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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ALTEO.12NP

CONFIRMATION NO. 2025

45200
K&L Gates LLP-Orange County
1 Park Plaza
Twelfth Floor
Irvine, CA 92614

IMPROPER CFR REQUEST



OC000000076584808

Date Mailed: 08/19/2024

RESPONSE TO REQUEST FOR CORRECTED FILING RECEIPT

Power of Attorney, Claims, Fees, System Limitations, and Miscellaneous

In response to your request for a corrected Filing Receipt, the Office is unable to comply with your request because:

- The ADS received on 07/22/2024 did not contain the entire section in which changes are being made. See 37 CFR 1.76(c)(2). For any section of information being changed, the section must include the entire section (including the section heading) showing the current information of record, and any insertions (relative to the current information of record) shown with underlining and any text removed (relative to the current information of record) shown with strike-through or brackets.

How to Make Changes in the Information of Record Using a Corrected Application Data Sheet: