670, ASAE Publication Number 701P0201.

***Invited Talks***

Cadwallader, K.R., Yin, Y., Hausch, B. and Chen, F. 2016. Assuring accuracy in the quantitation of the unstable odorant 2-acetyl-1-pyrroline in aromatic rice. ACS Symposium: *Flavor Stability: Chemical Changes in Flavor Molecules, Food-Flavor Matrix Interactions, Flavor Encapsulation.* 252nd Americal Chemical Society Meeting. Philadelphia, PA, August 21-25.

Cadwallader, K.R. 2016. Occurrence, formation and stabilization of the potent odorant 2-acetyl-1-pyrroline. Meeting of the Illinois Heartland Local Section of the American Chemical Society, Bloomington, IL, May 16, 2016.

Ickes, C. and Cadwallader, K.R. 2016. Characterizing aroma components of rum. ACS Symposium: *Flavor Chemistry of Alcoholic Beverages.* 251st American Chemical Society Meeting, San Diego, CA, March 13-17.

Cadwallader, K.R., Hausch, B. and Yin, Y. Quest for stability of 2-acetyl-1-pyrroline: The key odorant in aromatic rice and pandan. 17th Food Innovation Asia Conference 2015, Bangkok, Thailand, June 18-19.

Ickes, C. and Cadwallader, K.R. 2015. Understanding the effects of ethanol-flavor interactions on flavor perception in alcoholic beverages. ACS Symposium: *Challenges in Applied Flavor Sciences.* ACS National Meeting, Boston, MA, August 16-20, AGFD paper no. 297.

Pang, X., Wu, J. and Cadwallader, K.R. 2014. Identification of predominant contributors to off-odors formed in thermally processed melon juice. ACS Symposium: *Chemical Changes During Processing.* 248th American Chemical Society Meeting, San Francisco, CA, August 10-14. AGFD paper no. 177.

Cadwallader, K.R. and Lapsongphon, N. 2012. Identification of key odorants in fish sauce. US-Korea Conference (UKC) 2012, Los Angeles, August 8-11.

Fang, M. and Cadwallader, K.R. 2011. Convenient synthesis of stable deuterium labeled alkyl pyrazines for use in stable isotope dilution assays. ACS Symposium: *Recent Advances in Analysis of Food Flavors.* 242nd American Chemical Society Meeting, Denver, CO, August 28 – September 1, 2011, AGFD paper no. 11.

Hausch, B. and Cadwallader, K.R. 2010. Flavor chemistry of lemon-lime flavored carbonated beverages. ACS Symposium: *Symposium Honoring Prof. Terry E. Acree on the Occasion of His 70th Year.* 240th ACS National Meeting, Boston, MA, August 22-26, AGFD paper no. 40.

Lahne, J. and Cadwallader, K.R. 2010. Streamlined analysis of potent odorants in distilled alcoholic beverages. ACS Symposium: *Flavor Chemistry of Alcoholic Beverages*. 240th ACS National Meeting, Boston, MA, August 22-26, AGFD paper no. 106.

Cadwallader, K.R. and Kim, H. 2010. Flavor chemistry of fish sauce. ACS Symposium: *Fermented Foods.* 239th ACS National Meeting, San Francisco, CA, March 21-25, AGFD paper no. 112.

Cadwallader, K.R. 2010. Flavor chemistry of tree nuts. IFT Symposium: *Nuts: Phytochemicals, Health Effects and Flavor.* IFT Annual Meeting and Food Expo, Chicago, IL, July 17-20, paper no. 054-05.

Lozano, P.R. and Cadwallader, K.R. 2009. Effect of deamidation on binding of flavor compounds by dehydrated soy protein isolates. ACS Symposium: *Food Proteins and Food-based Protein Chemistry* 237th ACS National Meeting, Finley, J., organizer, Salt Lake City, UT, March 22-26.

Cadwallader, K.R. 2008. Sensory evaluation of aroma models for flavor characterization. *Symposium in Honor of Ronald Buttery G. Kenneth Recipient of the 2008 Spencer Award for Outstanding Achievement in Agricultural and Food Chemistry*, Kansas City Section, American Chemical Society, Kansas City, MO, Oct 27.

Cadwallader, K.R. 2008. AGFD and 100 years of chemical research on grains and legumes. ACS Symposium: *AGFD 100th Anniversary Symposium*, Brine, C. and Tunick, M.H., organizers, 236th ACS National Meeting, Philadelphia, PA, August 17-21.

Liu, Y and Cadwallader, K.R. 2008. Aroma components of "Carlos" muscadine (*Vitis rotundifolia* Michx) grape juice. ACS Symposium: Flavor and Health Benefits of Small Fruits, Rimando, A.M. and Qian, M.C., organizers, 236th ACS National Meeting, Philadelphia, PA, August 17-21.

Lozano, P.R. and Cadwallader, K.R. 2008. Flavor binding by soy proteins. ACS Symposium: Chemistry, Texture and Flavor of Soy, Cadwallader, K.R. and Chang, S. K. C. Chang, organizers, 236th ACS National Meeting, Philadelphia, PA, August 17-21.

Watcharananun, W., Cadwallader, K.R. and Huangrak, K. 2008. Predominant odorants in Thai desserts flavored by smoking with *tian op*, a traditional Thai scented candle. ACS Symposium: *Recent developments in flavor chemistry*, Cadwallader, K.R., organizer, 235th ACS National Meeting, New Orleans, LA, April 6-10.

Cadwallader, K.R. Lozano, P.R. and Kim, H. 2007. Challenges in the isolation and identification of key aroma components of complex functional foods. ACS Symposium: *Food Bioactives and Nutraceuticals: Production, Chemistry, Analysis and Health Effects: Symposium Honoring Fereidoon Shahidi*, Rimando, A.M., organizer. 234th ACS National Meeting, Boston, MA, August 19-23, AGFD Paper 92.

Cook, S., Cadwallader, K.R. and Kim, H. 2007. Identification of key thermally-derived odorants in cooked chicken liver. ACS Symposium: *Thermal Generation of Flavors and Off-flavors,* Ho, C.-T., Raghavan, S., McGorrin, R.J., organizers. 234th ACS National Meeting, August 19-23. AGFD Paper 206.

Cadwallader, K.R., Lorjaroenphon, Y., Kim, H. and Lee, S-Y. 2007. Evaluation of key odorants in chipotle pepper by quantitative analysis, calculation of odor-activity values and omission studies. 8th Wartburg Symposium on Flavor Chemistry & Biology, Eisenach, Germany, February 28 – March 2.

Cadwallader, K.R. 2007. Protein-based functional beverages and flavoring considerations. In IFT Symposium: *Functional Beverages and Human Health.* Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 28 - August 1, Session-Paper 174-02.

Cadwallader, K.R. 2006. Chemical and sensory characterization of food aroma: An academic approach. Meeting of the Society of Flavor Chemists, Chicago, IL, October 19.

Cadwallader, K.R. 2006. Flavor chemistry of fish and shellfish. ACS Symposium: Molecular Cuisine. (Tunick, M.H., Risch, S.J. and Johnson, S.C., organizers). 232nd ACS National Meeting, San Francisco, CA, September 10-14, AGFD paper 61.

Cadwallader, K.R. and Zhou, Q. 2006. Characteristic aroma components of tree nuts. ACS Symposium: Nutrition and Sensory Quality of Nuts. (Pattee, H.E.; Shahidi, F.; Yu, L., organizers). 331st ACS National Meeting, Atlanta, GA, March 26 – March 30, AGFD paper 40.

Cadwallader, K.R. 2006. Modern techniques to characterize complex food flavor systems. International Symposium on *Functional Foods*, ATAM (Nutrition Society of Mexico) and Institute of Food Technologists, Mexico City, Mexico, August 17.

Rotsachakul, P., Cadwallader, K.R. and Chaiseri, S. 2005. Comparison of DHS and solvent extraction-SAFE for GCO-dilution analysis of key aroma components of Thai fried chili paste. ACS Symposium: *Aroma-active Compounds in Foods and Reaction Flavors: Formation, Measurement and Stability.* (Ho, C.-T., Weerasinghe, D.K. and Cadwallader, K.R., organizers). 330th ACS National Meeting, Washington, DC, August 28 – September 1, AGFD paper 9.

Cadwallader, K.R., Bordignon, J.R., Wang, P. and Sugiharto, R. 2005. Identification of odorants responsible for off-flavor of corn gluten meal. ACS Symposium: *Grain-based Products: Health and Flavor, and Safety Aspects* (Cadwallader, K.R., Schieberle, P. and Morello, M.J., organizers). 330th ACS National Meeting, Washington, DC, August 28 – September 1, AGFD paper 167.

Cadwallader, K.R., Drake, M.A., Carunchia-Whetstine, M.E. and Singh, T.J. 2005. Characterisation of Cheddar cheese flavour by sensory directed instrumental analysis and model studies. 11th Weurman Flavour Research Symposium, Roskilde, Denmark, June 21-24.

Gnadt, T.A., Jasso, L. and Cadwallader, K.R. 2005. Characteristic aroma components of chipotle peppers. ACS Symposium: *Chemistry and Flavor of Hispanic Foods* (de Mejia, E. and Tunick, M.H., organizers). 229th ACS National Meeting, San Diego, CA, March 13-17.

Lozano, P.R., Nicolalde, C.L. and Cadwallader, K.R. 2005. Identification of characteristic aroma components of mate (*Ilex paraguariensis*) tea. ACS Symposium: *Chemistry and Flavor of Hispanic Foods* (de Mejia, E. and Tunick, M.H., organizers). 229th ACS National Meeting, San Diego, CA, March 13-17.

Lecona-Uribe, S., Loarca-Piña, G., Arcila-Lozano, C.C. and Cadwallader, K.R. 2005. Chemical composition of essential oil from Mexican orégano. ACS Symposium: *Chemistry and Flavor of Hispanic Foods* (de Mejia, E. and Tunick, M.H., organizers). 229th ACS National Meeting, San Diego, CA, March 13-17.

Cadwallader, K.R. Importance of sample preparation technique on the composition of aroma extracts from fresh herbs. ACS Sympsosium: *Challenges in Herb Research – Chemical Analysis and Quality* (Ho, C.T. and Hwang, L.S., organizers). 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004.

Cadwallader, K.R., Jarunrattanasri, A. and Theerakulkait, C. 2003. Aroma components of HVP made from rice bran protein. ACS Symposium: *Processed/Reaction Flavors, Ingredients and Intermediate Reactions.* (Weerasinghe, D.K. and Sucan, M.K., organizers). 226th ACS National Meeting, New York, NY, September 7-11.

Cadwallader, K.R. and Pojjanapimol, S. 2003. Characteristic aroma components of the cilantro mimics. ACS Symposium: *Natural Flavor and Fragrance Ingredients: Chemistry, Production and Application.* (Frey, C. and Rouseff, R.L., organizers). 226th ACS National Meeting, New York, NY, September 7-11.

Cadwallader, K.R. Relating Cheddar cheese flavor to chemical components. IFT Symposium: *Flavor Chemistry of Dairy Products.* (Drake, M.A., organizer). Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 12-16, #52-5.

Cadwallader, K.R., Pojjanapimol, S. and Chaiseri, S. 2002. Heat-induced changes in holy basil aroma components. ACS Symposium: *Challenges in the Characterization of Flavor Compound.* (Deibler, K.D. and Delwiche, J., organizers). 224th ACS National Meeting, Boston, MA, August 18-22.

Cadwallader, K.R., Zhou, Q. and Huda, M.S. 2002. Measuring flavor release from microencapsulants under controlled environmental conditions. ACS Symposium: *Controlled Release Systems for Foods.* (Shefer, S. and Yildiz, M.E., organizers). 223rd ACS National Meeting, Orlando, FL, April 7-11.

Cadwallader, K.R., Brehart, D.M., Schmidt, S.J. and Huda, M.S. 2002. Volatile release from a sucrose encapsulated flavoring. IFT Symposium: *Use of Carbohydrates for Encapsulation and Sustained Release.* (Obanni, M. and Asquith, T.N., organizers). Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #67-1.

Cadwallader, K.R., Lopez, J.R. and Menke, S.D. 2001. Aroma components of wines from Chardonel, a French-American hybrid grape variety. ACS Symposium: *Chemistry and Flavor of Nutritional Beverages.* (Shahidi, F. and Weerasinghe, D., organizers). 222nd ACS National Meeting, Chicago, IL, August 26-31.

Guthrie, B. and Cadwallader, K.R. 2001. Measuring flavor retention in dry food systems. IFT Symposium: *Developments in the Analysis of Complex Flavor Systems*. (Cadwallader, K.R. and McGorrin, R.J., organizers). Annual Meeting of the Institute of Food Technologies, New Orleans, LA, June 23-27, #76-2.

Cadwallader, K.R. 2001. Use of SPME Technology to Evaluate Antioxidant Effectiveness. Symposium: *Antioxidant Analysis*, (Engeseth, N.J., organizer). 92nd AOCS Annual Meeting and Expo, Minneapolis, MN, May 13-16.

Karagul-Yuceer,Y., Drake, M.A. and Cadwallader, K.R. 2001. Aroma characterization of fresh and stored nonfat dry milk. ACS Symposium: *Freshness and Shelf-life of Foods.* (Weenen, H. and Cadwallader, K.R., organizers). 222nd ACS National Meeting, Chicago, IL, August 26-30.

Cadwallader, K.R. 2000. Flavor Chemistry of Saffron. Symposium: *Carotenoid-Derived Aroma Compounds.* (Winterhalter, P. and Rouseff, R., organizers). 219th ACS National Meeting, San Francisco, CA, March 26-30, paper #46 AGFD.

Cadwallader, K.R. 1999. Sample dilution analysis for identification of aroma-impact components of edible oils. ACS Symposium: *Advances in Gas Chromatography/Olfactometry.* (Leland, J., Acree, T.E., organizers). 218th ACS National Meeting, New Orleans, LA, August 22-26.

Cadwallader, K.R. and Shahidi, F. 1999. Identification of potent odorants in seal blubber oil by direct thermal desorption-gas chromatography-olfactometry. ACS Symposium: *Chemistry and Nutrition of Highly Unsaturated Fatty Acids.* (Shahidi, F. and Finley, J.W., organizers). 217th ACS National Meeting, Anaheim, CA, March 21-25.

Cadwallader, K.R. and Howard, C.L. 1997. Analysis of aroma-active compounds in light-activated milk. ACS Symposium: *Challenges in the Isolation and Characterization of Flavor Compounds.* (Mussinan, C.J. and Morello, F., organizers). 214th National Meeting of the American Chemical Society, Las Vegas, NV, September 7-11.

Baek, H.-H. and Cadwallader, K.R. 1996. Character-impact aroma compounds of crustacea. ACS Symposium: *Flavor and Lipid Chemistry of Seafoods.* (Shahidi, F. and Cadwallader, K.R., organizers). 212th National Meeting of the American Chemical Society, Orlando, FL, August 25-29.

Cha, Y.J., Lee, G.H. and Cadwallader, K.R. 1996. Aroma-active compounds in salt-fermented anchovy. ACS Symposium: *Flavor and Lipid Chemistry of Seafoods.* (Shahidi, F. and Cadwallader, K.R., organizers). 212th National Meeting of the American Chemical Society, Orlando, FL, August 25-29.

Wang, H.-J., Cadwallader, K.R., Baek. H.H., D'Abramo, L.R. and Sullivan, J.A. 1996. Manipulating the flavor of crustacea using postharvest seawater acclimation. ACS Symposium: *Flavor and Lipid Chemistry of Seafoods.* (Shahidi, F. and Cadwallader, K.R., organizers). 212th National Meeting of the American Chemical Society, Orlando, FL, August 25-29.

Cadwallader, K.R. and Howard, C.L. 1996. Characterization of saffron flavor by aroma extract dilution analysis. ACS Symposium: *Spices: Flavor Chemistry and Antioxidant Properties.* (Risch, S.J. and Ho, C.T., organizers). 211th National Meeting of the American Chemical Society, New Orleans, LA, March 24-28.

Cadwallader, K.R., Baek, H.H., Chung, H.Y. and Moody, M.W. 1993. Contribution of lipid-derived components to the flavor of alligator meat. ACS Symposium: *Lipids and Food Flavors.* (Ho, C.T. and Hoffman, T.G., organizers). 205th National Meeting of the American Chemical Society, Denver, CO.

Braddock, R.J. and Cadwallader, K.R. 1993. Bioconversion of citrus d-limonene. Symposium paper presented at the 206th National Meeting of the American Chemical Society, Chicago, IL.

Braddock, R.J. and Cadwallader, K.R. 1991. Citrus by-products manufacture for food use. Symposium paper presented at the 52nd Annual Meeting of the Institute of Food Technologists, Dallas, TX, June 1-5.

***Volunteered Abstracts***

Kelley, L. and Cadwallader, K.R. 2016. Identification and quantitation of potent odorants in spearmint oils. 11th Wartburg Syposium on Flavor Chemistry & Biology, Eisenach, Germany, June 21-24.

McKenna, S. and Cadwallader, K.R. 2016. Identification and characterization of mint lactones: Trace-level odor-important compounds in peppermint oil. IFT Annual Meeting and Food Expo, Chicago, IL, July 17-19, paper no. PO2-020

Ickes, C., Lee, S. and Cadwallader, K.R. Novel creation of rum flavor lexicon through the use of web-based material. IFT Annual Meeting and Food Expo, Chicago, IL, July 17-19, paper no. P03-111

Yu, L., Thomas, L., Yin, L, Jerrell, J., Cadwallader, K. and Schmidt, S. 2015. Impact on sucrose crystal composition and chemistry on its thermal behavior. IFT Annual Meeting and Food Expo, Chicago, IL, July 11-14, paper no. 046-093.

Yu, L., Thomas, L., Yin, L, Jerrell, J., Cadwallader, K. and Schmidt, S. 2015. Impact on sucrose crystal composition and chemistry on its thermal behavior. IFT Annual Meeting and Food Expo, Chicago, IL, July 11-14, paper 046-093.

Cadwallader, K.R. and Fang, M.-C. 2014. A novel and attractive method for the stabilization of the potent odorant 2-acetyl-1-pyrroline. 14th Weurman Flavor Research Symposium, Cambridge, UK, September 15-19.

Donovan, J.D., Cadwallader, K.R. and Lee, Y. 2014. Improvement of protein microcapsule structure and core retention through the use of inulin. IFT Annual Meeting and Food Expo, New Orleans, LA, June 20-25, paper 181-01.

Erten, E. and Cadwallader, K.R. 2014. Characterization of aroma components of raw, dry roasted, and oil roasted almonds using solvent assisted flavor evaporation (SAFE) and aroma extract dilution analysis (AEDA). IFT Annual Meeting and Food Expo, New Orleans, LA, June 20-25, paper 206-26.

Lu, Y., Lee, J., Thomas, L., Jerrell, J., Cadwallader, K.R. and Schmidt, S.J. 2014. Investigating the thermal decomposition differences between beet and cane sugars using HPLC. IFT Annual Meeting and Food Expo, New Orleans, LA, June 20-25, paper 050-07.

Rosales, E., Cadwallader, K.R. and Engeseth, N. 2014. Effect of ultrasonic application on fatty acid composition and aroma compounds of dark chocolate. IFT Annual Meeting and Food Expo, New Orleans, LA, June 20-25, paper 206-94.

Burnsides, E. and Cadwallader, K. 2012 Comparison of aroma compounds in rums and rum ethers. IFT Annual Meeting and Food Expo, Las Vegas, NV, paper no. 193-28.

Su, C., Padua, G. and Cadwallader, K. 2012. Zein applications in flavor encapsulation. IFT Annual Meeting and Food Expo, Las Vegas, NV, paper no. 228-23.

Cadwallader, K.R., Hausch, B. and Lorjaroenphon, Y. 2011. Identification, characterization and relative aroma impact of 2,3-dehydro-1,8-cineol in lemon-lime flavored carbonated beverages. 13th Weurman Flavor Research Symposium, Zaragoza, SPAIN, September 26-30.

Suppavorasatit, I., deMejia, E. and Cadwallader, K.R. 2011. Effect of enzymatic deamidation of soy protein isolate by protein-glutaminase on the functional properties of the protein. IFT Annual Meeting and Food Expo, New Orleans, LA, June 11-14, paper no. 236-57.

Lapsongphon, N., Yongsawatdigul, J. and Cadwallader, K.R. 2011. Aroma characterization of premium fish sauce. IFT Annual Meeting and Food Expo, New Orleans, LA, June 11-14, paper no. 236-61.

Tinchan, P., Chaiseri, S. and Cadwallader, K.R. 2011. Quantification of δ-lactones in canned coconut milk by stable isotope dilution assay-GC-MS. IFT Annual Meeting and Food Expo, New Orleans, LA, June 11-14, paper no. 236-64.

Lorjaroenphon, Y. and Cadwallader, K.R. 2011. Identification of potent odorants in cola flavored carbonated beverages. IFT Annual Meeting and Food Expo, New Orleans, LA, June 11-14, paper no. 236-73.

Gao, Y., Cadwallader, K.R. and Schmidt, S.J. 2011. Investigating the chemical and physical stability of glass encapsulated spray-dried flavors stored below their glass transition temperatures. IFT Annual Meeting and Food Expo, New Orleans, LA, June 11-14, paper no. 290-18

Lee, H., Kim, H., Cadwallader, K.R. and Feng, H. 2011. Analysis of aroma compounds of apple cider treated by thermal-pasteurization, manosonication, thermosonication, and manothermosolication. IFT Annual Meeting and Food Expo, New Orleans, LA, June 11-14, paper no. 293-14.

Cadwallader, K.R. 2010. Potent odorants in soymilk as affected by processing and storage. *Nutraceuticals, Ingredients, Challenges, Formulations, Flavours and Health Effects.* International Conference, Exhibition and Short Course on Nutraceuticals and Functional Foods, Denpasar, Bali, Indonesia, October 11 – 12, paper no. 92.

Genthner, E.R. and Cadwallader, K.R. 2010. Characterizing aroma components of fresh-cut watermelon. 9th Wartburg Symp. on Flavor Chemistry & Biology, Eisenach, Germany, April 13-16.

He, Y., Garces, M., Toshkov, S., Kim, H., Cadwallader, K.R., Engeseth, N., Parker, T. and Jackson, M. 2010. Impact of irradiation processing on papaya nectar flavor. IFT Annual Meeting and Food Expo, Chicago, IL, July 17-20, paper no. 188-11

Kim, H. and Cadwallader, K.R. 2010. Comparison of key odorants between commercial aseptic Korean and American soy milks. IFT Annual Meeting and Food Expo, Chicago, IL, July 17-20, 188-05

Tinchan, P., Chaiseri, S. and Cadwallader, K.R. 2010. Changes in the volatile profile of canned coconut milk during storage. IFT Annual Meeting and Food Expo, Chicago, IL, July 17-20, 188-14.

Cadwallader, K.R. 2009. Flavor challenges in functional and nutraceutical beverages. International Conference and Exhibition on Nutraceuticals and Functional Foods 2009, International Society for Nutraceuticals & Functional Foods, San Francisco, CA, October 31-November 4, paper 87.

LaFond, S., Cadwallader, K. and Artz, W. 2009. The formation of 4-HNE in frying oils: A controlled study using a French fry model. 110th AOCS Annual Meeting & Expo, Orlando, FL, May 3-6.

Choi, I.-S., Kim, H. and Cadwallader, K.R. 2009. Comparison of the aroma components between dairy and soy yogurt. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 6-9, #024-02.

Lorjaroenphon, Y., Moy, M., Rosales, E. and Cadwallader, K.R. 2009. Identification of the key aroma components of fresh and baked Bartlett pear. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 6-9, #057-15.

Lozano, P.R. and Cadwallader, K.R. 2009. Effect of nonenzymatic deamidation of soy protein isolate on the binding of selected flavor compounds. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 6-9, #024-12

Lozano, P. and Cadwallader, K. 2008. Binding interactions of selected sulfur compounds with soy protein isolate under controlled relative humidity. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 28 – July 1, #006-12.

Carrasco Hernandez, G. and Cadwallader, K.R. 2008. Headspace reduction by different terpenoids of the main volatile sulfur compounds responsible for garlic breath. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 28 – July 1, #006-24.

Waimaleongora-Elk, P, Herrera Corredor, J., Prinyawiwatkul., W., Suvanich, V. and Cadwallader, K. Sensory attributes driving acceptance and purchase intent of watermelon juice containing no added sugar. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 28 – July 1, #138-12

Cadwallader, K.R. and Puangpraphant, S. 2008. Changes in the aroma components of pecans during roasting. 12th Weurman Flavour Research Symposium, Interlaken, Switzerland, July 1-4

Kim, H., Cadwallader, K.R. and Kido, H. 2008. Effect of commercial rosemary extract powders on formation of lipid-derived odorants in cooked pork sausages during cold storage. 235th ACS National Meeting, New Orleans, LA, April 6-10.

Carrasco, G. and Cadwallader, K.R. 2007. Mechanism of action of menthone in ameliorating oral cavity malodor caused by consumption of garlic. 234th ACS National Meeting, Boston, MA, August 19-23.

Lozano, P.R., Miracle, E.R., Krause, A.J. and Drake, M.A. 2007. Effect of cold storage and packaging material on the major aroma components of sweet cream butter. 234th ACS National Meeting, Boston, MA, August 19-23.

Gnadt, T.A., Lee, S.-Y. and Cadwallader, K.R. 2007. Effects of commercial masking agents and lactones on soymilk aroma and flavor. Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 28 - August 2, #4-224.

Hong, L., Sajuti, S.C. and Cadwallader, K.R. 2007. Identification of characteristic aroma components of Pomegranate (Punica granatum). Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 28 - August 2, #3-187

Mosca, C., Esgro, S. and Cadwallader, K.R. 2007. Flavor Characterization of unrefined shea butters. American Oil Chemists' Society's (AOCS) 98th Annual Meeting and Expo, Quebec City, QC, Canada, May 13-16.

Andrae, L.M., Cadwallader, K.R. and Engeseth, N.J. 2006. Flavor changes of stored dark chocolate by dynamic headspace sorption – gas chromatography/mass spectrometry. Annual Meeting of the Institute of Food Technologists, Orlando, FL, June 24-28, #39F-12.

Lozano, P. and Cadwallader, K.R and Drake, M.A. 2006. Instrumental and sensory characterization of heat-induced odorants in aseptic packaged soymilk. Annual Meeting of the Institute of Food Technologists, Orlando, FL, June 24-28, #39F-12.

Gnadt, T.A., Jasso, L. and Cadwallader, K.R. 2005. Comparison of direct solvent extraction and dynamic headspace sampling for the analysis of characteristic aroma components of chipotle pepper. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, July 16-20, #17D-34.

Klein, B.P., Khanna, P., Cadwallader, K.R. and Endres, J.M. 2005. Reducing fat in school lunches by using soy-enhanced entrees. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, July 16-20, #70E-27.

Nowak, M.C., Singh, T.K. and Cadwallader, K.R. 2005. Identification of potent odorants in commercial hickory and mesquite liquid smoke. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, July 16-20, #17D-36.

Song, H. and Cadwallader, K.R. 2005. Aroma components of American country-style ham. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, July 16-20, #17D-35

Yu, X., Song, Y.S. and Cadwallader, K.R. 2005. Identification of the characteristic aroma components of commercial dried California bay leaves (*Laurus nobilis* L.). Annual Meeting of the Institute of Food Technologists, New Orleans, LA, July 16-20, #17D-19.

Zhou, Q. and Cadwallader, K.R. 2005. Application of IGC for measurement of binding of volatile flavor compounds by soy proteins in low-moisture food systems. 229$^{th}$ ACS National Meeting, San Diego, CA, March 13-17.

Bohn, D.M. Cadwallader, K.R. and Schmidt, S.J. 2004. Kinetic analysis of benzaldehyde release in artificial cherry Durarome® upon humidification using dynamic vapor sorption-fast gas chromatography-flame ionization detection. Annual Meeting of the Institute of Food Technologists, Las Vegas, NV, July 12-16, #114B-27.

Lopez, J.R., Cadwallader K.R. and Menke, S.D. 2004. Menke Aroma-impact components of Illinois Frontenac wine. Annual Meeting of the Institute of Food Technologists, Las Vegas, NV, July 12-16, #83D-3.

Singh, T.K., Young, N.D., Drake, M.A., Cadwallader, K.R. 2004. Production of a bitter peptide from casein and its sensory characterization. Annual Meeting of the Institute of Food Technologists, Las Vegas, NV, July 12-16, #17B-17.

Ugarte-Romero, E.E. Feng, H, Martin, S.E. and Cadwallader, K.R. 2004. Power ultrasound as an alternative for apple cider pasteurization. Annual Meeting of the Institute of Food Technologists, Las Vegas, NV, July 12-16, #32-10.

Yoon, Y., Carunchia-Whetstine, M.E., Friedeck, K.G., Drake, M.A. and Cadwallader, K.R. 2004. Characterization of aroma-active compounds in fresh sweet cherry cultivars. Annual Meeting of the Institute of Food Technologists, Las Vegas, NV, July 12-16, #114B-3.

Zhou, Q. and Cadwallader, K.R. 2004. Investigation of flavor-soy protein interactions under controlled relative humidity by inverse gas chromatography (IGC). Annual Meeting of the Institute of Food Technologists, Las Vegas, NV, July 12-16, # 114B-2.

Brisske, L.K., Lee, S.Y., Klein, B.P. and Cadwallader, K.R. 2003 Consumer ratings of energy bars: Should the bar be raised? Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 12-16, #12-2.

Bohn, D.M., Cadwallader, K.R. and Schmidt, S.J. 2003. Measurement of volatile release from an amorphous carbohydrate matrix as a function of relative humidity using dynamic vapor sorption technology. Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 12-16, #12-2.

Singh, T.K., Drake, M.A. and Cadwallader, K.R. 2003. Characterization of aroma components of Muenster cheese by aroma extract dilution and headspace dilution analyses. Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 12-16, #71-3.

Suriyaphan, O., Zhou, Q. and Cadwallader, K.R. 2003. Identification of key aroma components of *Piper betel* L. leaf. Annual Meeting of the Institute of Food Technologists, Chicago, IL, July 12-16, #45C-16.

Drake, M.A., Karagul-Yuceer, Y., Civille, G.V., Cadwallader, K.R. and Tong, P.S. 2002. Development of a descriptive sensory language for milk powders. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #100D-2.

Karagul-Yuceer, Y., Drake, M.A. and Cadwallader, K.R. 2002. Evaluation of the character-impact odorants in nonfat dried milk by sensory studies on model mixtures. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #12-10.

Karagul-Yuceer, Y., Vlahovich, K., Drake, M.A. and Cadwallader, K.R. 2002. Compounds responsible for musky off-odor of rennet casein. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #15B-12.

Karagul-Yuceer, Y, Cadwallader, K.R. and Drake, M.A. 2002. Odor-active compounds of liquid whey. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #61B-4.

Pojjanapimol, S., Chaiseri, S. and Cadwallader, K.R. 2002. Aroma components of distilled essential oil of Holy basil. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #61B-12.

Zhou, Q., Cadwallader, K.R. and Guthrie, B.D. 2002. Simultaneous measurement of permeability of aroma compound mixtures through polymer packaging films. Annual Meeting of the Institute of Food Technologists, Anaheim, CA, June 15-19, #100B-8.

Benitez, D. and Cadwallader K.R. 2001. Aroma-active components of Vietnamese coriander (*Polygonum odoratum*). Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #88A-14.

Benitez, D., Kappes, S. and Cadwallader, K.R. 2001. Aroma of dried peaches. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #44C-34.

Chen, D., Andrae, L., Suriyaphan, O., Weingartner, K. and Cadwallader, K. 2001. Characteristic aroma components of vegetable soybean (edamame). Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #88A-17.

Drake, M.A., Gerard, P.D., Wright, S., Cadwallader, K.R. and Civille, G.V. 2001. Cross validation of a sensory language for Cheddar cheese. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #73G-19.

Grady, J., Klein, B.P. and Cadwallader, K.R. 2001. Bitterness and astringency thresholds for soy isoflavones. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #98-2.

Karagul-Yuceer, Y, Cadwallader, K.R. and Drake, M.A. 2001. Identification of volatile off-flavor compounds of nonfat dried milks. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #88A-3.

Suvanich, V., Maciel-Pedrote, I., Cadwallader, K.R., Moser, E.B., Thongthai, C. and Prinyawiwatkul, W. 2001. Aroma indices of Southeast Asian fish sauces. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #73F-16.

Suvanich, V., Maciel-Pedrote, I., Cadwallader, K.R., Moser, E.B., Thongthai, C. and Prinyawiwatkul, W. 2001. Developnebt if fish sauces quantitative descriptive sensory aroma profile. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #73G-34.

Zhou, X., Winterstein, C. and Cadwallader, K.R. 2001. Aroma of buckwheat honey. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #88A-12.

Zhu, L., Robbins, K. and Cadwallader, K.R. 2001. Effects of soy protein isolate on headspace aroma components of cooked ground beef patties. Annual Meeting of the Institute of Food Technologists, New Orleans, LA, June 23-27, #88A-18.

Drake, M.A., McIngvale, S.C., Cadwallader, K.R. and Civille, G.V. 2000. Development of a descriptive language for Cheddar cheese. Book of Abstracts, Annual Meeting of the Institute of Food Technologists, Dallas, TX, June 10-14, #11-3.

Suriyaphan, O., Cadwallader, K.R. and Drake, M.A. 2000. Lipid oxidation of deoiled soy lecithin in fermented milk systems. Book of Abstracts, Annual Meeting of the Institute of Food Technologists, Dallas, TX, June 10-14, #14B-32.

Cadwallader, K.R. and Thongthai, C. 2000. Comparison of aroma-active headspace components of three types of fish sauces. Book of Abstracts, Annual Meeting of the Institute of Food Technologists, Dallas, TX, June 10-14, #36-3.

Chen, X.Q., Drake, M.A. and Cadwallader, K.R. 2000. Characteristic aroma components of English Farmhouse Cheddar Cheeses. Book of Abstracts, Annual Meeting of the Institute of Food Technologists, Dallas, TX, June 10-14, #78C-4.

Karagul, Y., Drake, M.A. and Cadwallader, K.R. 2000. Aroma-active components of nonfat dry milk powders. Book of Abstracts, Annual Meeting of the Institute of Food Technologists, Dallas, TX, June 10-14, #78C-6.

Cadwallader, K.R. and Jung, J. 1999. Evaluation of warmed-over flavor in chicken wings by sensory and instrumental methods. 60th Annual Meeting of the Institute of Food Technologists, Chicago, IL, #50A-13, p. 122.

Wu, Y.F., Baek, H.H. and Cadwallader, K.R. 1999. Development of a meat-like process flavoring from soybean-based hydrolyzed vegetable protein. 60th Annual Meeting of the Institute of Food Technologists, Chicago, IL, #50A-9, p.121.

Suriyaphan, O., Cadwallader, K.R. and Drake, M.A. 1999. Lecithin associated off-flavors in fermented dairy products—A model study. 60th Annual Meeting of the Institute of Food Technologists, Chicago, IL, #17-2, p. 31.

Cadwallader, K.R. and Suriyaphan, O. 1998. Aroma-impact components of loroco. 59th Annual Meeting of the Institute of Food Technologists, Atlanta, GA, #45-2, p. 97.

Surakarnkul, R. and Cadwallader, K.R. 1998. Release of glycosidically-bound aroma compounds during fermentation of muscadine juice. 59th Annual Meeting of the Institute of Food Technologists, Atlanta, GA, #72-18, p. 180.

Suriyaphan, O., Drake, M.A., and Cadwallader, K.R. 1998. Identification of volatile off-flavors in reduced fat cheeses containing lecithin. 59th Annual Meeting of the Institute of Food Technologists, Atlanta, GA, #72-31, p. 183.

Baek, H.H. and Cadwallader, K.R. 1997. Free and glycosidically bound volatile aroma compounds in muscadine grape juice. 58th Annual Meeting of the Institute of Food Technologists, Orlando, FL, #23D-6, p.63.

Cai, M. and Cadwallader, K.R. 1997. (Z)-3-Nonenal and (Z,Z)-3,6-nonadienal: Character-impact aroma compounds in watermelon. 58th Annual Meeting of the Institute of Food Technologists, Orlando, FL, #23D-9, p.64.

Cha, Y.J., Kim, H., and Cadwallader, K.R. 1997. Aroma-active compounds in Kimchi during aging. 58th Annual Meeting of the Institute of Food Technologists, Orlando, FL, #23D-13, p.65.

Baek, H.H., Kim, C.J., Ahn, H.S., Nam, H.S., and Cadwallader, K.R. 1997. Aroma extract dilution analysis of beef-like process flavor from extruded enzymatically hydrolyzed soybean protein. 58th Annual Meeting of the Institute of Food Technologists, Orlando, FL, #23D-24, p.67.

Fu, S.G., Baek, H.H., and Cadwallader, K.R. 1997. Comparison of aroma-active compounds extracted from blue crab meat with processing by-products hydrolysate using aroma extract dilution analysis. 58th Annual Meeting of the Institute of Food Technologists, Orlando, FL, #23D-25, p.67.

Aryana, K.J., Cadwallader, K.R., and Haque, Z.U. 1996. Isolation of flavor volatiles in lowfat Cheddar cheese by vacuum simultaneous distillation-solvent extraction. 73rd Annual Meeting of the Southern Branch, American Dairy Science Association, February 3-7.

Baek, H.H. and Cadwallader, K.R. 1996. Evaluation of the enzymatic hydrolysis of defatted soybean meal by response surface methodology. 57th Annual Meeting of the Institute of Food Technologists, New Orleans, LA, #53A-16, p.120.

Baek, H.H., Cadwallader, K.R., Marroquin, E., and Silva, J.L. 1996. Gas chromatography/olfactometric analysis of muscadine grape aroma. 57th Annual Meeting of the Institute of Food Technologists, New Orleans, LA, #34-7, p.74.

Cadwallader, K.R. 1996. Potent odorants in hickory and mesquite smokes and liquid smoke extracts. 57th Annual Meeting of the Institute of Food Technologists, New Orleans, LA, #34-6, p. 74.

Cadwallader, K.R., Baek, H.H., Chang-Lee, G.-H. 1996. Aroma extract dilution analysis of cooked freshwater prawn. 57th Annual Meeting of the Institute of Food Technologists, New Orleans, LA, #80D-20, p.197.

Cha, Y.J., Kim, E.J., Baek, H.H., and Cadwallader, K.R. 1996. Development of a flavoring agent from sea mussel. 57th Annual Meeting of the Institute of Food Technologists, New Orleans, LA, #80D-22, p.197.

Kim, H.R., Ahn, C.B., Jung, K.J., Baek, H.H., Cadwallader, K.R. 1996. Characterization and utilization of waste water from oyster processing plants as flavoring agents. 57th Annual Meeting of the Institute of Food Technologists, New Orleans, LA, #80D-21, p.197.

Aryana, K.J., Cadwallader, K.R., and Haque, Z.U. 1996. Development of methodology for measuring+ flavor volatiles in Cheddar cheese made with and without fat replacers. International Conference on Food Science and Technology of The Fine Particle Society, Chicago, IL, August 24-26.

Cha, Y.J., Baek, H.H., and Cadwallader, K.R. 1995. Volatile flavor components in oyster hydrolysate produced with protease. 56th Annual Meeting of the Institute of Food Technologists, Anaheim, CA, #54E-16, p.166.

Conner, T.M., McGregor, J.U., and Cadwallader, K.R. 1995. Identifying flavor components in light-activated milk. J. Dairy Sci. 48(supplement 1): 317.

Baek, H.H. and Cadwallader, K.R. 1994. Comparison of volatile compounds in flavor concentrates produced from crawfish processing by-products with and without protease treatment. 55th Annual Meeting of the Institute of Food Technologists, June 25-29, Atlanta, GA, #79C-5, p.244.

Cadwallader, K.R., Tan, Q., Chen, F., and Meyers, S.P. 1994. Identification of character-impact aroma compounds in spiny lobster (*Panulirus argus*) tail meat. 55th Annual Meeting of the Institute of Food Technologists, June 25-29, Atlanta, GA, #7-7, p.13.

Chung, H.Y. and Cadwallader, K.R. 1994. Comparison of the aroma of three different extracts prepared from blue crab (*Callinetes sapidus*) processing by-product. 55th Annual Meeting of the Institute of Food Technologists, June 25-29, Atlanta, GA, #79C-7, p.244.

Chung, H.Y., Chen, F., and Cadwallader, K.R. 1994. Evaluation of aroma of blue crab (*Callinetes sapidus*) claw and lump meats. 55th Annual Meeting of the Institute of Food Technologists, June 25-29, Atlanta, GA, #79C-6, p.244.

Tan, Q. and Cadwallader, K.R. 1994. Biotransformation of ß-pinene by *Aspergillus cellulosae*. 55th Annual Meeting of the Institute of Food Technologists, June 25-29, Atlanta, GA, #24C-7, p.67.

Andrews, L.S. and Cadwallader, K.R. 1993. Microbial and sensory quality of ground ginger as affected by gamma irradiation. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #817, p.206.

Baek, H.H. and Cadwallader, K.R. 1993. Identification of characteristic volatile flavor components of roasted chicory by aroma extract dilution analysis. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #506, p.129.

Cha, Y.J. and Cadwallader, K.R. 1993. Volatile flavor components in Korean fermented fish paste. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #510, p.130.

Cha, Y.J., Baek, H.H., and Cadwallader, K.R. 1993. Comparison of DHS and SDE for the analysis of volatile compounds in fermented shrimp paste. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #511, p.131.

Chung, H.Y. and Cadwallader, K.R. 1993. Aroma extract dilution analysis of freshly picked cooked blue crab meat. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #563, p.144.

Chung, H.Y., Chou, C.-C., and Cadwallader, K.R. 1993. Changes in the volatile flavor constituents of coconut during roasting. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #504, p.129.

Yoo, S.K. and Cadwallader, K.R. 1993. Bioconversion of α- and ß-pinene. 54th Annual Meeting of the Institute of Food Technologists, July 10-14, Chicago, IL, Technical Program: Book of Abstracts, #516, p.132.

Baek, H.H. and Cadwallader, K.R. 1992. Enzymatic hydrolysis of crawfish waste for bioflavor production. Ninth International Biotechnology Symposium and Exposition, August 16-21, Crystal City, VA, Book of Abstracts, #472.

Baek, H.H., Pike, M.M., Bidner, T.D., Moody, M.W., and Cadwallader, K.R. 1992. Evaluation of the off-odor associated with wild alligator. 53rd Annual Meeting of the Institute of Food Technologists, June 20-24, New Orleans, LA. Book of Programs and Abstracts, #359, p.93.

Cha, Y.J., Baek, H.H., and Cadwallader, K.R. 1992. Volatile flavor components in concentrated snow crab extracts. 53rd Annual Meeting of the Institute of Food Technologists, June 20-24, New Orleans, LA, Book of Abstracts, #357, p.92.

Chung, H.Y. and Cadwallader, K.R. 1992. Comparison of volatile compounds in freshly picked crabmeat and crab processing waste. 53rd Annual Meeting of the Institute of Food Technologists, June 20-24, New Orleans, LA, Book of Abstracts, #358, p.93.

Kim, H.R., Baek, H.H., Cadwallader, K.R., Meyers, S.P., and Godber, J.S. 1992. Improved flavor extractibility from crab waste using the hepatopancreatic enzyme of crawfish, *Procambarus clarkii*. 53rd Annual Meeting of the Institute of Food Technologists, June 20-24, New Orleans, LA, Book of Abstracts, #360, p.93.

Cadwallader, K.R. and Braddock, R.J. 1990. Enzymatic hydration of limonene to α-terpineol. 51st Annual Meeting of the Institute of Food Technologists, June 16-20, Anaheim, CA, Book of Programs and Abstracts, #354, p.170.

Cadwallader, K.R. 1988. Bioconversion of (+)-limonene. 49th Annual Meeting of the Institute of Food Technologists, June 19-22, New Orleans, LA, Book of Programs and Abstracts, #293.

**Students/Postdoctoral/Visiting Scholar Researchers Supervised (1991-1999)**

***Visiting Scientists***
Yong-Jun Cha (LSU, MSU) – Chang Won National University
Hetty Voermans (LSU) – University of Wegeningen, The Netherlands

***Postdoctoral Researchers***
Hyung-Hee Baek (MSU)

***Graduate Students Completed (LSU/MSU)***

MS Students
Sun-Kyun Yoo (LSU)
Min Cai (MSU)
Hsin-Jen (Connie) Weng (MSU)
Shi-Guei (Scott) Fu (MSU)
Shin-Pei (Peggy) Yang (MSU)
Yi-Fang (Grace) Wu (MSU)
Leyla Yuksel (MSU)
JiHyun Jung (MSU)
Min-Sheng Su (MSU)
Gwo-Yuh Li (MSU)
Jeong Heo (MSU)

Ph.D. Students
Hyung-Hee Baek (LSU)
Hau Yin Chung (LSU)
Gyu-Hee (Chang) Lee (MSU)
Ranee Surakarnkul (MSU)
Yonca Karagul-Yuceer (MSU)

**Students/Postdoctoral/Visiting Scholar Researchers Supervised (UIUC, 2000-present)**

***Visiting Scholars***
Byung Hak Ahn (2006-2007) - Korea Food Research Institute, South Korea
Supeeraya Arsa (2013-2014) – Kasetsart University, Bangkok, Thailand
Mantana Buttara (2011-present) – Suranaree Univeristy of Technology, Thailand
Dong Chen (2015-present) – China Agricultural University, Beijing, China

Rongrong Chen (2016-present) - Ever Maple Food Science and Technology Co., Ltd., China
Arporn Jarunrattanasri (2003-2004) – Naresuan University, Thailand
Young-Suk Kim (2015-present) – Ewha Womans University
Patthamawadi Kiatbenjaku. (2009-2011, 2012) – Suranaree University of Technology, Thailand
Fareeya Kulapichitr (2016-present) – Chulalongkorn University, Thailand
Sasinee Kunyaboon (2016-present) - Suranaree University of Technology, Thailand
Nawaporn Lapsongphon (2010-2011) - Suranaree University of Technology, Thailand
Yuping Liu (2014-2015) – Beijing Technology and Business University, China
Yaowapa Lorjaroenphone (2006-2007) – Kasetsart University, Thailand
Xueli Pang (2013-2014) – China Agricultural University, Beijing, China
Sompoche Pojjanapimol (2003-2004) - Kasetsart University, Thailand
Primseri Rotsachakul (2004-2005) – Kasetsart University, Thailand
Huanlu Song (2005-2006) – Beijing Technology and Business University, Beijing, China
Patcharaporn Tinchan (2010-2012) – Kasetsart University, Thailand
Jihong Wu (2011-2012) – China Agricultural University, Beijing, China

***Postdoctoral Researchers (UIUC)***
Masud Huda (2002-2003)
Orasa Suriyaphan (2001, 2003)
Tanoj Singh (2001-2005)
Hun Kim (2005-2012)

***Graduate Students Completed (UIUC)***
Daniel Benitez (MS 2003)
Laura Brisske (MS 2003)
Erin Burnside (MS 2012)
Gabriela Carrasco (MS 2007)
Shondra Cook (MS 2007)
Edibe Erten (Ph.D. 2016)
Ming Chih Fang (Ph.D.2013)
Samantha Gardiner (MS 2015)
Elizabeth Genthner (MS 2010; Ph.D. 2014)
Theresa Gnadt (MS 2007)
Julia Gregg (Nonthesis MS, CHEFS Program, 2009)
Bethany Hausch (MS 2010)
Lauren Kelley (MS)
Sean LaFond (MS 2009)
Jacob Lahne (MS 2010)
Yaowapa Lorjaroenphone (Ph.D. 2012)
Patricio Lozano (MS 2005 & Ph.D. 2009)
Samantha McKenna (MS, 2016)
Joshua Moore (MS 2006)
Linda Moran (MS 2013)
Ana Carolina Mosca (MS 2007)
Jason Niermann (Nonthesis MS, CHEFS Program 2001)
Sirima Puangpraphant (MS 2007)
Bethany Richardson (MS 2013)
Inthawoot Suppavorasatit (Ph.D. 2012)
Chenxing Sun (3+2 program, Nonthesis MS)
Qiaoxuan Zhou (MS 2001 & Ph.D. 2005)

***Current Graduate Students (2016)***
Courtney Beckett (MS)
Chelsea Ickes (Ph.D.)
Fengjia Chen (MS, 3+1)
Bethany Hausch (Ph.D.)
Nagiat Hwasa (Ph.D.)
Jing (Jenny) Jin (MS, 3+1)
Tiandan Wu (MS)
Wenqi Zhu (Ph.D.)
Yun Yin (Ph.D.)

***Undergraduate Student Researchers***
Kelsey Choquette (2012-2013)
Diniene Chreaton, Rap II (2001)
Ashley Davis, Rap II (ACES) (2001) & UIUC Ronald E. McNair Summer Research Program (2004)
Yaozheng (Tess) Liu (2013-present)
Rosemary Nash (2011-2012)
Mary Nowak (2004-2005)
Jieun Oh (2013)
Abigail Pishevar (2014-2015)
David Potts (2008-2010)
Stephanie Sajuti (2005-2007)
Dylan Troth (2015-present)
Katrina Vlahovich (2001-2002)

**Involvement in Professional Organizations (2000-present)**

***Leadership***

Chair and Program Chair for the Division of Agricultural and Food Chemistry (AGFD) of the American Chemical Society, 2003-2005. Responsibilities include organizing AGFD technical programs for two ACS National Meetings (fall 2004 and spring 2005 meetings).

***Editorial Board***

Flavour and Frangrance Journal

***Associate Editor***

Journal of Food Science – *Food Chemistry*

***Symposia Organized***

Cadwallader, K.R. and Shahidi, F. 2017. ACS Symposium: *Chemistry of Clean Ingredients.* Washington, DC, August 20-24.

Cadwallader, K.R. and Chang, S.K.C. 2008. ACS Symposium: *Chemistry, Texture and Favor of Soy,* Philadelphia, PA, August 17-21.

Cadwallader, K.R. 2008. ACS Symposium: *Recent Developments in Flavor Chemistry*. 235th ACS National Meeting, New Orleans, LA, April 6-10.

Ho, C.-T., Weerasinghe, D.K. and Cadwallader, K.R. 2005. ACS Symposium: *Aroma-active Compounds in Foods and Reaction Favors: formation, measurement and stability*. 330th ACS National Meeting, Washington, DC, August 28 – September 1.

Cadwallader, K.R., P. Schieberle and M.J. Morello. 2005. ACS Symposium: *Grain-based Products: Health and Flavor, and Safety Aspects*. 330th ACS National Meeting, Washington, DC, August 28 – September 1.

Cadwallader, K.R. *Obesity Management: Role of Soy Foods*. University of Illinois, Champaign, IL, May 25-26, 2005.

Cadwallader, K.R., Drake, M.A. and McGorrin, R.J. 2004. ACS Symposium: *Chemistry and Flavor of Dairy Products*. 228th ACS National Meeting, Philadelphia, PA, August 22-26.

Weenen, H. and Cadwallader, K.R. (organizers). 2001. ACS Symposium: *Freshness and Shelf-life of Foods*. 222nd ACS National Meeting, Chicago, IL, August 26-30.

Cadwallader, K.R. and McGorrin, R.J. (organizers). 2001. IFT Symposium: *Developments in the Analysis of Complex Flavor Systems*. Annual Meeting of the Institute of Food Technologies, New Orleans, LA, June 23-27.

Rouseff, R.L. and Cadwallader, K.R. 1998. ACS Symposium: *Headspace Analysis of Foods and Flavors*. 214th ACS National Meeting, Boston, MA, August 23-27.

Shahidi, F. and Cadwallader, K.R. 1996. ACS Symposium: *Flavor and Lipid Chemistry of Seafoods*. 212th National Meeting of the American Chemical Society, Orlando, FL, August 25-29.

***Workshops/Short courses (organized)***

*A Place for Soy in a Better School Lunch Program*. University of Illinois, Urbana, IL, March 12, 2003.

*Traditional and Emerging Methods for the Manufacture and Analysis of Food Flavorings*. Faculty of Agriculture Industry, King Mongkut's Institute of Technology Ladkraband (KMITL), Bangkok, Thailand, July 29, 2002

*Soy Flavor Workshop*. ICSF Workshop (Klein, B.P. et al. coorganizers). Illinois Center for Soy Foods, University of Illinois, Urbana, IL, April, 2002/2003.

***Workshops/Short courses (lecturer)***

*Nutraceuticals, Ingredients, Challenges, Formulations, Flavours and Health Effects*. International Society for Nutraceutical and Functional Foods. Denpasar, Bali, Indonesia, October 11 – 12.

*Flavor Chemistry. (course co-taught with Drs. Chi-Tang Ho and Soo-Yeun Lee), Taiwan National University, May 10-19, 2008.*

*Flavor Research Workshop*. ACS Short Course (Acree, T.E., course director), American Chemical Society, Boston, MA, August 17-18, 2007.

*Flavor Research Workshop.* ACS Short Course (Acree, T.E. and Deibler, K., organizers), American Chemical Society, August 25-26, 2005.

Cadwallader, K.R. Flavoring soy products: masking and creating. Preconference AOAC Short Course. *Soyfoods: Ingredients, Preparation, and Utilization,* Koseoglu, S. and Shahidi, F. (organizers), Cincinnati, OH, May 9, 2005.

Cadwallader, K.R. 2004. Aroma and flavor aspects of soy beverages. Preconference Shortcourse: *Functional Beverages,* Koseoglu, S and Shahidi, F. (organizers), Worldnutra: International Conference and Exhibition on Nutraceutacals and Functional Foods, San Francisco, CA, Nov 8, 2004

*Flavor Research Workshop*. ACS Short Course (Acree, T.E., organizer), American Chemical Society, Boston, MA, August 16-17, 2002; New York, NY, September 7-11, 2003.

*Cheese Flavor and Texture: Sensory and Instrumental Analysis.* SDFRC Short Course (Drake, M.A., course director), Southeast Dairy Foods Research Center, North Carolina State University, Raleigh, NC, August 7-9, 2002.

**Proposal Reviewer/Panel Participation (2010-present)**

Panelist/Reviewer (2015) - Office of Scientific Quality Review (OSQR)-USDA-ARS, NP 306 Panel 14: Functional Foods (2015)

Panelist/Reviewer (2015) - Office of Scientific Quality Review (OSQR)-USDA-ARS, NP 107 Panel 14: Grain Engineering (2014)

Panelist/Reviewer (2014) - Office of Scientific Quality Review (OSQR)-USDA-ARS, NP 107 Panel 5: Food Chemistry Analysis (2014)

Panelist/Reviewer (2013) – 2012/2013 King Abdulaziz City for Science and Technology (KACST) Research Proposal Competition

EXHIBIT B

# MATERIALS CONSIDERED

- U.S. Patent Application No. 14/797,006 ("the '006 application")
- Office Action mailed June 6, 2016
- Proulx et al. (2006, J. Agric. Food Chem., 54:1518-22) ("Proulx")
- Hsieh et al. (US 2012/0093994) ("the '994 application")
- Declaration under 37 CFR § 1.132 of Dr. Celeste Holz-Schietinger ("the Holz-Schietinger Declaration")
- Lane and Nursten, "Variety of odors produced in Maillard model systems and how they are influenced by reaction conditions" in Maillard Reaction in Foods and Nutrition, Waller and Feather, eds., ACS Symposium Series No. 215, pp 141-158
- Kokkinidou and Peterson, 2013, Food Funct., 4:1093-104
- Elmore et al., 2001, "A comparison of headspace entrainment on Tenax with solid phase micro-extraction for the analysis of the aroma volatiles of cooked beef," in Headspace Analysis of Foods and Flavors; Rouseff and Cadwallader, eds, Springer
- Elmore et al. (2002, J. Agric. Food Chem., 50:1126-32)
- Chen et al. (2003, "Influence of DNA on Volatile Generation from Maillard Reaction of Cysteine and Ribose," *in* Nutraceutical Beverages, ACS Symposium Series Vol 871)
- Mottram and Nobrega (2002, J. Agric. Food Chem., 50(14):4080–86)
- Schieberle and Hofmann ("Characterization of Key Odorants in Dry-Heated Cysteine—Carbohydrate Mixtures: Comparison with Aqueous Reaction Systems," *in* Flavor Analysis, ACS Symposium Series, Vol 705)

- Mottram and Mottram (2002, "An Overview of the Contribution of Sulfur-Containing Compounds to the Aroma in Heated Foods," *in* Heteroatomic Aroma Compounds, ACS Symposium Series, Vol 826)
- Shu-C and Ho (1989, "Parameter Effects of the thermal reaction of cysteine and 2,5-dimethyl-4-hydroxy-3(2H)-furanone," *in* Thermal Generation of Aromas, ACS Symposium Series, Vol 409)
- Chemistry and Technology of Flavours and Fragrances, 2005, Ed David Rowe, Blackwell Publishing Ltd
- Flavor of Meat and Meat Products, 1994, Ed Shahidi, Springer-Science+Business Media, BV
- Handbook of Meat and Meat Processing, 2012, 2nd Ed, Ed Hui, CRC Press
- Chen and Ho (2002, J. Agric. Food Chem., 50(8):2372–76)
- Kerscher and Grosch (1998, J. Agric. Food Chem., 46:1954-58)
- Tang et al. (2013, J. Sulfur Chem., 34:38-47)
- Withcombe and Mussinan (1988, J. Food Sci., 53:658-60)

Attorney's Docket No.: 38767-0015001 / M3CON-Track 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | 1791 |
| Serial No. | : | 14/797,006 | Examiner | : | Elizabeth A. Gwartney |
| Filed | : | July 10, 2015 | Conf. No. | : | 8496 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR § 1.132

I, Devin Grant Peterson, PhD, hereby declare as follows:

1. I am currently a Professor in the Department of Food Science and Technology at the Ohio State University in Columbus, Ohio. I have held this position since early 2016. I have worked and taught in the field of Food Science since 2001. Prior to my current position, I held Professor/Associate Professor positions at the University of Minnesota in Saint Paul, Minnesota from 2009 to 2016; and was a faculty member in the Department of Food Science at the Pennsylvania State University in University Park, Pennsylvania from 2001 to 2009. In addition, I have been the Director of the Flavor Research and Education Center for the past seven years, at both the University of Minnesota and the Ohio State University.

2. I am a nationally recognized expert and scholar in the field of flavor science. In 2015, I received the Excellence in Flavor Science Award from the Flavor and Extract Manufacturers Association. In 2008, I received a Pan-American Nutrition, Food Science and Technology Award. In 2004, during my tenure at Pennsylvania State University, I was awarded the Presidential Early Career Award for Scientists and Engineers (PECASE), which was presented by the White House Office of Science and Technology Policy.

3. I received a Bachelor's of Science (B.S.) degree in Food Science in 1994 from the University of Manitoba in Winnipeg, Manitoba. I earned a Master's of Science (M.S.) degree in 1997 and a Doctor of Philosophy (Ph.D.) degree in 2001 in Flavor Chemistry from the Department of Food Science from the University of Minnesota in Saint Paul, Minnesota. I was named to the Dean's List during my academic career at both the University of Manitoba and at the University of Minnesota. While I was obtaining my Ph.D., I completed a six-month Internship as a Research Flavor Scientist at Givaudan Flavors in Cincinnati, Ohio.

4. A copy of my curriculum vitae is attached in **Exhibit A**.

5. My research focuses on food flavor and related chemistry, with an emphasis on identification of flavor stimuli (e.g., taste, aroma, chemesthetic, mouthfeel), pathways of formation and degradation of flavor stimuli, taste and aroma modulation, and mechanisms of delivery.

6. In preparing my Declaration, I have reviewed U.S. Patent Application No. 14/797,006 ("the '006 application"), as well as the Office Action mailed June 6, 2016, in which the claims of the '006 application were rejected as being anticipated by Proulx et al. (2006, J. Agric. Food Chem., 54:1518-22) ("Proulx") and as being obvious considering Hsieh et al. (US 2012/0093994) ("the '994 application") in view of Proulx. I also reviewed the Declaration under 37 CFR § 1.132 of Dr. Celeste Holz-Schietinger ("the Holz-Schietinger Declaration"). A list of the materials I reviewed in preparing this Declaration is provided in **Exhibit B**.

7. In forming my opinion, I reviewed and considered Applicants' experiments related to their discovery and demonstration that the addition of heme protein (in some cases as

leghemoglobin or LegH) surprisingly contributes to the development of meaty aroma in a "ground beef-like food product" comprising no animal products. These experiments are described in the '006 application and in the Holz-Schietinger Declaration.

8. Flavor is a complex sensation, consisting of different modalities such as olfaction (aroma), gustation (sweet, sour, salty, bitter, umami), and chemesthesis (heat, cooling, pain), as well as others. The aroma attributes are known to be a key component of flavor perception and have been the most widely studied by flavor chemists.

9. In my opinion, the scientific protocols in the '006 application and in the Holz-Schietinger Declaration for a) sample preparation and treatment; and b) chemical analysis of aqueous thermal reaction samples are reasonable and consistent with methods that would be used by skilled individuals in the art. Each of these aspects are reviewed in more detail below.

10. The Hotz-Schietinger Declaration describes chemical analysis of aqueous thermal reaction samples using art recognized instrumental aroma analysis methods, specifically HS-SPME combined with GC-MS, to monitor the effect of LegH addition on the formation of volatile compounds, specifically those with meaty aroma characteristics, during heating (i.e., cooking). The objective was to demonstrate that LegH was capable of promoting or catalyzing the formation of meaty aroma compounds via aqueous thermal reactions between ribose and cysteine. Three flavor reaction systems were compared, consisting of: 1) 1% (10 mg/mL) LegH alone (**LegH control**), 2) 50 mM ribose + 50 mM cysteine alone (**Rib + Cyst**) and 3) 1% (10 mg/mL) LegH + 50 mM ribose + 50 mM cysteine (**LegH + Rib + Cyst**). The above reaction mixtures were diluted in a buffer (50 mM potassium phosphate and 100 mM sodium chloride)

and adjusted to pH 6.5, which is near the physiological pH of ground beef. A 2 mL aliquot of each reaction mixture was transferred to sample vials (sealed) which were subsequently heated (150°C for 3 min) and then analyzed by HS-SPME-GC-MS.

11. The concentrations (i.e. 0.1 to 50 mM) of flavor precursors (i.e., ribose and cysteine) of the aqueous thermal reaction samples described in the '006 application and the Hotz-Schietinger Declaration are consistent with peer-reviewed publications that have used similar aqueous reaction samples to investigate the thermal generation of volatile aroma compounds contributing to the flavor sensation of a food product. While aqueous thermal reaction samples are simplistic compared to food matrices, they provide relevant guidance and generalized outcomes for understanding the influence of flavor precursors on the formation of volatile compounds contributing to aroma, and to the flavor sensation generally in a number of different food products.

12. For example, a widely utilized and referenced publication for understanding the impact of flavor precursor composition on the formation of volatile aroma compounds generated therefrom is Lane and Nursten, "Variety of odors produced in Maillard model systems and how they are influenced by reaction conditions" in Maillard Reaction in Foods and Nutrition, Waller and Feather, eds., ACS Symposium, Series No. 215, pp 141-158. This publication describes aqueous combinations of sugar and amino acid mixtures heated under different time and temperature conditions. Lane and Nursten provides directional guidance for flavor development, and how flavor is impacted by flavor precursors, in various types of food matrices.

13. It is my opinion that the experimental approach and subsequent data analysis techniques described in the Holz-Schietinger declaration are appropriate and acceptable for the purpose of evaluating and comparing aroma compound formation in the three aqueous thermal reaction systems under heating conditions. The aqueous thermal reaction samples described in the Holz-Schietinger Declaration are comparable with those described by Lane and Nursten. It is also my opinion that these conditions would simulate the cooking of a "ground beef-like food product" containing no animal products as described in the '006 application, and that the data obtained from the experimental approach would be reasonably predictive of the expected aroma compound formation from a "ground beef-like food product" containing no animal products and including the flavor reaction system components LegH, ribose, and cysteine.

14. It is well known that thermal generation of volatile aroma compounds in an aqueous reaction system is influenced by reaction temperature and pH. When utilizing aqueous reaction samples, the reaction systems often are sealed so they can be pressurized, which increases the temperature of the sample to simulate temperatures in excess of 100°C, which would be experienced with conventional food heating methods such as baking, grilling or pan-frying. The aqueous thermal reaction samples described in the '006 application and in the Holz-Schietinger Declaration were heated in sealed vials at 150°C, which would be consistent with temperatures experienced by common meat preparation (heating) techniques.

15. My research program has similarly utilized the benchtop autosampler apparatus utilized in the '006 application and the Holz-Schietinger Declaration to rapidly heat sealed vials of aqueous samples to between 100-150°C for the purpose of evaluating and comparing aroma

compound formation. See, for example, Kokkinidou and Peterson, 2013, Food Funct., 4:1093-104.

16. The slightly acidic pH value of 6 - 6.5 for the aqueous thermal reaction samples used in the '006 application and the Holz-Schietinger Declaration also are consistent with the typical intrinsic pH values of meat products, as well as with peer-reviewed publications evaluating flavor development, and how it is impacted by flavor precursors, in various types of food matrices, including in meat food products.

17. It is my opinion that the experimental approach and analytical methods used in the '006 application and the Holz-Schietinger Declaration for evaluating and comparing aroma compound formation in aqueous thermal reaction samples were consistent with those used by flavor scientists of ordinary skill in the art. For example, the headspace solid phase micro-extraction (SPME) sampling technique coupled with GCMS utilized in the '006 application and the Holz-Schietinger Declaration has been widely utilized for characterizing the aroma of foodstuffs, such as meat food products. See, for example, Elmore et al., 2001, "A comparison of headspace entrainment on Tenax with solid phase micro-extraction for the analysis of the aroma volatiles of cooked beef," in Headspace Analysis of Foods and Flavors; Rouseff and Cadwallader, eds, Springer. Indeed, more than 100 articles are reported in SciFinder when the key words "meat, aroma, SPME" are set as filters to screen the existing scientific literature.

18. It is well known that the aroma profiles of meat food products are impacted by sulfur-containing compounds (typically, reaction products of sulfur-containing amino acids) and lipid degradation/oxidation products that are generated during heating. The different chemical

classes of volatile compounds formed in the aqueous thermal reaction samples of the '006 application and the Holz-Schietinger Declaration are consistent with volatile aroma compounds reported in the literature evaluating volatile compound formation contributing to meat aroma and flavor sensation. See, for example, Elmore et al. (2002, J. Agric. Food Chem., 50:1126-32); Chen et al. (2003, "Influence of DNA on Volatile Generation from Maillard Reaction of Cysteine and Ribose," *in* Nutraceutical Beverages, ACS Symposium Series Vol 871); Mottram and Nobrega (2002, J. Agric. Food Chem., 50(14):4080–86); Schieberle and Hofmann ("Characterization of Key Odorants in Dry-Heated Cysteine—Carbohydrate Mixtures: Comparison with Aqueous Reaction Systems," *in* Flavor Analysis, ACS Symposium Series, Vol 705); Mottram and Mottram (2002, "An Overview of the Contribution of Sulfur-Containing Compounds to the Aroma in Heated Foods," *in* Heteroatomic Aroma Compounds, ACS Symposium Series, Vol 826); and Shu-C and Ho (1989, "Parameter Effects of the thermal reaction of cysteine and 2,5-dimethyl-4-hydroxy-3(2H)-furanone," *in* Thermal Generation of Aromas, ACS Symposium Series, Vol 409).

19. In my opinion, Applicant's experiments in the '006 application and the Holz-Schietinger Declaration demonstrate that the addition of LegH to an aqueous thermal reaction mixture comprising ribose and cysteine has the surprising result of enhancing the formation of volatile compounds associate with a meaty aroma. Significantly, the 2,851-fold increase in concentration of 2-acetylthiazole when LegH was combined with Ribose and Cysteine, which is shown in the Holz-Schietinger Declaration, in my opinion signifies that novel and unexpected chemical reactions occur in the presence of LegH. 2-acetylthiazole is particularly interesting as

it has been associated in the literature with a meaty/roasty aroma. See, for example, Chemistry and Technology of Flavours and Fragrances, 2005, Ed Rowe, Blackwell Publishing Ltd; Flavor of Meat and Meat Products, 1994, Ed Shahidi, Springer-Science+Business Media, BV; Handbook of Meat and Meat Processing, 2012, 2nd Ed, Ed Hui, CRC Press; Mottram and Mottram (2002, "An Overview of the Contribution of Sulfur-Containing Compounds to the Aroma in Heated Foods," *in* Heteroatomic Aroma Compounds, ACS Symposium Series, Vol 826); and Chen and Ho (2002, J. Agric. Food Chem., 50(8):2372–76).

20. Yield changes of 0.5- to 10-fold would be consistent with optimizing a reaction pathway, however, changes of greater than 1000-fold, as is seen with 2-acetylthiazole, indicate that new pathways of formation for meaty aromas result from the inclusion of LegH in the aqueous thermal reaction mixture.

21. Additionally, the Holz-Schietinger Declaration demonstrates that 2-methyl-3-furanthiol (MFT) and the major degradation product of MFT, the dimer, bis(2-methyl-3-furyl) disulfide, were detected only in the aqueous thermal reaction samples that contained Leghemoglobin. MFT is a very potent meaty odorant, with an extremely low odor threshold at 0.007 μg/kg in water, and is known to have an important contribution to meat aroma. See, for example, Kerscher and Grosch (1998, J. Agric. Food Chem., 46:1954-58); Tang et al. (2013, J. Sulfur Chem., 34:38-47); and Withcombe and Mussinan (1988, J. Food Sci., 53:658-60). It is surprising to me that an intense meaty aroma compound such as MFT was uniquely identified in the reaction mixture upon the addition of LegH.

22. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: Dec 2, 2016

Devin Grant Peterson, Ph.D.

EXHIBIT A

2249 Carter Avenue
Saint Paul, MN 55108

PHONE: (651) 308 3546
E-MAIL: devin.g.peterson@gmail.com

# Devin G Peterson

---

**Experience:**

| | | |
|---|---|---|
| Aug/16<br>**Professor**<br>**Food Science & Technology**<br>**Director of the Flavor Research & Education Center** | The Ohio State University | Columbus, OH |
| June/12 – Aug/16<br>**Professor**<br>**Food Science & Nutrition**<br>**Director of the Flavor Research & Education Center** | The University of Minnesota | St. Paul, MN |
| Aug/09 – June/12<br>**Associate Professor**<br>**Food Science & Nutrition**<br>**Director of the Flavor Research & Education Center** | The University of Minnesota | St. Paul, MN |
| July/07 – Aug/09<br>**Associate Professor/Food Science** | The Pennsylvania State University | University Park, PA |
| March/01 – June/07<br>**Assistant Professor/Food Science** | The Pennsylvania State University | University Park, PA |
| Dec/99 – Feb./01<br>**Research Assistant** | University of Minnesota | St. Paul, MN |
| July/99 - Dec./99<br>**Research Flavor Scientist (Internship)** | Givaudan Flavors | Cincinnati, OH |
| Sept./94 - July/99<br>**Research Assistant** | University of Minnesota | St. Paul, MN |
| June/94 –Aug./94<br>**Information Technician** | The Canadian Wheat Board | Winnipeg, MB |
| May – Aug./92&93<br>**QC Technician** | Coca-Cola Bottling Company | Winnipeg, MB |

| | | | |
|---|---|---|---|
| **Education:** | 1997 - 2001<br>**PhD/Food Science**<br>(Dean's List) | University of Minnesota | St. Paul, MN |
| | 1994 - 1997<br>**MS/Food Science**<br>(Dean's List) | University of Minnesota | St. Paul, MN |
| | 1990 – 1994<br>**BS/Food Science**<br>(Dean's List) | University of Manitoba | Winnipeg, MB |

| | | |
|---|---|---|
| **Awards:** | Flavor and Extract Manufacturers Association - Excellence in Flavor Science Award | 2015 |
| | Waters Centers of Innovation Award | 2012 |
| | Pan-American Nutrition, Food Science and Technology Award | 2008 |
| | Presidential Early Career Award for Scientist and Engineers (PECASE) | 2004 |
| | John Brandt Memorial Foundation Scholarship; National | 2000 |
| | M. E. Franks Scholarship; National | 1998, 1999 & 2000 |
| | IFT Grad. Fellowship–Soc. of Flavor Chemists Memorial; National | 1998/99 & 2000/01 |
| | AACC Graduate Fellowship; National | 1997/98 |
| | IFT Scholarship; Minnesota | 1997 & 2000 |
| | Triticus Award; Departmental | 1996 |
| | The Canadian Wheat Board Scholarship; National | 1994 |

**Peer Reviewed Publications (*italics* is corresponding author):**

1. Raithore, S. and ***Peterson, D.G.*** 2016. Delivery of taste and aroma components in sugar-free chewing gum: mass balance analysis. Chemosensory Perception. *Accepted.*
2. Paravisini, L. and ***Peterson, D.G.*** 2016. Characterization of Browning Formation in Orange Juice during Storage. ACS Symposium Proceedings, Browned Flavors: Analysis, Formation, & Physiology. *Accepted.*
3. Kokkinidou, S. ***Peterson, D.G.*** 2016. Identification of compounds that contribute to trigeminal burn in aqueous ethanol solutions. Food Chem. 211: 757-762 http://www.sciencedirect.com/science/article/pii/S0308814616308068
4. Bin, Q. and ***Peterson, D.G.*** 2016. Identification of Bitter Compounds in Whole Wheat Bread Crumb. Food Chem. 203: 8–15, http://www.sciencedirect.com/science/article/pii/S0308814616301182
5. Yeo, L., Thompson, D. and ***Peterson, D.G.*** 2016. Inclusion Complexation of Flavor Compounds by Dispersed High-Amylose Maize Starch (HAMS) in an Aqueous Model System. Food Chem. *199*: 393–400. http://www.sciencedirect.com/science/article/pii/S0308814615303320
6. Yucel, U. and ***Peterson, D.G.*** 2015. Effect of Protein–Lipid–Salt Interactions on Sodium Availability in the Mouth and Consequent Perception of Saltiness: In Solutions. J. Agric. Food Chem., 63: 7487–7493. Impact Factor: 3.1 http://pubs.acs.org/doi/abs/10.1021/acs.jafc.5b02311
7. Yucel, U. and ***Peterson, D.G.*** 2015. Effect of Protein–Lipid–Salt Interactions on Sodium Availability in the Mouth and Consequent Perception of Saltiness: As Affected by Hydration in Powders. J. Agric. Food Chem., 63: 7494–7498. http://pubs.acs.org/doi/abs/10.1021/acs.jafc.5b02312

8. Forero, D.P, Orrego, C.E. **Peterson, D.G.** and *Osoria, C.* 2015. Chemical and sensory comparison of fresh and dried lulo (*Solanum quitoense* Lam.) fruit aroma. Food Chemistry, 169: 85–91. http://www.sciencedirect.com/science/article/pii/S0308814614011595
9. Kokkinidou, S. and ***Peterson, D.G.*** 2015. Characterization of compounds that influence alcohol trigeminal burn in spirits. Weurman Symposium Proceedings Flavour Science Proceedings of the XIV Weurman Flavour Research Symposium, Andrew Taylor and Donald Mottram (Eds), pg 31-37.
10. Ronningen, I. and ***Peterson, D.G.*** 2015. Application of untargeted LC/MS techniques (Flavoromics) to identify changes related to freshness of food, *in* The Chemical Sensory Informatics of Food: Measurement, Analysis, Integration. Eds. Guthrie, et al.; ACS Symposium Series; American Chemical Society: Washington, DC, Vol. 1191, pg 269-277. http://pubs.acs.org/doi/pdf/10.1021/bk-2015-1191.ch019
11. Zhang, L., Xia, Y. and ***Peterson, D.G.*** 2014. Identification of bitter modulating Maillard-catechin reaction products. J. Agric. Food Chem. 62, 10092−10100. http://pubs.acs.org/doi/abs/10.1021/jf502040e
12. Karametsi, K., Kokkinidou, S., Ronningen, I. and ***Peterson, D.G.*** 2014. Identification of Bitter Peptides in Aged Cheddar Cheese. J. Agric. Food Chem. 62, 8034−8041. http://pubs.acs.org/doi/abs/10.1021/jf5020654
13. Troise, A. D. Fiore, A. Colantuono, A. Kokkinidou, S., **Peterson, D.G.** and *Fogliano, V.* 2014. Effect of olive mill wastewater phenol compounds on reactive carbonyl species and Maillard reaction end-products in ultrahigh-temperature-treated milk. J. Agric. Food Chem. 62, 10092−10100. http://pubs.acs.org/doi/abs/10.1021/jf501919y
14. Kokkinidou, S. and ***Peterson, D.G.*** 2014. Control of Maillard-type Off-Flavor Development in Ultra High Temperature Processed Bovine Milk By Phenolic Chemistry. J. Agric. Food Chem. 62, 8023−8033. http://pubs.acs.org/doi/abs/10.1021/jf501919y
15. Lui, X., Jiang, D. and ***Peterson, D.G.*** 2014. Identification of Bitter Peptides in Whey Protein Hydrolysate. J. Agric. Food Chem. 62, 5719−5725. http://pubs.acs.org/doi/abs/10.1021/jf4019728
16. Kokkinidou, S. and ***Peterson, D.G.*** 2013. Response Surface Methodology as Optimization Strategy for Reduction of Reactive Carbonyl Species in Heat-processed Foods by Means of Phenolic Chemistry. Food and Function. 4(7): 1093-1104. http://pubs.rsc.org/en/content/articlelanding/2013/fo/c3fo60032g
17. Jiang, D. and ***Peterson, D.G.*** 2013. Identification of Bitter Compounds in Whole Wheat Bread. Food Chem. 141; 1345-1353. http://www.sciencedirect.com/science/article/pii/S0308814613003233
18. Moskowitz, M., Bing, Q., Elias, R. and ***Peterson, D.G.*** 2012. Influence of endogenous ferulic acid in whole wheat flour on bread crust aroma. J. Agric. Food Chem. 60: 11245-11252. http://pubs.acs.org/doi/abs/10.1021/jf303750y
19. Ferruzzi, M.G., **Peterson, D.G.**, Singh, R.P. Schwartz, S.J. and *Freedman, M.* 2012. Nutritional Translation Blended With Food Science: 21st Century Applications. Adv. Nutr. 3: 813–819. http://advances.nutrition.org/content/3/6/813
20. Bin, Q., Jiang, D. Cho, I.H., ***Peterson, D. G.*** 2012. Chemical markers for bitterness in wheat bread. 2012. Flavour Fragr. J. 27, 454–458. http://onlinelibrary.wiley.com/doi/10.1002/ffj.3124/abstract

21. **Peterson, D.G**. 2012. Refining Maillard-type flavor chemistry: Phenolic reaction pathways, *in* Advances and Challenges in Flavor Chemistry & Biology. Plenary Lecture, 9th Wartburg Symposium Proceedings on Flavor Chemistry & Biology, Eisenach, Germany, pp 155-160
22. Bin, Q. **Peterson, D.G.** and *Elias, R.J.* 2012. Influence of phenolic compounds on the mechanisms of pyrazinium radical generation in the Maillard reaction. J. Agric. Food Chem. *60* (21), pp 5482–5490. http://pubs.acs.org/doi/full/10.1021/jf3010838
23. Jiang, D. Huang, Y. and **Peterson, D.G**. 2012. Application of Two-Dimensional Orthogonal Reversed-Phase Liquid Chromatography for Taste Compound Analysis. In Recent Advances in the Analysis of Food and Flavors; Toth, S., et al.; ACS Symposium Series; American Chemical Society: Washington, DC. http://pubs.acs.org/doi/abs/10.1021/bk-2012-1098.ch010
24. Moskowitz, M. and **Peterson, D. G.** 2011. Hydroxycinnamic acid-Maillard reactions in simple aqueous model systems. *in* Controlling Maillard Pathways. Washington, D.C.: American Chemical Society Symposium Proceedings 1042, pp 53-62. http://pubs.acs.org/doi/abs/10.1021/bk-2010-1042.ch006
25. Holt, A., Potineni, R. and **Peterson, D.G.** 2011. Flavor ingredient interactions in confections. Accepted. 12th Weurman Symposium Proceedings, Interlaken, Switzerland. *Pg 139-142.* https://home.zhaw.ch/~vere/pdf/Teil37 - Expression of Multidisciplinary.pdf
26. Cho, I. H. and ***Peterson, D.G.*** Chemistry of bread aroma: A review. 2010. Food Sci. Biotechnol. 19, 575-582. http://link.springer.com/article/10.1007/s10068-010-0081-3
27. Jiang, D. and ***Peterson, D.G.*** 2010. Role of hydroxycinnamic acids on food flavor: a brief overview. Phytochem. Rev. 9:187–193 http://link.springer.com/article/10.1007/s11101-009-9159-z
28. Jiang, D. , Chiaro, C., Maddali, P, Prabhu, S.K. and ***Peterson, D.G.*** 2009. Identification of hydroxycinnamic acid-Maillard reaction products in low-moisture baking model systems. J. Agric. Food Chem. 57, 9932–9943. http://pubs.acs.org/doi/full/10.1021/jf900932h
29. Potineni, R.V. and ***Peterson, D.G.*** 2008. Mechanisms of flavor release in chewing gum: Cinnamaldehyde. J. Agric. Food Chem *56, 3260–3267.* http://pubs.acs.org/doi/full/10.1021/jf0727847
30. Potineni, R.V. and ***Peterson, D.G.*** 2008. Influence of flavor solvent on flavor release and perception in sugar-free chewing gum. J. Agric. Food Chem *56, 3254–3259.* http://pubs.acs.org/doi/full/10.1021/jf072783e
31. Tapanapunnitikul, O., Chaiseri, S., **Peterson, D**., *Thompson, D.* 2008. Water solubility of flavor compounds influences formation of flavor inclusion complexes from dispersed high-amylose maize starch. J. Agric. Food Chem *56, 220-226.* Impact Factor *3.1. http://pubs.acs.org/doi/full/10.1021/jf071619o*
32. Ghosh, S., **Peterson, D.G.**, *J.N. Coupland.* 2008. Temporal Aroma Release Profile of Solid and Liquid Droplet Emulsions. Food Biophysics. 3:335–343 http://pubs.acs.org/doi/full/10.1021/jf071619o
33. Jiang, D. and **Peterson, D.G.** 2008. Hydroxycinnamic acid-Maillard reactions: Insights into flavor development of whole grain foods. 12th Weurman Symposium Proceedings, Interlaken, Switzerland, pg 297-300. https://home.zhaw.ch/~vere/pdf/Teil76 - Expression of Multidisciplinary.pdf

34. **Peterson, D.G.** and Noda, Y. 2008. Role of Phenolic Reactions on Maillard Reaction Flavours. Wartburg Flavor Symposium. 8th Wartburg Symposium Proceedings on Flavor Chemistry & Biology, February 28 - March 2, 2007, Eisenach, Germany.
35. Vunta H, Davis F, Palempalli UD, Bhat D, Arner RJ, Thompson JT, **Peterson DG**, Reddy CC, *Prabhu KS*. 2007. The Anti-inflammatory Effects of Selenium Are Mediated through 15-Deoxy-Δ12,14-prostaglandin J2 in Macrophages. J. Biol. Chem. V. 282, No. 25, pp. 17964–17973. Impact Factor 4.651. http://www.jbc.org/content/282/25/17964
36. Ghosh, G., **Peterson, D.G.** and *Coupland, J.N.* 2007. Aroma Release from Solid Droplet Emulsions: Effect of Lipid Type. JAOCS. 84:1001–1014. http://link.springer.com/article/10.1007/s11746-007-1135-4
37. Noda, Y. and ***Peterson, D.G.*** 2007. Structure-reactivity relationships of flavan-3-ols on product generation in aqueous glucose/glycine model systems. J. Agric. Food Chem. 55. 3686-3691. http://pubs.acs.org/doi/full/10.1021/jf063423e
38. Totlani, V.M. and ***Peterson, D.G.*** 2007. Influence of Epicatechin Reactions on the Mechanisms of Maillard Product Formation in Low Moisture Model Systems. J. Ag. Fd. Chem. 55: 414-420. http://pubs.acs.org/doi/full/10.1021/jf0617521
39. Totlani, V.M. and ***Peterson, D.G.*** 2006. Epicatechin carbonyl-trapping reactions in aqueous Maillard systems: Identification and structural elucidation. J. Agric. Food Chem. 54: 7311-7318. http://pubs.acs.org/doi/full/10.1021/jf061244r
40. Schwambach, S.L. and ***Peterson, D.G.*** 2006. Reduction of stale flavor development in low-heat skim milk powder via epicatechin addition. J. Ag. Fd. Chem. 54: 502-508. *http://pubs.acs.org/doi/abs/10.1021/jf0519764*
41. Ghosh, G., **Peterson, D.G.** and *Coupland, J.N.* 2006. Effects of droplet crystallization and melting on the aroma release properties of a model oil-in-water emulsion. J. Ag. Fd. Chem. 54; 1829-1837. http://pubs.acs.org/doi/abs/10.1021/jf052262w
42. **Peterson, D.G.**, Colahan-Sederstrom, P.M. and Potineni, R.V. 2006. Effect of processing technology and phenolic chemistry on ultra-high temperature Bovine milk flavor quality. *in* Chemistry and Flavor of Dairy Products, Symposium Proceedings, 228th ACS National Meeting, Philadelphia, PA, August 22-26, 2004. http://pubs.acs.org/doi/abs/10.1021/jf0487248
43. Dubost, N.J., *Beelman, R.B.*, **Peterson, D.G.**, and Royse, D.J. 2006. Identification and quantification of ergothioneine in cultivated mushrooms by liquid chromatography-mass spectroscopy. Int. J. Med. Mushr. 8:215-222. http://www.dl.begellhouse.com/journals/708ae68d64b17c52,67fa6af2515135b9,62e00b0414f6d4ec.html
44. Totlani, V.M. and ***Peterson, D.G.*** 2005. Reactivity of epicatechin in aqueous glycine and glucose Maillard reaction models: quenching of $C_2$, $C_3$ and $C_4$-sugar fragments. J. Ag. Fd. Chem. 53: 4130-4135. Impact Factor 3.1. http://pubs.acs.org/doi/full/10.1021/jf050044x
45. Colahan-Sederstrom, P.M. and ***Peterson, D.G.*** 2005. Inhibition of key aroma compound generated during ultra-high temperature processing of bovine milk via epicatechin addition. J. Ag. Fd. Chem. 53: 389-402. http://pubs.acs.org/doi/full/10.1021/jf0487248
46. Potineni, R.V. and ***Peterson, D.G.*** 2005. Influence of thermal processing conditions on flavor stability in fluid milk: benzaldehyde. J. Dairy Sci. 88:1-6.

http://www.sciencedirect.com/science/article/pii/S0022030205726552
47. Morawicki, R.O., *Beelman, R.B.*, **Peterson, D.G**. 2005. Recovery and purification of 10-oxo-*trans*-8-decenoic acid enzymatically produced using a crude homogenate of *Agaricus bisporus*. J. Food Sci. 70(8): C490-494.
Impact factor: 1.775. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2621.2005.tb11506.x/abstract
48. Morawicki, R.O., *Beelman, R.B.*, **Peterson, D.G.** and Demirci, A. 2005. Biosynthesis of 1-octen-3-ol and 10-oxo-trans-8-decenoic acid using a crude homogenate of Agaricus bisporus: Reaction Scale Up. J. Food Sci. 70(5):367-371.
http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2621.2005.tb09978.x/abstract
49. Gallaher, J.J, **Peterson, D.G.**, Roberts, R.F. and *Coupland, J.N.* 2005. Effect of composition and antioxidants on the oxidative stability of fluid milk supplemented with an omega-3 oil rich emulsion. International Dairy Journal. 15: 333-341.
http://www.sciencedirect.com/science/article/pii/S095869460400216X
50. Morawicki, R.O., *Beelman, R.B.*, **Peterson, D.G**. and Ziegler, G. 2005. Biosynthesis of 1-octen-3-ol and 10-oxo-trans-8-decenoic acid using a mushroom homogenate. Optimization of the reaction, part I: kinetic factors. Process Biochemistry. 40:131-137.
http://www.sciencedirect.com/science/article/pii/S0032959203004618
51. **Peterson, D.G.** and V.A. Totlani. 2005. Influence of flavonoids on the thermal generation of aroma compounds. in Phenolics in Foods and Natural Health Products, New York, ACS Symposium Series #909, September 7-11, 2003, pg 143-160.
http://pubs.acs.org/doi/abs/10.1021/bk-2005-0909.ch013
52. Schober, A.L. and ***Peterson, D.G.*** 2004. Flavor release and perception in hard candy: Influence of flavor compound-compound interactions. J. Ag. Fd. Chem. 52: 2623-2627.
http://pubs.acs.org/doi/full/10.1021/jf0353133
53. Schober, A.L. and ***Peterson, D.G.*** 2004. Flavor release and perception in hard candy: Influence of flavor compound-flavor solvent interactions. J. Ag. Fd. Chem. 52: 2628-2631.
http://pubs.acs.org/doi/full/10.1021/jf0354287
54. Nattress, L.A , *Ziegler, G.R.*, Hollender, R and **D.G. Peterson**. 2003. The impact of hazelnut paste on the sensory properties and shelf life of dark chocolate. J. Sensory Studies. 19: 133-148. Impact factor 3.1. http://onlinelibrary.wiley.com/doi/10.1111/j.1745-459X.2004.tb00141.x/abstract
55. **Peterson, D.G**. and *Reineccius, G.A.* 2003. Characterization of the volatile compounds which constitute fresh sweet cream butter aroma. Flavour Frag. J. 18(3):215-220.
http://onlinelibrary.wiley.com/doi/10.1002/ffj.1192/abstract
56. **Peterson, D.G.** and *Reineccius, G.A.* 2002. Biological pathways for the formation of oxygen-containing aroma compounds. in Heteroatomic Aroma Compounds. G.A. Reineccius. ACS Symposium 826, pg. 227-242. http://pubs.acs.org/doi/abs/10.1021/bk-2002-0826.ch014
57. **Peterson, D.G.** and *Reineccius, G.A.* 2002. Determination of the aroma impact compounds in heated sweet cream butter. Flavour Frag. J. 18(4):320-324.
http://onlinelibrary.wiley.com/doi/10.1002/ffj.1228/abstract
58. **Peterson, D.G.** and *Fulcher, R.G.* 2001. Variation in Minnesota HRS wheats: Starch granule size distribution. Food Research International 34(4): 357-363.
http://www.sciencedirect.com/science/article/pii/S0963996900001757
59. **Peterson, D.G.** and *Fulcher, R.G.* 2001. A simple digital conversion of a traditional laboratory mixograph. Cereal Research Communications 29(3-4): 397-404.

60. **Peterson, D.G.** and *Fulcher, R.G.* 2001. Variation in Minnesota HRS wheats: Bran content. J. Food Sci. 67(1): 67-70. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2621.2002.tb11360.x/abstract

**Patents (inventor):**
International Application (PCT). April 21st, 2015. Peterson, D. and Kokkinidou, S. Methods of Making Modified Alcohol Containing Products.

USA application. An umami-enhanced food product and method of enhancing the umami taste of food products.

**Courses Taught:**
Flavor Chemistry (FScN 8337), Flavor Technology (FScN 5521); Current Issues in Food Science (FScN 8318); Food Chemistry and Functional Foods (FScN 4112)

**Professional Memberships**:
American Chemical Society
Institute of Food Technologists

EXHIBIT B

MATERIALS CONSIDERED

- U.S. Application Serial No. 14/797,006, Fraser, R. Brown, P.O., Karr, J. and Holz-Schietinger, C., 2014, Publication No. US 2015/0351435
- Hsieh, F-h and Huff, H.E. 2012. Meat analog compositions and process. U.S. Patent Application No. US 2012/0093994 ("the '994 application")
- Office Action Mailed June 6, 2016 and draft Response to same
- Declaration Under 37 CFR §1.132 of Celeste Holz-Schietinger, Ph.D.
- Calkins, C.R. and Hodgen, J.M. A fresh look at meat flavor. Meat Sci. 2007, 63-80.
- Proulx, A.K. and Reddy, M.B. Iron bioavailability of hemoglobin from soy root nodules using caco-2 cell culture model. J. Agric. Food Chem. 2006, 54, 1518-1522.
- Belitz, H.-D., Grosch, W., and Schieberle, P. Food Chemistry, 3rd revised edition. Springer-Verlag, Berlin (2006), p. 368.
- Tang, W., Jiang, D., Yuan, P. and Ho, C.-T. (2013) Flavor chemistry of 2-methyl-3-furanthiol, an intense meaty aroma compound. J. Sulfur Chem. 34: 38-47.
- Chaudhari, N. and Roper, S.D. (2010). The cell biology of taste. J. Cell Biol. 190(3): 285-296.
- Shahidi, F., Rubin, L.J., D'Souza, L.A., Teranishi, R. and Buttery, R.G. 1986. Meat flavor volatiles: A review of the composition, techniques of analysis, and sensory evaluation. CRC Crit. Rev. Food Sci. Nutr. 24: 142-243.
- Cadwallader, K.R. and MacLeod, A.J. 1998. Instrumental methods for analyzing the flavor of muscle foods. Ch. 16. In *Flavor of Meat, Meat Products, and Seafoods, 2nd Ed.* Shahidi, F. (Ed.). Blackie Academic & Professional, New York, pp.
- Jublot, L., Rosing, E.A.E, Blom, L. v.d., Desclaux, G., Martins, S.I.F.S., Batenburg, A.M.

and Smit, G. 2010. Quantitation of sulphur aroma compounds in Maillard model reaction systems of different composition. In *Expression of Multidisciplinary Flavour Science.* Proceedings of the 12th Weurman Symposium. Blank, I., Wüst, M., and Yeretzian, C. (Eds.). Winterthur: Zurich University of Applied Sciences.

- Spence, C. 2015. Multisensory flavor perception. Cell 161: 24-35.

Attorney Docket No.: 38767-0015002 / Client Ref: Meat3CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | | | |
|---|---|---|---|---|---|
| First Named Inventor | : | Rachel Fraser | Art Unit | : | 1791 |
| Serial No. | : | 15/398,479 | Examiner | : | Elizabeth A. Gwartney |
| Filed | : | January 4, 2017 | Conf. No. | : | 2358 |
| Title | : | METHODS AND COMPOSITIONS FOR AFFECTING THE FLAVOR AND AROMA PROFILE OF CONSUMABLES | | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**DECLARATION UNDER 35 U.S.C. § 1.132 OF DAVID J. LIPMAN M.D.**

I, Dr. David J. Lipman, hereby declare as follows:

1. I am currently Chief Scientific Officer of Impossible Foods, the assignee of U.S. Application Serial No. 15/398,479 ("the '479 application"). I have held this position since May 2017, and am responsible for research and development and information technology. I am submitting this Declaration in support of the '479 application.

2. It is my understanding that the Office has rejected the pending claims in the '479 application as being anticipated and/or obvious over a number of references, including Tong et al. ("Blood Composition of Different Beef Breed Types", Can. J. Anim. Sci, 1986;66: 915-924); Shimbayashi et al. ("Free Amino Acids and Phosphorylethanolamine in Milk Whey of Cow", Agr. Biol. Chem, Vol. 29, No. 1, 1965;13-19); Koutsidis et al. ("Water-soluble precursors of beef flavor: I. Effect of diet and breed", Meat Science, 79, 2008;79:124-130); Field et al. ("Heme Pigment Content of Bovine Hemopoietic Marrow and Muscle", J. Food Sci., 1980;45:1109-1112); and Jamieson ("Iroquois Stew With Beef, Chicken and Pork", Bon Appetit, November 1995, http://w ww.epicurious.conilrecipesifoodiviewsiiroquois-stewwith-beef-chicken-and-pork-865). I have read the '479 application, the Office Action, and the cited art. I have also read the Declarations of Dr. Keith R. Cadwallader, Dr. Devin Grant Peterson, Dr. S. Christopher Davis and Dr. Celeste Holz-Schietinger, the cited art, and prior Office Action Responses that Impossible Foods has submitted with prior responses to Office Actions, including

those submitted in U.S. Application Serial No. 14/797,006, now U.S. Patent No. 9,700,067, which is the parent application of the '479 application.

3. I have a Bachelor of Science degree conferred on me by Brown University in 1976, and a M.D. degree conferred on me in 1980 by the State University of New York at Buffalo.

4. I am a nationally and internationally recognized expert in the field of bioinformatics. I was actively involved in the development of a series of sequence similarity algorithms, including the Wilbur-Lipman algorithm in 1983, FASTA search in 1985, BLAST in 1990, and Gapped BLAST and PSI-BLAST in 1997.

5. I am an elected member of the National Academy of Sciences and the National Academy of Medicine, and a fellow of the International Society of Computational Biology, the American Academy of Arts and Sciences, and the American College of Medical Informatics. I received the Jim Gray eScience Award from Microsoft in 2013.

6. I served as Director of the National Center for Biotechnology Information (NCBI) at the National Institutes of Health (NIH) from 1989 to 2017. NCBI is the home of GenBank, the U.S. node of the International Sequence Database Consortium, and PubMed, one of the most heavily used sites in the world for the search and retrieval of biomedical information.

7. A copy of my curriculum vitae is attached as **Exhibit A**.

8. Under my direction, a pairwise alignment was performed on 27 heme-containing protein sequences provided in the '479 application (i.e., SEQ ID NOs. 1-27 disclosed in the '479 application), representing a diverse range of organisms, to evaluate amino acid sequence similarity. All but three of the proteins are heme-containing globin proteins from a wide phylogenetic spread. The amino acid sequences of the three non-globin proteins are provided in SEQ ID Nos: 6-8.

9. The pairwise alignments were performed using the Needleman & Wunsch alignment algorithm [Needleman SB, Wunsch CD. "A general method applicable to the search for similarities in the amino acid sequence of two proteins", J Mol Biol. 1970 Mar;48(3):443-53, attached as **Exhibit B**] as implemented by the National Center for Biotechnology Information [see https://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE_TYPE=BlastSearch&PROG_DEF=blastn&BLA

ST_PROG_DEF=blastn&BLAST_SPEC=GlobalAln&LINK_LOC=BlastHomeLink, attached as **Exhibit C**) ] and run using the default parameters.

10. The results of the pairwise alignments are shown in **Exhibit D**. The table provided in Exhibit D reports the percentage of identical amino acids shared among each pair of aligned sequences. This global alignment approach was used in order to maximize the number of shared amino acids across the entire amino acid sequence, and thus it is a highly conservative approach in this context. Despite this conservative approach, this set of proteins is so diverse that many pairs exhibit very little sequence similarity.

11. Example 9 of the '479 application describes an experiment employing Gas Chromatography-Mass Spectroscopy (GCMS) and Gas Chromatography-Olfactory (GCO) methods to evaluate the production of volatile compounds, including those associated with a meaty aroma, during thermal treatment (cooking) of four aqueous flavor reaction mixtures containing four distinct globin heme-containing proteins (SEQ ID NOs: 3-5 and 18).

12. A summary of the pairwise alignment shared among each pair of aligned sequences for SEQ ID NOs: 3-5 and 18 shown in Exhibit B is provided in Table 1 below. As one can see from Exhibit B and Table 1, these 4 globin heme-containing proteins demonstrate less than 36% pairwise identity between each pair of aligned sequences. These four globin proteins represent heme-containing proteins obtained from animals, plants, and bacteria, which have been separated by over a billion years of evolution; (see, for example, Proc Natl Acad Sci U S A. 2001 Feb 27;98(5):2497-502, attached as **Exhibit E**; and Mol Biol Evol. 2015 Apr;32(4):835-45, attached as **Exhibit F**).

**Table 1**

| | | **Pairwise Identity** | | | |
|---|---|---|---|---|---|
| | | SEQ ID NO:3 | SEQ ID NO:4 | SEQ ID NO:5 | SEQ ID NO:18 |
| *Aquifex aeolicus* | SEQ ID NO:3 | 100% | 25% | 19% | 21% |
| Leghemoglobin | SEQ ID NO:4 | 25% | 100% | 36% | 19% |
| Barley (*Hordeum vulgare*) | SEQ ID NO:5 | 19% | 36% | 100% | 20% |
| *Bovin Myoglobin* | SEQ ID NO:18 | 21% | 18% | 20% | 100% |

13. The first flavor reaction mixture in Example 9 contained 1% (10 mg/ml) Leghemoglobin (SEQ ID NO: 4) mixed with 10 mM Cysteine and 10 mM Ribose; the second

flavor reaction mixture contained 1% (10 mg/ml) Barley hemoglobin (*H. vulgare*, (SEQ ID NO: 5) mixed with 10 mM Cysteine and 10 mM Ribose; the third flavor reaction mixture contained 1% (10 mg/ml) *B. myoglobin* hemoglobin (SEQ ID NO: 18) mixed with 10 mM Cysteine and 10 mM Ribose; and the fourth flavor reaction mixture contained 1% (10 mg/ml) an *A. aeolicus* heme-containing protein (SEQ ID NO: 3) mixed with 10 mM Cysteine and 10 mM Ribose. All flavor reaction mixtures were adjusted to pH 6.0, heated to 150°C for 3 minutes and evaluated by GCMS to identify volatile aroma compounds produced that are associated with meaty aroma.

14. The results of the above-identified experiments are set forth in Table 9 of the '479 application, which is reproduced below. The results show that that inclusion of <u>any</u> of the four members of this widely diverse set of heme containing proteins, proteins that in my opinion are from perhaps the farthest branches of the tree of life, in an aqueous thermal flavor reaction with Cysteine and Ribose, produced multiple aroma compounds associated with a meaty aroma upon heating.

**Table 9 of the '479 Application**

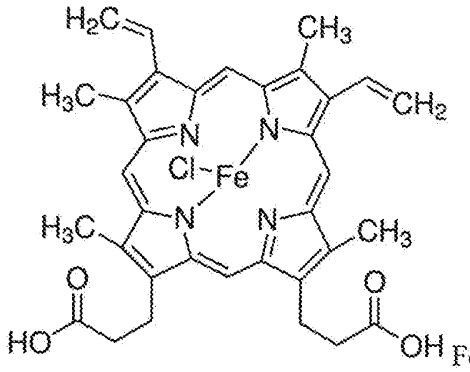
| Name | LegH | Barley | *B. myoglobin* | *A. aeolicus* |
|---|---|---|---|---|
| Furan | x | x | x | x |
| Thiazole | x | x | x | x |
| benzaldehyde | x | x | x | x |
| 2-acetylthiazole | x | x | x | x |
| 2-methyl-propanal | x | x | x | x |
| furfural | x | x | x | x |
| 2,3-butanedione | x | x | x | x |
| 2-pentyl-furan | x | x | x | x |
| 2-pentanone | x | x | | |
| pyrazine | x | x | x | x |
| dimethyl trisulfide | x | x | x | x |
| 3-methyl-butanal | x | x | | x |
| 2-methyl-thiazole | x | x | x | x |
| pentanal | x | x | x | x |
| 1,3,5-cycloheptatriene | x | x | x | x |
| methacrolein | x | x | x | x |
| heptanal | x | x | x | x |
| 2-methyl-butanal | x | x | | x |
| isothiazole | x | x | x | x |
| thiophene | x | x | x | x |

| | | | | |
|---|---|---|---|---|
| propanal | x | x | x | x |
| 2-heptenal | x | | x | x |
| methyl-pyrazine | x | x | x | x |
| 1-octene | x | | x | x |
| butanal | x | x | x | x |
| 2-acetyl-propen-2-ol | x | x | x | x |
| pyrrole | x | x | x | x |
| 2-methyl-furan | x | x | x | x |
| nonanal | | x | x | x |
| 2-propenal | | x | x | x |
| 2-decenal | | x | x | x |
| 2-nonanone | | x | | x |
| 2-octanone | | x | x | x |
| 2-tridecen-1-ol, | | | x | x |
| 2-octanone | | | x | |
| 2-octenal | | | x | x |
| 4-methyl-2-heptanone | | | x | x |
| octanal | | | x | x |
| 2-undecenal | | | | x |
| butyrolactone | | | | x |
| 1-octen-3-one | | | | x |
| 3-methylheptyl acetate | | | | x |
| 2-pentyl-thiophene | | | | x |

15. Example 13 of the '479 application describes an experiment employing GCMS methods to evaluate the production of volatile aroma compounds associated with a meaty aroma during cooking of reaction mixtures containing either myoglobin free in solution or hemin (heme unbound to protein) coupled to a solid support. A first reaction mixture included heme protein (equine myoglobin -Sigma) at 0.35% in a phosphate buffer (20 mM) at pH 6.0 with 100 mM NaCl; this was then mixed with Magic Mix (see Table 13 of the '479 application). A second reaction mixture was created with immobilized hemin (bovine hemin (Sigma Aldrich)) at 0.35% in a phosphate buffer (20 mM) at pH 6.0 with 100 mM NaCl; this was mixed with Magic Mix (Table 13 of the '479). The reaction mixtures were heated to 150°C for 3 minutes and evaluated by GCMS to identify volatile aroma compounds that are associated with meaty aroma.

16. Hemin is an example of a conjugated heterocyclic ring complexed to an iron ion, as described in the '479 application. More specifically, hemin is an iron-containing porphyrin

(protoporphyrin IX) containing a ferric iron ion (heme B) with a chloride ligand, having the structure of Formula I below.



Formula I

17. The results of the above-identified experiments are set forth in Table 17 of the '479 application, which is reproduced below. The results provided in Table 17 show that reaction mixtures containing the immobilized hemin and the heme-protein both produce multiple aroma compounds associated with a meaty aroma upon heating. Notably, the profiles of volatile compounds, measured by GCMS, produced by the reaction mixtures containing the immobilized hemin and the heme-protein, respectively, were very similar.

**Table 17 of the '479 Application**

| Flavor compound | myoglobin | hemin-linker-resin |
|---|---|---|
| 2-methyl-5-(methylthio)-thiophene | Low | |
| dihydro-5-propyl-2(3H)-furanone | Low | |
| octane | Low | |
| pyrrole | Low | Low |
| methanethiol | Low | Low |
| 2-thiophenecarboxaldehyde | Low | Low |
| methyl-pyrazine | Low | Low |
| 1-hydroxy-2-propanone | Low | Low |
| propanal | Low | Low |
| thiophene | Low | medium |
| pyridine | Low | Low |
| 2-methyl-furan | Low | medium |
| oxalic acid, butyl propyl ester | Low | Low |
| pyrazine | medium | Low |
| oxalic acid, diallyl ester | medium | medium |
| 2-butenal | medium | large |
| furfural | medium | medium |

| | | |
|---|---|---|
| nonanal | medium | medium |
| 2-ethyl-furan | medium | Low |
| ethanol | medium | very large |
| tert-butanol | medium | |
| 3,3'-dithiobis[2-methyl]-furan | medium | medium |
| m-aminophenylacetylene | medium | medium |
| 2,5-dihydro-3,4-dimethyl-furan | medium | medium |
| 2-acetylthiazole | medium | medium |
| cyclohexane | medium | |
| ethyl tert-butyl ether | medium | |
| carbon disulfide | medium | medium |
| thiazole | medium | medium |
| acetonitrile | medium | large |
| 2-pentyl-furan | medium | Low |
| 3-thiophenecarboxaldehyde | medium | medium |
| 2-methyl-butanal | medium | medium |
| thiazole | medium | large |
| 2-methyl-3-furanthiol | large | large |
| 2-propenal | large | large |
| 3-methyl-2-butenal | large | medium |
| 2-methyl-3-(methylthio) furan | large | large |
| ethyl acetate | large | medium |
| methacrolein | large | medium |
| methyl-thiirane | large | large |
| methional | large | large |
| methyl alcohol | large | medium |
| 2-butanone | large | Low |
| 2,3-butanedione | large | medium |
| acetone | large | large |
| furan | large | medium |
| benzaldehyde | large | medium |
| methyl thiolacetate | large | medium |
| acetaldehyde | very large | very large |
| 2-methyl-propanal | very large | very large |
| dimethyl trisulfide | very large | very large |
| 3-methyl-butanal | very large | very large |
| propyl-cyclopropane | | medium |
| (E)-2-octenal | | medium |
| 2-n-propylaziridine | | medium |

| | | |
|---|---|---|
| thiirane | | medium |
| ethyl formate | | medium |
| methyl vinyl ketone | | medium |
| 2-propenoic acid, ethyl ester | | medium |
| 1-nonanol | | large |
| 1-octene | | large |
| 1-heptanol | | large |
| 1-dodecene | | large |
| phorone | | very large |

18. In my opinion, the experimental data provided in Example 9 of the '479 application relating to the surprising ability of four very distinct members of the set of heme containing proteins to generate meat-associated volatile aroma compounds upon heating, when coupled with the experimental data provided in Example 13 of the '479 application, demonstrating that even heme unbound to protein (i.e., hemin), also shared such meat aroma and flavor production properties when heated in a reaction mixture, make it reasonable to conclude that these functional properties are not based on protein sequence similarity, but are instead based on the commonality among the proteins and the hemin experiments, namely, the inclusion of the heme co-factor.

19. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: July 11, 2017

David J. Lipman, M.D.

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096

*J. Mol. Biol.* (1970) **48**, 443–453

# A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins

SAUL B. NEEDLEMAN AND CHRISTIAN D. WUNSCH

*Department of Biochemistry, Northwestern University, and Nuclear Medicine Service, V. A. Research Hospital Chicago, Ill. 60611, U.S.A.*

(*Received 21 July 1969*)

A computer adaptable method for finding similarities in the amino acid sequences of two proteins has been developed. From these findings it is possible to determine whether significant homology exists between the proteins. This information is used to trace their possible evolutionary development.

The maximum match is a number dependent upon the similarity of the sequences. One of its definitions is the largest number of amino acids of one protein that can be matched with those of a second protein allowing for all possible interruptions in either of the sequences. While the interruptions give rise to a very large number of comparisons, the method efficiently excludes from consideration those comparisons that cannot contribute to the maximum match.

Comparisons are made from the smallest unit of significance, a pair of amino acids, one from each protein. All possible pairs are represented by a two-dimensional array, and all possible comparisons are represented by pathways through the array. For this maximum match only certain of the possible pathways must be evaluated. A numerical value, one in this case, is assigned to every cell in the array representing like amino acids. The maximum match is the largest number that would result from summing the cell values of every pathway.

## 1. Introduction

The amino acid sequences of a number of proteins have been compared to determine whether the relationships existing between them could have occurred by chance. Generally, these sequences are from proteins having closely related functions and are so similar that simple visual comparisons can reveal sequence coincidence. Because the method of visual comparison is tedious and because the determination of the significance of a given result usually is left to intuitive rationalization, computer-based statistical approaches have been proposed (Fitch, 1966; Needleman & Blair, 1969).

Direct comparison of two sequences, based on the presence in both of corresponding amino acids in an identical array, is insufficient to establish the full genetic relationships between the two proteins. Allowance for gaps (Braunitzer, 1965) greatly multiplies the number of comparisons that can be made but introduces unnecessary and partial comparisons.

## 2. A General Method for Sequence Comparison

The smallest unit of comparison is a pair of amino acids, one from each protein. The maximum match can be defined as the largest number of amino acids of one protein that can be matched with those of another protein while allowing for all possible deletions.



Motif Exhibit 1002, Page 326 of 1290

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



The maximum match can be determined by representing in a two-dimensional array, all possible pair combinations that can be constructed from the amino acid sequences of the proteins, $A$ and $B$, being compared. If the amino acids are numbered from the N-terminal end, $Aj$ is the $j$th amino acid of protein $A$ and $Bi$ is the $i$th amino acid of protein $B$. The $Aj$ represent the columns and the $Bi$ the rows of the two-dimensional array, MAT. Then the cell, MAT$ij$, represents a pair combination that contains $Aj$ and $Bi$.

Every possible comparison can now be represented by pathways through the array. An $i$ or $j$ can occur only once in a pathway because a particular amino acid cannot occupy more than one position at one time. Furthermore, if MAT$mn$ is part of a pathway including MAT$ij$, the only permissible relationships of their indices are $m > i$, $n > j$ or $m < i$, $n < j$. Any other relationships represent permutations of one or both amino acid sequences which cannot be allowed since this destroys the significance of a sequence. Then any pathway can be represented by MAT$ab$ . . . MAT$yz$, where $a \geqslant 1$, $b \geqslant 1$, the $i$ and $j$ of all subsequent cells of MAT are larger than the running indices of the previous cell and $y \leqslant K$, $z \leqslant M$, the total number of amino acids comprising the sequences of proteins $A$ and $B$, respectively. A pathway is signified by a line connecting cells of the array. Complete diagonals of the array contain no gaps. When MAT$ij$ and MAT$mn$ are part of a pathway, $i - m \neq j - n$ is a sufficient, but not necessary condition for a gap to occur. A necessary pathway through MAT is defined as one which begins at a cell in the first column or the first row. Both $i$ and $j$ must increase in value; either $i$ or $j$ must increase by only one but the other index may increase by one or more. This leads to the next cell in a MAT pathway. This procedure is repeated until either $i$ or $j$, or both, equal their limiting values, $K$ and $M$, respectively. Every partial or unnecessary pathway will be contained in at least one necessary pathway.

In the simplest method, MAT$ij$ is assigned the value, one, if $Aj$ is the same kind of amino acid as $Bi$; if they are different amino acids, MAT$ij$ is assigned the value, zero. The sophistication of the comparison is increased if, instead of zero or one, each cell value is made a function of the composition of the proteins, the genetic code triplets representing the amino acids, the neighboring cells in the array, or any theory concerned with the significance of a pair of amino acids. A penalty factor, a number subtracted for every gap made, may be assessed as a barrier to allowing the gap. The penalty factor could be a function of the size and/or direction of the gap. No gap would be allowed in the operation unless the benefit from allowing that gap would exceed the barrier. The maximum-match pathway then, is that pathway for which the sum of the assigned cell values (less any penalty factors) is largest. MAT can be broken up into subsections operated upon independently. The method also can be expanded to allow simultaneous comparison of several proteins using the amino acid sequences of $n$ proteins to generate an $n$-dimensional array whose cells represent all possible combinations of $n$ amino acids, one from each protein.

The maximum-match pathway can be obtained by beginning at the terminals of the sequences ($i = y, j = z$) and proceeding toward the origins, first by adding to the value of each cell possessing indices $i = y - 1$ and/or $j = z - 1$, the maximum value from among all the cells which lie on a pathway to it. The process is repeated for indices $i = y - 2$ and/or $j = z - 2$. This increment in the indices is continued until all cells in the matrix have been operated upon. Each cell in this outer row or column will contain the maximum number of matches that can be obtained by originating

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



any pathway at that cell and the largest number in that row or column is equal to the maximum match; the maximum-match pathway in any row or column must begin at this number. The operation of successive summations of cell values is illustrated in Figures 1 and 2.

| | A | B | C | N | J | R | Q | C | L | C | R | P | M |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 1 | | | | | | | | | | | | |
| J | | | | | 1 | | | | | | | | |
| C | | | 1 | | | | | 1 | | 1 | | | |
| J | | | | | 1 | | | | | | | | |
| N | | | | 1 | | | | | | | | | |
| R | | | | | | 1 | 4 | 3 | 3 | 2 | 2 | 0 | 0 |
| C | 3 | 3 | 4 | 3 | 3 | 3 | 3 | 4 | 3 | 3 | 1 | 0 | 0 |
| K | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 1 | 0 | 0 |
| C | 2 | 2 | 3 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 1 | 0 | 0 |
| R | 2 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 2 | 0 | 0 |
| B | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| P | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

FIG. 1. The maximum-match operation for necessary pathways.
The number contained in each cell of the array is the largest number of identical pairs that can be found if that cell is the origin for a pathway which proceeds with increases in running indices. Identical pairs of amino acids were given the value of one. Blank cells which represent non-identical pairs have the value, zero. The operation of successive summations was begun at the last row of the array and proceeded row-by-row towards the first row. The operation has been partially completed in the R row. The enclosed cell in this row is the site of the cell operation which consists of a search along the subrow and subcolumn indicated by borders for the largest value, 4 in subrow C. This value is added to the cell from which the search began.

| | A | B | C | N | J | R | Q | C | L | C | R | P | M |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 8 | 7 | 6 | 6 | 5 | 4 | 4 | 3 | 3 | 2 | 1 | 0 | 0 |
| J | 7 | 7 | 6 | 6 | 6 | 4 | 4 | 3 | 3 | 2 | 1 | 0 | 0 |
| C | 6 | 6 | 7 | 6 | 5 | 4 | 4 | 4 | 3 | 3 | 1 | 0 | 0 |
| J | 6 | 6 | 6 | 5 | 6 | 4 | 4 | 3 | 3 | 2 | 1 | 0 | 0 |
| N | 5 | 5 | 5 | 6 | 5 | 4 | 4 | 3 | 3 | 2 | 1 | 0 | 0 |
| R | 4 | 4 | 4 | 4 | 4 | 5 | 4 | 3 | 3 | 2 | 2 | 0 | 0 |
| C | 3 | 3 | 4 | 3 | 3 | 3 | 3 | 4 | 3 | 3 | 1 | 0 | 0 |
| K | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 1 | 0 | 0 |
| C | 2 | 2 | 3 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 1 | 0 | 0 |
| R | 2 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 2 | 0 | 0 |
| B | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| P | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

FIG. 2. Contributors to the maximum match in the completed array.
The alternative pathways that could form the maximum match are illustrated. The maximum match terminates at the largest number in the first row or first column, 8 in this case.

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



It is apparent that the above array operation can begin at any of a number of points along the borders of the array, which is equivalent to a comparison of N-terminal residues or C-terminal residues only. As long as the appropriate rules for pathways are followed, the maximum match will be the same. The cells of the array which contributed to the maximum match, may be determined by recording the origin of the number that was added to each cell when the array was operated upon.

## 3. Evaluating the Significance of the Maximum Match

A given maximum match may represent the maximum number of amino acids matched, or it may just be a number that is a complex function of the relationship between sequences. It will, however, always be a function of both the amino acid compositions of the proteins and the relationship between their sequences. One may ask whether a particular result found differs significantly from a fortuitous match between two random sequences. Ideally,one would prefer to know the exact probability of obtaining the result found from a pair of random sequences and what fraction of the total possibilities are less probable, but that is prohibitively difficult, especially if a complex function were used for assigning a value to the cells.

As an alternative to determining the exact probabilities, it is possible to estimate the probabilities experimentally. To accomplish the estimate one can construct two sets of random sequences, a set from the amino acid composition of each of the proteins compared. Pairs of random sequences can then be formed by randomly drawing one member from each set. Determining the maximum match for each pair selected will yield a set of random values. If the value found for the real proteins is significantly different from the values found for the random sequences, the difference is a function of the sequences alone and not of the compositions. Alternatively, one can construct random sequences from only one of the proteins and compare them with the other to determine a set of random values. The two procedures measure different probabilities. The first procedure determines whether a significant relationship exists *between* the real sequences. The second procedure determines whether the relationship *of* the protein used to form the random sequences *to* the other proteins is significant. It bears reiterating that the integral amino acid composition of each random sequence must be equal to that of the protein it represents.

The amino acid sequence of each protein compared belongs to a set of sequences which are permutations. Sequences drawn randomly from one or both of these sets are used to establish a distribution of random maximum-match values which would include all possible values if enough comparisons were made. The null hypothesis, that any sequence relationship manifested by the two proteins is a random one, is tested. If the distribution of random values indicates a small probability that a maximum match equal to, or greater than, that found for the two proteins could be drawn from the random set, the hypothesis is rejected.

## 4. Cell Values and Weighting Factors

To provide a theoretical framework for experiments, amino acid pairs may be classified into two broad types, identical and non-identical pairs. From 20 different amino acids one can construct 180 possible non-identical pairs. Of these, 75 pairs of amino acids have codons (Marshall, Caskey & Nirenberg, 1967) whose bases differ at only one position (Eck & Dayhoff, 1966). Each change is presumably the result of a

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



single-point mutation. The majority of non-identical pairs have a maximum of only one or zero corresponding bases. Due to the degeneracy of the genetic code, pair differences representing amino acids with no possible corresponding bases are uncommon even in randomly selected pairs. If cells are weighted in accordance with the maximum number of corresponding bases in codons of the represented amino acids, the maximum match will be a function of identical and non-identical pairs. For comparisons in general, the cell weights can be chosen on any basis.

If every possible sequence gap is allowed in forming the maximum match, the significance of the maximum match is enhanced by decreasing the weight of those pathways containing a large number of gaps. A simple way to accomplish this is to assign a penalty factor, a number which is subtracted from the maximum match for each gap used to form it. The penalty is assigned before the maximum match is formed. Thus the pathways will be weighted according to the number of gaps they contain, but the nature of the contributors to the maximum match will be affected as well. In proceeding from one cell to the next in a maximum-match pathway, it is necessary that the difference between each cell value and the penalty, be greater than the value for a cell in a pathway that contains no gap. If the value of the penalty were zero, all possible gaps could be allowed. If the value were equal to the theoretical value for the maximum match between two proteins, it would be impossible to allow a gap and the maximum match would be the largest of the values found by simply summing along the diagonals of the array; this is the simple frame-shift method.

## 5. Application of the Method

To illustrate the role of weighting factors in evaluating a maximum match, two proteins expected to show homology, whale myoglobin (Edmundson, 1965) and human $\beta$-hemoglobin (Konigsberg, Goldstein & Hill, 1963), and two proteins not expected to exhibit homology, bovine pancreatic ribonuclease (Smyth, Stein & Moore, 1963) and hen's egg lysozyme (Canfield, 1963) were chosen for comparisons.

The FORTRAN programs used in this study were written for the CDC3400 computer. The operations employed in forming the maximum match are those for the special case when none of the cells of the array have a value less than zero. Four types of amino acid pairs were distinguished and variable sets consisting of values to be assigned to each type of pair and a value for the penalty were established. The pair types are as follows:

*Type 3.* Identical pairs: those having a maximum of three corresponding bases in their codons.

*Type 2.* Pairs having a maximum of two corresponding bases in their codons.

*Type 1.* Pairs having a maximum of one corresponding base in their codons.

*Type 0.* Pairs having no possible corresponding base in their codons.

The value for type 3 pairs was 1·0 and the value for type 0 pairs was zero for all variable sets.

At program execution time, the amino acids (coded by two-digit numbers) of the sequences to be compared were read into the computer, and were followed by a twenty-by-twenty symmetrical array, the maximum correspondence array, analogous to one used by Fitch (1966), that contained all possible pairs of amino acids and identified each pair as to type. The RNA codons for amino acids used to construct the maximum-correspondence array were taken from a single Table (Marshall *et al.*,

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



1967). The UGA, UAA and UAG codons were not used, but UUG was used as a codon for leucine. The subsequent data cards indicated the numerical values for a variable set.

The two-dimensional comparison array was generated row-by-row. The amino acid code numbers for $Ai$ and $Bj$ referenced the correspondence array to determine the type of amino acid pair constituted by $Ai$ and $Bj$. The type number referenced a short array, the variable set, containing the type values, and the appropriate value from that set was assigned to the appropriate cell of the comparison array. The maximum match was then determined by the procedure of successive summations.

Following the determination of the maximum match for the real proteins, the amino acid sequence of only one member of the protein pair was randomized and the match was repeated. The sequences of $\beta$-hemoglobin and ribonuclease were the ones randomized. The randomization procedure was a sequence shuffling routine based on computer-generated random numbers. A cycle of sequence randomization–maximum-match determination was repeated ten times in all of the experiments in this report, giving the random values used for comparison with the real maximum-match. The average and standard deviation for the random values of each variable set was estimated.

## 6. Results and Discussion

The use of a small random sample size (ten) was necessary to hold the computer time to a reasonable level. The maximum probable error in a standard deviation estimate for a sample this small is quite large and the results should be judged with this fact in mind. For each set of variables, it was assumed that the random values would be distributed in the fashion of the normal-error curve; therefore, the values of the first six random sets in the $\beta$-hemoglobin–myoglobin comparison were converted to standard measure, five was added to the result, and these values were plotted as *one* group against their calculated probit. The results of the plot are shown in Figure 3. The fit is good indicating the probable adequacy of the measured standard deviations for these variable sets in estimating distribution functions for random values through two standard deviations. The above fit indicates no bias in the randomization procedure. In other words, randomization of the sequence was complete before the maximum match was determined for any sequence in a random set.

The results obtained in the comparison of $\beta$-hemoglobin with myoglobin are summarized in Table 1 and the results for the ribonuclease–lysozyme comparison are in Table 2. These Tables indicate the values assigned to the pair types, the penalty factor used in forming each of the maximum matches, and the statistical results obtained. The number of gaps roughly characterizes the nature of the pathway that formed the maximum match. A large number is indicative of a devious pathway through the array. One gap means that all of the pathway may be found on only two partial diagonals of the array.

The most important information is obtained from the standardized value of the maximum match for the real proteins, the difference from the mean in standard-deviation units. For this sample size all deviations greater than 3·0 were assumed to include less than 1% of the true random population and to indicate a significant difference. As might be expected, all matches of myoglobin and $\beta$-hemoglobin show a significant deviation. Among the sets of variables, set 1, which results in a search for identical amino acid pairs while allowing for all deletions, indicates that 63

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



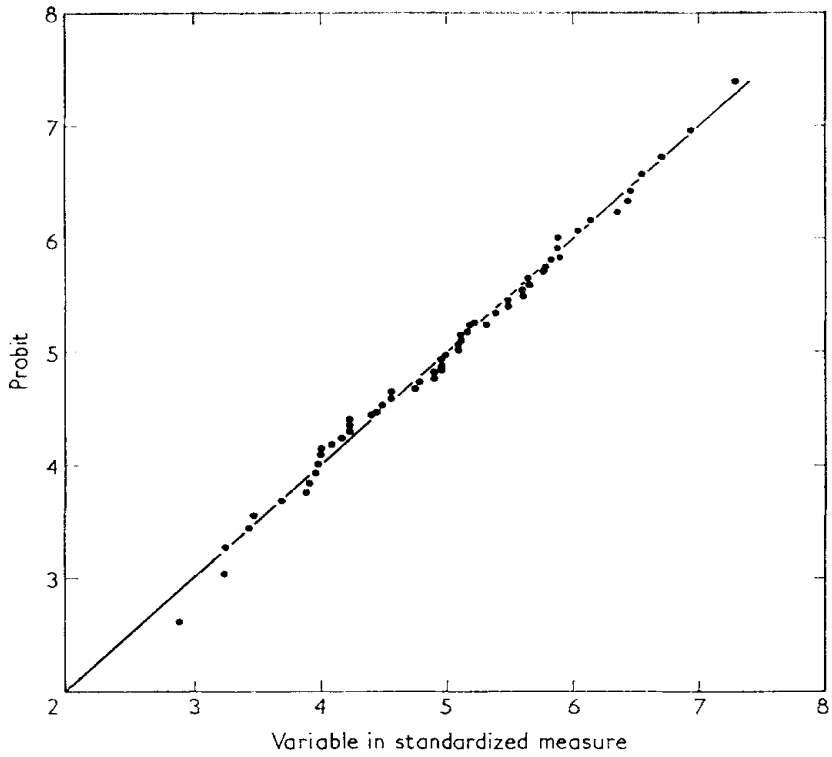



FIG. 3. Probit plot for six grouped random samples.

The solid line indicates the plot that would result from a probit analysis on an infinite number of samples from a normally-distributed population. The points represent the results of probit calculations on 60 random maximum match values that were assumed to have come from one population.

TABLE 1

*β-Hemoglobin–myoglobin maximum matches*

| Variable set | Match values for pair types | | Penalty | Maximum-match value sum | | $s$ | Real $X$ | Minimum deletions | |
|---|---|---|---|---|---|---|---|---|---|
| | 2 | 1 | | Real | Random† | | | Real | Random† |
| 1 | 0 | 0 | 0 | 63·00 | 55·60 | 1·80 | 4·11 | 35 | 36·2 |
| 2 | 0 | 0 | 1·00 | 38·00 | 27·80 | 2·09 | 4·88 | 4 | 5·5 |
| 3 | 0·67 | 0·33 | 0 | 97·00 | 91·47 | 1·55 | 3·57 | 18 | 24·3 |
| 4 | 0·67 | 0·33 | 1·03 | 89·63 | 80·25 | 1·11 | 8·46 | 1 | 3·6 |
| 5 | 0·25 | 0·05 | 0 | 71·55 | 64·78 | 1·59 | 4·27 | 46 | 45·0 |
| 6 | 0·25 | 0·05 | 1·05 | 51·95 | 40·54 | 1·46 | 7·80 | 3 | 7·5 |
| 7 | 0·25 | 0·05 | 25 | 47·30 | 33·80 | 1·52 | 8·87 | 0 | 0 |

$s$ is the estimated standard deviation; $X$, the standardized value, (real − random)/$s$, of the maximum match of the real proteins. The values for type 3 and type 0 pairs were 1·0 and 0, respectively, in each variable set.

† An average value from 10 samples.

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



TABLE 2

*Ribonuclease–lysozyme maximum matches*

| Variable set | Match values for pair types | | Penalty | Maximum-match value sum | | $s$ | Real $X$ | Minimum deletions | |
|---|---|---|---|---|---|---|---|---|---|
| | 2 | 1 | | Real | Random† | | | Real | Random† |
| 1 | 0 | 0 | 0 | 48·00 | 44·20 | 2·56 | 1·48 | 34 | 29·2 |
| 2 | 0 | 0 | 1·00 | 23·00 | 22·00 | 1·73 | 0·58 | 5 | 5·2 |
| 3 | 0·67 | 0·33 | 0 | 78·33 | 76·17 | 0·82 | 2·64 | 21 | 18·8 |
| 4 | 0·67 | 0·33 | 1·03 | 67·93 | 67·37 | 1·27 | 0·43 | 2 | 2·2 |
| 5 | 0·25 | 0·05 | 0 | 56·00 | 52·26 | 2·12 | 1·77 | 35 | 35·5 |
| 6 | 0·25 | 0·05 | 1·05 | 33·70 | 33·02 | 1·66 | 0·41 | 8 | 6·8 |
| 7 | 0·25 | 0·05 | 25 | 28·15 | 27·67 | 1·75 | 0·22 | 0 | 0 |

$s$ is the estimated standard deviation; $X$, the standardized value, (real − random)/$s$, of the maximum match of the real proteins. The values for type 3 and type 0 pairs were 1·0 and 0, respectively in each variable set.

† An average value from 10 samples.

amino acids in β-hemoglobin and myoglobin can be matched. To attain this match, however, it is necessary to permit at least 35 gaps. In contrast, when two gaps are allowed according to Braunitzer (1965), it is possible to match only 37 of the amino acids. Curiously, when this variable set was used for comparing *human* myoglobin (Hill, personal communication) with human β-hemoglobin, the maximum match obtained was not significant. Differences between real and random values were highly significant, however, when other variable sets were used.

Variable set 2 attaches a penalty equal to the value of one identical amino acid pair to the search for identical amino acid pairs. This penalty will exclude from consideration any possible pathway that leaves and returns to a principal diagonal, thereby needing two gaps, in order to add only one or two amino acids to the maximum match. This set results in a total of $30 + 4 = 42$ amino acids matched (the maximum-match value plus the number of gaps is reduced to four) and the significance of the result relative to set 1 appears to be increased. Braunitzer's comparison would have a value of $37 - 2 = 35$ using this variable set, hence it was not selected by the method.

Variable sets 3 and 4 have an interesting property. Their maximum-match values can be related to the minimum number of mutations needed to convert the selected parts of one amino acid sequence into the selected parts of the other. The minimum number of mutations concept in protein comparisons was first advanced by Fitch (1966). If the type values for these sets are multiplied by three, they become equal to their pair type and directly represent the maximum number of corresponding bases in the codons for a given amino acid pair. Thus the maximum match and penalty factors may be multiplied by three, making it possible to calculate the maximum number of bases matched in the combination of amino acid pairs selected by the maximum-match operation.

β-Hemoglobin, the smaller of the two proteins, contains 146 amino acids; consequently the highest possible maximum match (disregarding integral amino-acid composition data) with myoglobin is $146 \times 3 = 438$. Insufficient data are available

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



to analyze the result from set 3 on the basis of mutations. If it is assumed that the gap in set 4 does not exclude any part of $\beta$-hemoglobin from the comparison, this set has a maximum of $3(89{\cdot}63 + 1{\cdot}03) = 272$ bases matched, indicating a minimum of $438 - 272 = 166$ point mutations in this combination. Using this variable set and placing gaps according to Braunitzer, a score of 88·6 was obtained, thus his match was not selected. Again it may be observed that the penalty greatly enhanced the significance of the maximum match.

Variable sets 5 and 6 have no intrinsic meaning and were chosen because the weight attached to type 2 and type 1 pairs is intermediate in value with respect to sets 1 and 2 and sets 3 and 4. The maximum match for set 6 is seen to have a highly significant value.

The data of set 7 are results that would be obtained from using the frame-shift method to select a maximum match; the penalty was large enough to prevent any gaps in the comparisons. The slight differences in significance found among the maximum-match values of $\beta$-hemoglobin and myoglobin resulting from use of sets 4, 6 and 7 are probably meaningless due to small sample size and errors introduced by the assumptions about the distribution functions of random values. Finding a value in set 7 that is approximately equal to those from sets 4 and 6 in significance is not surprising. A larger penalty factor would have increased the difference from the mean in sets 4 and 6 because almost every random value in each set was the result of more gaps than were required to form the real maximum match. Further, the gaps that are allowed are at the N-terminal ends so that about 85% of the comparison can be made without gaps. If an actual gap were present near the middle of one of the sequences, it would have caused a sharp reduction in the significance of the frame-shift type of match.

Set 3 is the only variable set in Table 2 that shows a possible difference. Assuming the value is accurate, other than chance, there is no simple explanation for the difference. A small but meaningful difference in any comparison could represent evolutionary divergence or convergence. It is generally accepted that the primary structure of proteins is the chief determinant of the tertiary structure. Because certain features of tertiary structure are common to proteins, it is reasonable to suppose that proteins will exhibit similarities in their sequences, and that these similarities will be sufficient to cause a significant difference between most protein pairs and their corresponding randomized sequences, being an example of submolecular evolutionary convergence. Further, the interactions of the protein backbone, side chains, and the solvent that determine tertiary structure are, in large measure, forces arising from the polarity and steric nature of the protein side-chains. There are conspicuous correlations in the polarity and steric nature of type 2 pairs. Heavy weighting of these pairs would be expected to enhance the significance of real maximum-match values if common structural features are present in proteins that are compared. The presence of sequence similarities does not always imply common ancestry in proteins. More experimentation will be required before a choice among the possibilities suggested for the result from set 3 can be made. If several short sequences of amino acids are common to all proteins, it seems remarkable that the relationship of ribonuclease to lysozyme in six of the seven variable sets appears to be truly a random one. It should be noted, however, that the standard value of the real maximum-match is positive in each variable set in this comparison.

This method was designed for the purpose of detecting homology and defining its nature when it can be shown to exist. Its usefulness for the above purposes depends in

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



part upon assumptions related to the genetic events that could have occurred in the evolution of proteins. Starting with the assumption that homologous proteins are the result of gene duplication and subsequent mutations, it is possible to construct several hypothetical amino-acid sequences that would be expected to show homology. If one assumes that following the duplication, point mutations occur at a constant or variable rate, but randomly, along the genes of the two proteins, after a relatively short period of time the protein pairs will have nearly identical sequences. Detection of the high degree of homology present can be accomplished by several means. The use of values for non-identical pairs will do little to improve the significance of the results. If no, or very few, deletions (insertions) have occurred, one could expect to enhance the significance of the match by assigning a relatively high penalty for gaps. Later on in time the hypothetical proteins may have a sizable fraction of their codons changed by point mutations, the result being that an attempt to increase the significance of the maximum match will probably require attaching substantial weight to those pairs representing amino acids still having two of the three original bases in their codons. Further, if a few more gaps have occurred, the penalty should be reduced to a small enough value to allow areas of homology to be linked to one another. At a still later date in time more emphasis must be placed on non-identical pairs, and perhaps a very small or even negative penalty factor must be assessed. Eventually, it will be impossible to detect the remaining homology in the hypothetical example by using the approach detailed here.

From consideration of this simple model of protein evolution one may deduce that the variables which maximize the significance of the difference between real and random proteins gives an indication of the nature of the homology. In the comparison of human $\beta$-hemoglobin to whale myoglobin, the assignment of some weight to type 2 pairs considerably enhances the significance of the result, indicating substantial evolutionary divergence. Further, few deletions (additions) have apparently occurred.

It is known that the evolutionary divergence manifested by cytochrome (Margoliash, Needleman & Stewart, 1963) and other heme proteins (Zuckerkandl & Pauling, 1965) did not follow the sample model outlined above. Their divergence is the result of *non-random* mutations along the genes. The degree and type of homology can be expected to differ between protein pairs. As a consequence of the difference there is no *a priori* best set of cell and operation values for maximizing the significance of a maximum-match value of homologous proteins, and as a corollary to this fact, there is no best set of values for the purpose of detecting only slight homology. This is an important consideration, because whether the sequence relationship between proteins is significant depends solely upon the cell and operation values chosen. If it is found that the divergence of proteins follows one or two simple models, it may be possible to derive a set of values that will be most useful in detecting and defining homology.

The most common method for determining the degree of homology between protein pairs has been to count the number of non-identical pairs (amino acid replacements) in the homologous comparison and to use this number as a measure of evolutionary distance between the amino acid sequences. A second, more recent concept has been to count the minimum number of mutations represented by the non-identical pairs. This number is probably a more adequate measure of evolutionary distance because it utilizes more of the available information and theory to give some measure of the number of genetic events that have occurred in the evolution of the proteins. The approach outlined in this paper supplies either of these numbers.

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



This work was supported in part by grants to one of us (S.B.N.) from the U.S. Public Health Service (1 501 FR 05370 02) and from Merck Sharp & Dohme.

## REFERENCES

Braunitzer, G. (1965). In *Evolving Genes and Proteins*, ed. by V. Bryson & H. J. Vogel, p. 183. New York: Academic Press.

Canfield, R. (1963). *J. Biol. Chem.* **238**, 2698.

Eck, R. V. & Dayhoff, M. O. (1966). *Atlas of Protein Sequence and Structure*. Silver Spring, Maryland: National Biomedical Research Foundation.

Edmundson, A. B. (1965). *Nature*, **205**, 883.

Fitch, W. (1966). *J. Mol. Biol.* **16**, 9.

Konigsberg, W., Goldstein, J. & Hill, R. J. (1963). *J. Biol. Chem.* **238**, 2028.

Margoliash, E., Needleman, S. B. & Stewart, J. W. (1963). *Acta Chem. Scand.* **17**, S 250.

Marshall, R. E., Caskey, C. T. & Nirenberg, M. (1967). *Science*, **155**, 820.

Needleman, S. B. & Blair, T. H. (1969). *Proc. Nat. Acad. Sci., Wash.* **63**, 1127.

Smyth, D. G., Stein, W. G. & Moore, S. (1963). *J. Biol. Chem.* **238**, 227.

Zuckerkandl, E. & Pauling, L. (1965). In *Evolving Genes and Proteins*, ed. by V. Bryson & H. J. Vogel, p. 97. New York: Academic Press.

- NCBI Home
- Sign in to NCBI
- Skip to Main Content
- Skip to Navigation
- About NCBI Accesskeys

NIH U.S. National Library of Medicine

NCBI National Center for Biotechnology Information

- 
- My NCBI
- Sign in to NCBI
- Register
- Sign Out

BLAST ® » Global Alignment

- Home
- Recent Results
- Saved Strategies

Needleman-Wunsch Global Align Nucleotide Sequences

- 
- 
- Nucleotide
- 
- Protein
- 

Needleman-Wunsch alignment of two nucleotide sequences
[?]
Reset page Bookmark

Enter Query Sequence

Enter accession number, gi, or FASTA sequence
[?]
Clear

Input limited to 100,000 letters for either input sequence. The total length of both query and subject may not exceed 150,000 letters.

Query subrange
[?]
Query subrangeFrom

Query subrangeTo

Or, upload file

Browse...

[?]

Genetic code

Standard (1)

Job Title

Enter a descriptive title for your BLAST search

[?]

☑ Align two or more sequences

[?]

Enter Subject Sequence

Enter accession number, gi, or FASTA sequence

[?]

Clear

Input limited to 100,000 letters for either input sequence. The total length of both query and subject may not exceed 150,000 letters.

Subject subrange

[?]

Subject subrangeFrom

Subject subrangeTo

Or, upload file

Browse...

[?]

Choose Search Set

Database

○ Human genomic + transcript ○ Mouse genomic + transcript ◉ Others (nr etc.):

♦Database sequences non-default value

Nucleotide collection (nr/nt)

[?]

Limit by

○ Organism ○ BioProjectID ○ WGS Project

Organism

Optional

Enter organism name or id--completions will be suggested ☐ Exclude +

Enter organism common name, binomial, or tax id. Only 20 top taxa will be shown

[?]

Exclude

Optional

☐ Exclude Models (XM/XP) ☐ Exclude Uncultured/environmental sample sequences
Limit to
Optional
☐ Sequences from type material
Entrez Query
Optional
Create custom database
Enter an Entrez query to limit search
[?]

Align

☐ Show results in a new window
Algorithm parameters

11 | 16 | 11 | Linear | Linear
Linear | Existence: 5 Extension: 2 | Linear
Existence: 5 Extension: 2

BLAST is a registered trademark of the National Library of Medicine

Support center Mailing list YouTube

- National Library Of Medicine
- National Institutes Of Health
- U.S. Department of Health & Human Services
- USA.gov

NCBI

*National Center for Biotechnology Information, U.S. National Library of Medicine 8600 Rockville Pike, Bethesda MD, 20894 USA*
Policies and Guidelines | Contact

| Designation | Organism/Strain |
|---|---|
| H6WZ70 | H6WZ70_VIGRA Non-symbiotic hemoglobin OS=Vigna radiata GN=NSH PE=2 SV=1 |
| B3DUZ7 | B3DUZ7_METI4 Hemoglobin-like flavoprotein OS=Methylacidiphilum infernorum (isolate V4) GN=hmp PE=1 SV=1 |
| O66586 | Y211_AQUAE Uncharacterized globin-like protein aq_211 OS=Aquifex aeolicus (strain VF5) GN=aq_211 PE=3 SV=1 |
| P02236 | LGB2_SOYBN Leghemoglobin C2 OS=Glycine max PE=1 SV=2 |
| Q42831 | HBL_HORVU Non-symbiotic hemoglobin OS=Hordeum vulgare GN=HB PE=1 SV=1 |
| G4N2X9 | G4N2X9_MAGO7 Heme peroxidase OS=Magnaporthe oryzae (strain 70-15 / ATCC MYA-4617 / FGSC 8958) GN=MGG_10859 PE=4 SV=1 |
| N4UFN7 | N4UFN7_FUSC1 Peroxidase OS=Fusarium oxysporum f. sp. cubense (strain race 1) GN=FOC1_g10007184 PE=3 SV=1 |
| Q4ING3 | CCPR_GIBZE Cytochrome c peroxidase mitochondrial OS=Gibberella zeae (strain PH-1 / ATCC MYA-4620 / FGSC 9075 / NRRL 31084) GN=CCP1 PE=3 SV=1 |
| Q08753 | TRHN1_CHLMO Group 1 truncated hemoglobin LI637 OS=Chlamydomonas moewusii GN=LI637 PE=1 SV=1 |
| P17724 | LGB2_SOYBN Leghemoglobin C2 OS=Glycine max PE=1 SV=2 |
| P15160 | TRHBN_PARCA Group 1 truncated hemoglobin trHbN OS=Paramecium caudatum PE=1 SV=2 |
| Q5DVM4 | Q5DVM4_ASPNG Putative haemoglobin OS=Aspergillus niger GN=hmb1 PE=3 SV=1 |
| Q9FY42 | HBL_MAIZE Non-symbiotic hemoglobin OS=Zea mays GN=HB PE=2 SV=1 |
| O04985 | HBL2_ORYSJ Non-symbiotic hemoglobin 2 OS=Oryza sativa subsp. japonica GN=HB2 PE=2 SV=1 |
| O24520 | HBL1_ARATH Non-symbiotic hemoglobin 1 OS=Arabidopsis thaliana GN=AHB1 PE=1 SV=1 |
| O48668 | LGB2_PEA Leghemoglobin Lb5-10 OS=Pisum sativum PE=2 SV=3 |
| Q43236 | LGB1_VIGUN Leghemoglobin-1 OS=Vigna unguiculata GN=LBI PE=2 SV=1 |
| P02192 | MYG_BOVIN Myoglobin OS=Bos taurus GN=MB PE=1 SV=3 |
| P02189 | MYG_PIG Myoglobin OS=Sus scrofa GN=MB PE=1 SV=2 |
| P68082 | MYG_HORSE Myoglobin OS=Equus caballus GN=MB PE=1 SV=2 |
| Nicotiana_benthamiana | Nicotiana_benthamiana non symbiotic hemoglobin |
| A0A063XGS7 | A0A063XGS7_BACIU Group 2 truncated hemoglobin YjbI OS=Bacillus subtilis GN=yjbI PE=4 SV=1 |
| Q8NMW6 | Q8NMW6_CORGL Hemoglobin-like proteins OS=Corynebacterium glutamicum (strain ATCC 13032 / DSM 20300 / JCM 1318 / LMG 3730 / NCIMB 10025) GN=Cgl2448 PE=4 SV=1 |
| P73925 | TRHBN_SYNY3 Group 1 truncated hemoglobin GlbN OS=Synechocystis sp. (strain PCC 6803 / Kazusa) GN=glbN PE=1 SV=1 |
| B4WLV9 | B4WLV9_SYNS7 Globin domain protein OS=Synechococcus sp. (strain ATCC 29403 / PCC 7335) GN=S7335_2344 PE=3 SV=1 |
| Q00812 | TRHBN_NOSCO Group 1 truncated hemoglobin GlbN OS=Nostoc commune GN=glbN PE=3 SV=1 |
| G2RXE0 | G2RXE0_BACME Hemoglobin-like protein OS=Bacillus megaterium WSH-002 GN=BMWSH_4530 PE=4 SV=1 |

| | SEQ ID NO: |
|---|---|
| H6WZ70 | SEQ ID NO:1 *Vigna radiata* |
| B3DUZ7 | SEQ ID NO:2 *Methylacidiphilum infernorum* |
| O66586 | SEQ ID NO:3 *Aquifex aeolicus* |
| P02236 | SEQ ID NO:4 *Glycine max* |
| Q42831 | SEQ ID NO:5 *Hordeum vulgare* |
| G4N2X9 | SEQ ID NO:6 *Magnaporthe oryzae* |
| N4UFN7 | SEQ ID NO:7 *Fusarium oxysporum* |
| Q4ING3 | SEQ ID NO:8 *Fusarium graminearum* |
| Q08753 | SEQ ID NO:9 *Chlamydomonas eugametos* |
| P17724 | SEQ ID NO:10 *Tetrahymena pyriformis* |
| P15160 | SEQ ID NO:11 *Paramecium caudatum* |
| Q5DVM4 | SEQ ID NO:12 *Aspergillus niger* |
| Q9FY42 | SEQ ID NO:13 *Zea mays* |
| O04985 | SEQ ID NO:14 *Oryza sativa subsp. japonica* |
| O24520 | SEQ ID NO:15 *Arabidopsis thaliana* |
| O48668 | SEQ ID NO:16 *Pisum sativum* |
| Q43236 | SEQ ID NO:17 *Vigna unguiculata* |
| P02192 | SEQ ID NO:18 *Bos taurus* |
| P02189 | SEQ ID NO:19 *Sus scrofa* |
| P68082 | SEQ ID NO:20 *Equus caballus* |
| Nicotiana_benthamiana | SEQ ID NO:21 *Nicotiana benthamiana* |
| A0A063XGS7 | SEQ ID NO:22 *Bacillus subtilis* |
| Q8NMW6 | SEQ ID NO:23 *Corynebacterium glutamicum* |
| P73925 | SEQ ID NO:24 *Synechocystis* PCC6803 |
| B4WLV9 | SEQ ID NO:25 *Synechococcus* sp. PCC 7335 |
| Q00812 | SEQ ID NO:26 *Nostoc commune* |
| G2RXE0 | SEQ ID NO:27 *Bacillus megaterium* |

| | H6WZ70 | B3DUZ7 | O66586 | P02236 | Q42831 | G4N2X9 | N4UFN7 | Q4ING3 | Q08753 | P17724 | P15160 | Q5DVM4 | Q9FY42 | O04985 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| H6WZ70 | 100% | 21% | 23% | 40% | 70% | 5% | 11% | 13% | 18% | 14% | 16% | 18% | 70% | 68% |
| B3DUZ7 | 21% | 100% | 30% | 24% | 24% | 5% | 9% | 11% | 18% | 19% | 19% | 22% | 21% | 22% |
| O66586 | 23% | 28% | 100% | 25% | 19% | 5% | 8% | 11% | 16% | 15% | 16% | 37% | 19% | 17% |
| P02236 | 40% | 24% | 25% | 100% | 36% | 6% | 10% | 11% | 19% | 21% | 18% | 23% | 37% | 38% |
| Q42831 | 70% | 24% | 19% | 36% | 100% | 5% | 10% | 13% | 18% | 15% | 19% | 15% | 84% | 80% |
| G4N2X9 | 5% | 5% | 5% | 6% | 5% | 100% | 13% | 11% | 6% | 5% | 5% | 6% | 5% | 6% |
| N4UFN7 | 11% | 9% | 8% | 10% | 10% | 13% | 100% | 15% | 9% | 8% | 9% | 9% | 10% | 11% |
| Q4ING3 | 13% | 11% | 11% | 11% | 13% | 11% | 15% | 100% | 13% | 12% | 12% | 11% | 14% | 13% |
| Q08753 | 18% | 18% | 16% | 19% | 18% | 6% | 9% | 13% | 100% | 32% | 28% | 18% | 19% | 17% |
| P17724 | 14% | 19% | 15% | 21% | 14% | 5% | 8% | 12% | 32% | 100% | 35% | 19% | 15% | 14% |
| P15160 | 16% | 19% | 16% | 18% | 19% | 5% | 9% | 12% | 28% | 35% | 100% | 16% | 17% | 18% |
| Q5DVM4 | 18% | 22% | 37% | 23% | 15% | 6% | 9% | 11% | 18% | 19% | 16% | 100% | 17% | 16% |
| Q9FY42 | 70% | 21% | 19% | 37% | 84% | 5% | 10% | 14% | 19% | 15% | 17% | 17% | 100% | 80% |
| O04985 | 68% | 22% | 17% | 38% | 80% | 6% | 11% | 13% | 17% | 14% | 18% | 16% | 80% | 100% |
| O24520 | 73% | 27% | 22% | 40% | 68% | 6% | 10% | 10% | 16% | 14% | 14% | 21% | 67% | 65% |
| O48668 | 44% | 27% | 27% | 65% | 38% | 5% | 9% | 12% | 17% | 19% | 17% | 17% | 39% | 38% |
| Q43236 | 37% | 22% | 22% | 79% | 36% | 4% | 10% | 12% | 19% | 22% | 23% | 20% | 36% | 39% |
| P02192 | 20% | 15% | 21% | 18% | 20% | 6% | 10% | 10% | 20% | 23% | 17% | 24% | 21% | 19% |
| P02189 | 18% | 17% | 20% | 19% | 21% | 5% | 9% | 10% | 19% | 22% | 18% | 25% | 22% | 22% |
| P68082 | 17% | 17% | 22% | 18% | 21% | 5% | 10% | 12% | 21% | 21% | 19% | 25% | 22% | 20% |
| Nicotiana_benthamiana | 78% | 24% | 23% | 41% | 67% | 5% | 10% | 11% | 18% | 17% | 17% | 21% | 67% | 66% |
| A0A063XGS7 | 18% | 17% | 13% | 19% | 19% | 5% | 8% | 12% | 18% | 24% | 19% | 17% | 17% | 14% |
| Q8NMW6 | 21% | 15% | 18% | 16% | 18% | 5% | 8% | 10% | 16% | 19% | 20% | 16% | 18% | 17% |
| P73925 | 21% | 19% | 17% | 24% | 18% | 5% | 7% | 10% | 34% | 46% | 33% | 16% | 20% | 17% |
| B4WLV9 | 19% | 24% | 22% | 19% | 19% | 6% | 10% | 12% | 17% | 14% | 19% | 21% | 20% | 18% |
| Q00812 | 14% | 17% | 16% | 17% | 15% | 4% | 8% | 11% | 24% | 31% | 28% | 20% | 17% | 17% |
| G2RXE0 | 17% | 18% | 18% | 18% | 17% | 5% | 8% | 10% | 18% | 23% | 17% | 21% | 15% | 13% |

| | O24520 | O48668 | Q43236 | P02192 | P02189 | P68082 | Nicotiana_benthamiana | A0A063XGS7 | Q8NMW6 | P73925 | B4WLV9 | Q00812 | G2RXE0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| H6WZ70 | 73% | 44% | 37% | 20% | 18% | 17% | 78% | 18% | 21% | 21% | 18% | 14% | 17% |
| B3DUZ7 | 27% | 27% | 22% | 15% | 17% | 17% | 24% | 17% | 15% | 19% | 24% | 17% | 18% |
| O66586 | 22% | 27% | 22% | 21% | 20% | 22% | 23% | 13% | 18% | 17% | 22% | 16% | 17% |
| P02236 | 40% | 65% | 79% | 19% | 20% | 19% | 41% | 19% | 16% | 24% | 19% | 17% | 18% |
| Q42831 | 68% | 38% | 36% | 20% | 21% | 21% | 67% | 19% | 18% | 18% | 19% | 15% | 17% |
| G4N2X9 | 6% | 5% | 4% | 6% | 5% | 5% | 5% | 5% | 5% | 5% | 6% | 4% | 5% |
| N4UFN7 | 10% | 9% | 10% | 10% | 9% | 10% | 10% | 8% | 8% | 7% | 10% | 8% | 8% |
| Q4ING3 | 10% | 12% | 12% | 10% | 10% | 12% | 11% | 12% | 10% | 10% | 12% | 11% | 10% |
| Q08753 | 16% | 17% | 19% | 20% | 19% | 21% | 18% | 18% | 16% | 34% | 17% | 24% | 18% |
| P17724 | 14% | 19% | 22% | 23% | 22% | 21% | 17% | 24% | 19% | 46% | 14% | 31% | 23% |
| P15160 | 14% | 17% | 23% | 17% | 18% | 19% | 17% | 19% | 20% | 33% | 19% | 28% | 17% |
| Q5DVM4 | 21% | 17% | 20% | 23% | 25% | 25% | 21% | 16% | 16% | 16% | 21% | 20% | 21% |
| Q9FY42 | 67% | 39% | 36% | 21% | 22% | 22% | 67% | 17% | 18% | 20% | 20% | 17% | 15% |
| O04985 | 65% | 38% | 39% | 19% | 22% | 20% | 66% | 14% | 17% | 17% | 18% | 17% | 13% |
| O24520 | 100% | 43% | 39% | 20% | 20% | 23% | 71% | 17% | 19% | 21% | 17% | 15% | 17% |
| O48668 | 43% | 100% | 62% | 19% | 17% | 18% | 45% | 21% | 21% | 20% | 19% | 17% | 17% |
| Q43236 | 39% | 62% | 100% | 18% | 19% | 20% | 39% | 18% | 15% | 22% | 18% | 18% | 14% |
| P02192 | 20% | 19% | 18% | 100% | 88% | 88% | 19% | 20% | 17% | 20% | 18% | 19% | 20% |
| P02189 | 20% | 17% | 19% | 88% | 100% | 91% | 19% | 18% | 17% | 18% | 16% | 18% | 21% |
| P68082 | 23% | 18% | 20% | 88% | 91% | 100% | 22% | 18% | 15% | 18% | 19% | 19% | 21% |
| Nicotiana_benthamiana | 71% | 45% | 39% | 19% | 19% | 22% | 100% | 19% | 19% | 21% | 19% | 20% | 15% |
| A0A063XGS7 | 17% | 21% | 18% | 20% | 18% | 18% | 19% | 100% | 39% | 24% | 18% | 23% | 63% |
| Q8NMW6 | 19% | 21% | 14% | 17% | 17% | 15% | 19% | 39% | 100% | 25% | 16% | 23% | 33% |
| P73925 | 21% | 20% | 22% | 20% | 18% | 18% | 21% | 24% | 25% | 100% | 16% | 36% | 23% |
| B4WLV9 | 17% | 19% | 18% | 18% | 16% | 19% | 19% | 18% | 16% | 16% | 100% | 17% | 19% |
| Q00812 | 15% | 17% | 18% | 19% | 18% | 19% | 20% | 23% | 23% | 36% | 17% | 100% | 23% |
| G2RXE0 | 17% | 17% | 14% | 20% | 21% | 21% | 15% | 63% | 33% | 23% | 19% | 23% | 100% |

# Tree of Life Reveals Clock-Like Speciation and Diversification

S. Blair Hedges,*[1,2,3] Julie Marin,[1,2,3] Michael Suleski,[1,2,3] Madeline Paymer,[1,2,3] and Sudhir Kumar[1,2,3]
[1]Center for Biodiversity, Temple University
[2]Institute for Genomics and Evolutionary Medicine, Temple University
[3]Department of Biology, Temple University
***Corresponding author:** E-mail: sbh@temple.edu.
**Associate editor**: Emma Teeling

## Abstract

**Genomic data are rapidly resolving the tree of living species calibrated to time, the timetree of life, which will provide a framework for research in diverse fields of science. Previous analyses of taxonomically restricted timetrees have found a decline in the rate of diversification in many groups of organisms, often attributed to ecological interactions among species. Here, we have synthesized a global timetree of life from 2,274 studies representing 50,632 species and examined the pattern and rate of diversification as well as the timing of speciation. We found that species diversity has been mostly expanding overall and in many smaller groups of species, and that the rate of diversification in eukaryotes has been mostly constant. We also identified, and avoided, potential biases that may have influenced previous analyses of diversification including low levels of taxon sampling, small clade size, and the inclusion of stem branches in clade analyses. We found consistency in time-to-speciation among plants and animals, ~2 My, as measured by intervals of crown and stem species times. Together, this clock-like change at different levels suggests that speciation and diversification are processes dominated by random events and that adaptive change is largely a separate process.**

***Key words:*** **biodiversity, diversification, speciation, timetree, tree of life.**

## Introduction

The evolutionary timetree of life (TTOL) is needed for understanding and exploring the origin and diversity of life (Hedges and Kumar 2009; Nei 2013). For this reason, scientists have been leveraging the genomics revolution and major statistical advances in molecular dating techniques to generate divergence times between populations and species. Collectively, tens of thousands of species have been timed, and new divergence time estimates are appearing in hundreds of publications each year (supplementary fig. S1, Supplementary Material online). A global synthesis of these results will allow direct comparison of the TTOL with the fossil record and Earth history and provide new opportunities for discovery of patterns and processes that operated in the past. The TTOL is also essential for studying the multidimensional nature of biodiversity and predicting how anthropogenic changes in our environment will impact the distribution and composition of biodiversity in the future (Hoffmann et al. 2010). A robust TTOL will provide a framework for research in diverse fields of science and medicine and a stimulus for science education. Data now exist for building a synthetic species-level TTOL of substantial size from the growing knowledge (supplementary fig. S1, Supplementary Material online).

There are challenges in synthesizing a global TTOL. The most common approach for constructing a large timetree using a sequence alignment or super alignment is possible (Smith and O'Meara 2012; Tamura et al. 2012), but not generally practical because of data matrix sparseness. For example, genes appropriate for closely related species are unalignable at higher levels, and those appropriate for higher levels are too conserved for resolving relationships of species. Disproportionate attention to some species, such as model organisms and groups of general interest (e.g., mammals and birds), also results in an uneven distribution of knowledge. In addition, computational limits are reached for Bayesian timing methods involving more than a few hundred species (Battistuzzi et al. 2011; Jetz et al. 2012).

Here, we have taken an approach to build a global TTOL by means of a data-driven synthesis of published timetrees into a large hierarchy. We have synthesized timetrees and related information in 2,274 molecular studies, which we collected and curated in a knowledgebase (Hedges et al. 2006) (supplementary Materials and Methods, Supplementary Material online). We mapped timetrees and divergence data from those studies on a robust and conservative guidetree based on community consensus (National Center for Biotechnology Information 2013) and used those times to resolve polytomies and derive nodal times in the TTOL (supplementary fig. S2, Supplementary Material online). We present this synthesis here, for use by the community, and explore how it bears on evolutionary hypotheses and mechanisms of speciation and diversification.

## Results

### A Global Timetree of Species

Our TTOL contains 50,632 species (fig. 1). Nearly all (~99.5%) of the 1.9 million described species of living organisms are

Article

Fast Track

© The Author 2015. Published by Oxford University Press on behalf of the Society for Molecular Biology and Evolution.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Open Access

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



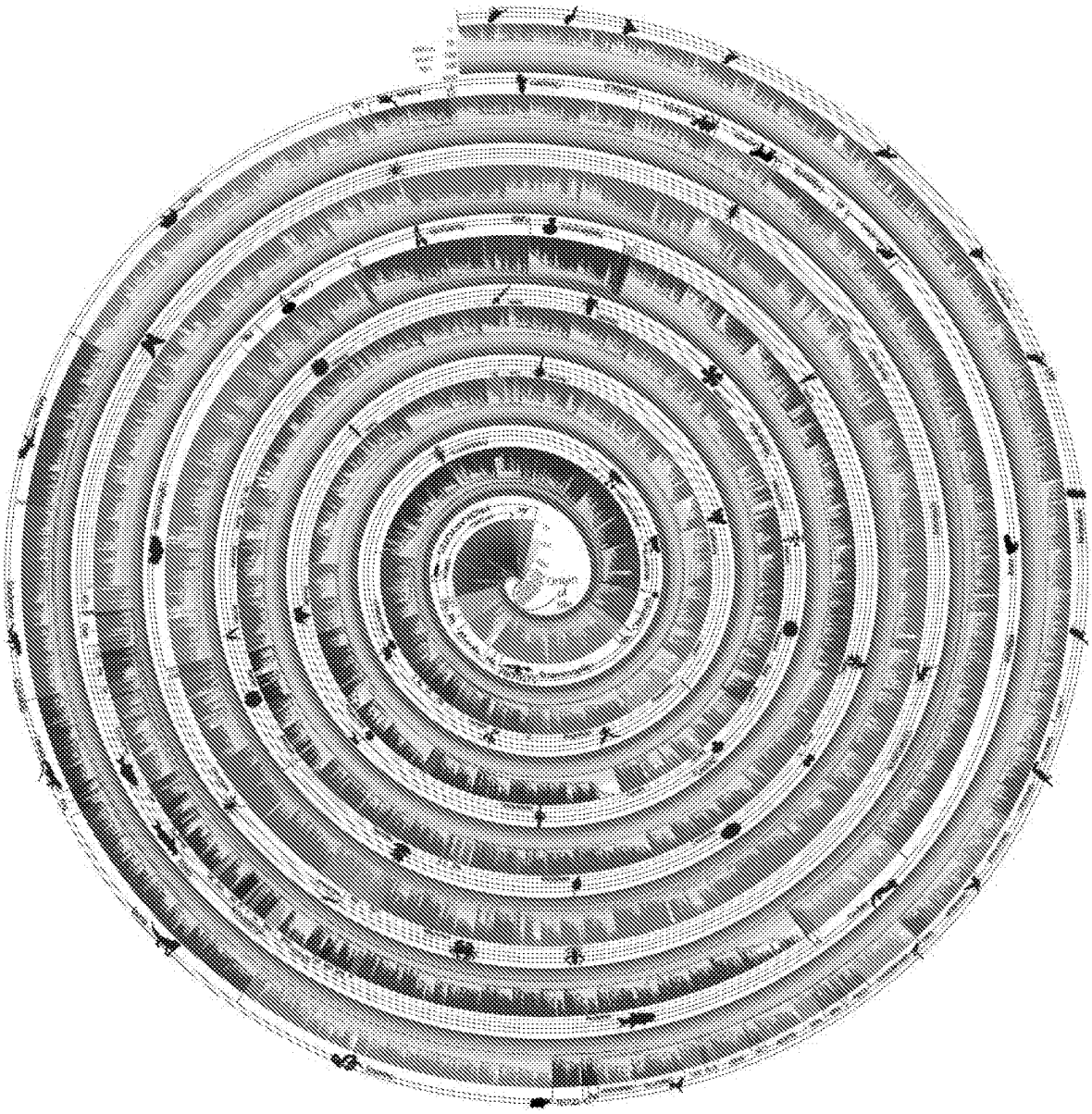


Fig. 1. (2 columns) A timetree of 50,632 species synthesized from times of divergence published in 2,274 studies. Evolutionary history is compressed into a narrow strip and then arranged in a spiral with one end in the middle and the other on the outside. Therefore, time progresses across the width of the strip at all places, rather than along the spiral. Time is shown in billions of years on a log scale and indicated throughout by bands of gray. Major taxonomic groups are labeled and the different color ranges correspond to the main taxonomic divisions of our tree.

eukaryotes (Costello et al. 2013), and the proportion is similar (99.7%) in our TTOL (fig. 1). The naturally unbalanced shape of the TTOL, for example, with more eukaryote than prokaryote species, allowed us to present it in a unique spiral format to accommodate its large size. A "timeline" can be envisioned for each species in the TTOL, based on its sequence of branching events back in time to the origin of life. For example, a timeline from humans (fig. 2) captures evolutionary events that have received the most queries (74%) by users of the TimeTree knowledgebase (Hedges et al. 2006) (supplementary Materials and Methods, Supplementary Material online).

Linnaean taxonomic ranks exhibit temporal inconsistencies (fig. 3) as has been suggested in smaller surveys (Hedges and Kumar 2009; Avise and Liu 2011). For example, a class (higher rank) of angiosperm averages younger than an order (lower rank) of fungus, and an order of animal averages younger than a genus (low rank) of basidiomycete fungus. Ranks for prokaryotes are all older than the corresponding ranks of eukaryotes, with a genus of eubacteria averaging $715.7 \pm 139.4$ Ma compared with $12.6 \pm 1.2$ Ma for a genus of eukaryotes (fig. 3 and supplementary Materials and Methods, Supplementary Material online). These inconsistencies will cause difficulties in any scientific study comparing



Motif Exhibit 1002, Page 345 of 1290

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



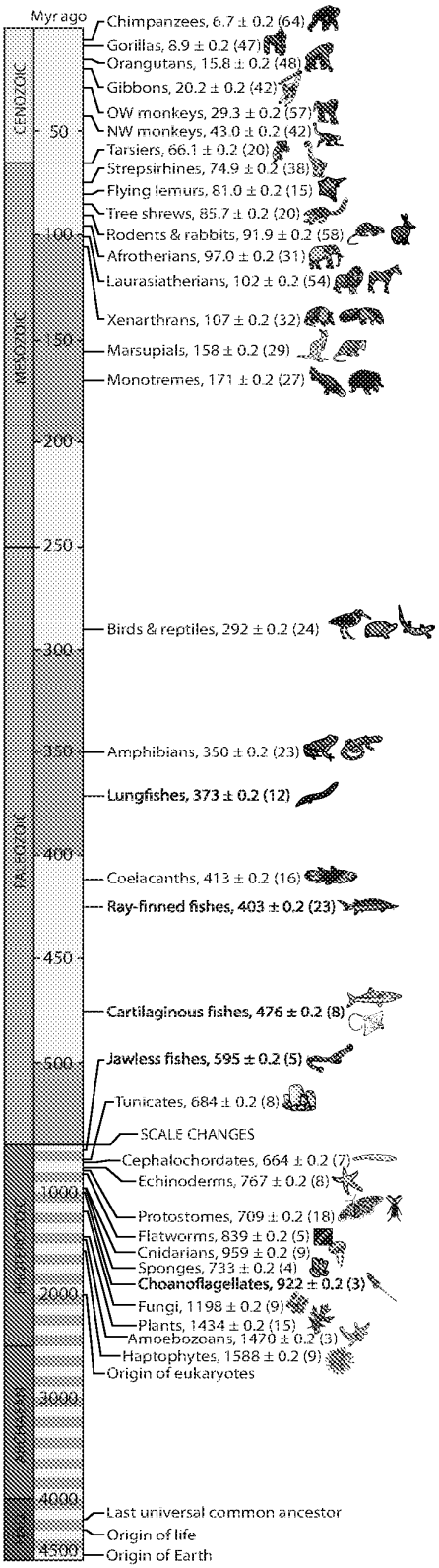



FIG. 2. (1 column) A timeline from the perspective of humans, showing divergences with other groups of organisms. In each case, mean ± standard error (among studies) is shown, with number of studies in parentheses. Also shown are the times for the origin of life, eukaryotes, and last universal common ancestor (Hedges and Kumar 2009).

different types of organisms, where Linnaean rank is assumed to have a temporal equivalence.

## Diversification

The large TTOL afforded us the opportunity to examine patterns of lineage splitting across the diversity of eukaryotes (we omit prokaryotes in our TTOL analyses because they have an arbitrary species definition). Under models of "expansion," diversity will continue to expand, either at an increasing diversification rate (hyper-expansion), the same rate (constant expansion), or decreasing rate (hypo-expansion). Saturation, on the other hand, refers to a drop in rate to zero as diversity reaches a plateau (equilibrium), possibly because of density-dependent biotic factors such as species interactions (Morlon 2014). Most recent analyses, but not all (Venditti et al. 2010; Jetz et al. 2012), have suggested that hypo-expansion is the predominant pattern in the tree of life, although there has been considerable debate as to the importance of timescales, biotic or abiotic factors, and potential biases in the analyses (Sepkoski 1984; Benton 2009; Morlon et al. 2010; Rabosky et al. 2012; Cornell 2013; Rabosky 2013).

Instead, we find that constant expansion and hyper-expansion are the dominant patterns of lineage diversification in the TTOL (fig. 4*a*). Our result was statistically significant irrespective of the method used, including diversification rate tests and simulations, a coalescent approach (not conducted for the TTOL), gamma tests, a clade age-size relationship (see Materials and Methods), and branch length distribution analysis (supplementary Materials and Methods, Supplementary Material online). The rate of diversification did not decrease over the history of eukaryotes (fig. 4). The same results were retrieved with another method (supplementary fig. S3, Supplementary Material online); we did not interpret the data before 1,000 Ma because only 37 lineages were present at this time, also explaining the large confidence intervals for this period. The observed diversification closely matched a simulated pure birth–death (BD) model, increasing slightly during the last 200 My (fig. 4*a* and *b*). The terminal drop in rate at ~1 Ma is a normal characteristic of diversification plots (Etienne and Rosindell 2012) related to the taxonomic level selected for the study, in this case species. This "taxonomic bias" (rate drop) occurs at different times (Hedges and Kumar 2009) when genera, families, or other taxa are selected for study, because lower level clades (in this case, populations destined to become species) are omitted.

The TTOL was partitioned into 58 diverse Linnaean clades (Actinopterygii, Afrotheria, *Amazona*, *Ambystoma*, Amphibia, Amphibolurinae, Amphisbaenia, angiosperms, Anguimorpha, *Anolis*, Anseriformes, birds, Boidae, *Bolitoglossa*, Canidae, Cetardiodactyla, *Chamaeleo*, Chondrichthyes, Ciconiiformes, Columbiformes, Cracidae, Cuculidae, *Eleutherodactylus*, Erinaceidae, *Falco*, Feliformia, Gymnophiona, gymnosperms, *Hylarana*, Hyloidea, *Hynobius*, *Hyperolius*, Iguanidae, Kinyongia, Lacertidae, *Liolaemus*, mammals, Megapodiidae, Metatheria, Moniliformopses, Musophagidae, Palaeognathae, Pelobatoidea, Perissodactyla, Phaeophyceae, Phasianidae, *Plethodon*, Podicipedidae,


Motif Exhibit 1002, Page 346 of 1290

Case No.: IPR2023-00207
U.S. Patent No. 9,943,096



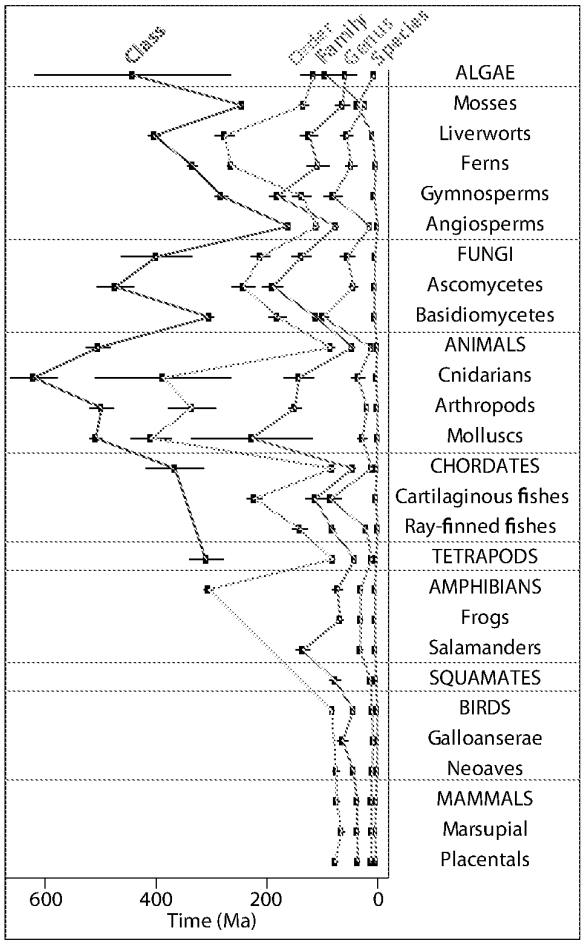



Fig. 3. (1 column) Temporal relationships of Linnaean ranks of eukaryotes, showing mode and 95% confidence intervals. Prokaryotes are not shown because of large differences in scale (supplementary Materials and Methods, Supplementary Material online).

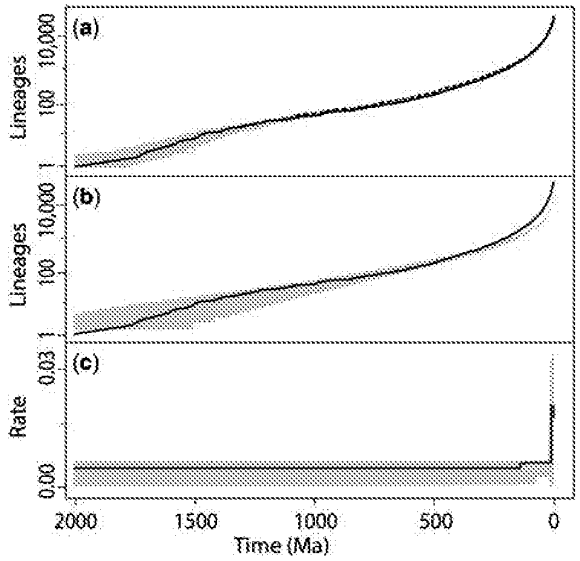



Fig. 4. (1 column) Patterns of lineage diversification. (*a*) Cumulative lineages-through-time (LTT) curve for eukaryotes (50,455 sp.), in black, showing the number of lineages through time (unsmoothed, dashed; smoothed, solid) and variance (red, 500 replicates). (*b*) Same LTT curve (black line), but compared with a simulated constant-expansion LTT curve ($\lambda$ (speciation rate) = 0.073 and $\mu$ (extinction rate) = 0.070) shown as ± 99% confidence intervals (red). (*c*) Diversification rate plot of same data showing only significant changes in rate as determined in maximum-likelihood tests; variance (red, 500 replicates) shown as ± 99% intervals.

Primates, Ranoidea, Squamata, *Suncus*, Thamnophis, Tupaiidae, Ursidae, *Varanus*, Xenarthra, and *Xenopus*) for coalescence and gamma tests encompassing 44,958 total species (supplementary Materials and Methods, Supplementary Material online). The clades were chosen to represent taxonomic diversity and a range of clade size, clade age, and taxonomic sampling. Species sampling levels were high, with a median clade size of 66% of known species and 84% of the clades having 40% or more of known species. Among the 10 largest clades (Actinopterygii, Amphibia, angiosperms, birds, Ciconiiformes, Hyloidea, mammals, Moniliformopses, Ranoidea, Squamata), only one (angiosperms) showed hypo-expansion using the coalescent method, while the others were exclusively hyper-expanding. Low levels of sampling are known to bias toward hypo-expansion (Cusimano and Renner 2010; Moen and Morlon 2014), and the same clade (angiosperms) was also the most poorly sampled (5%). Also, there was no support in those clades for a decline in diversification rate using the gamma test. Although some methods can account for incomplete random sampling, the nonrandom sampling typically used by systematists (e.g., selecting for deeply branching lineages) is not accounted for by current methods and will bias results in favor of hypo-expansion (Cusimano and Renner 2010).

Focusing on the 48 smaller clades (e.g., genera and families) of tetrapods, we found that these likewise favored the expanding models (84% of clades showing significant results) rather than the saturation model (see Materials and Methods). Of those, most (87%) were either expanding or hyper-expanding, with only 13% hypo-expanding. Concerning the gamma test, 67% of these smaller clades did not show a decline in diversification rate through time, as was true for eukaryotes as a whole (fig. 4; gamma statistic = 136.4, $P = 1$). Hyper-expanding clades were significantly larger (fig. 5*a*; $x^{\text{Pleasechecktrpezium}}$, 831 vs. 91 species; $P < 0.05$) and older (fig. 5*b*; $x^{\text{Pleasechecktrpezium}}$, 104 vs. 57 Ma; $P < 0.001$) than other clades (see Materials and Methods). We also found that TTOL branch-length distribution fits an exponential distribution significantly better than other models (see Materials and Methods), agreeing with an earlier study (Venditti et al. 2010) using a small data set and approach.

Diversification by expansion predicts a significant correlation between clade age and clade size (see Materials and Methods). Therefore, we evaluate the expansion hypothesis in two densely sampled groups: Mammals (5,363 species) and birds (9,879 species). We also tested the effect of stem versus crown age (fig. 5*c*) on clade sizes (supplementary Materials and Methods, Supplementary Material online); stem age



Motif Exhibit 1002, Page 347 of 1290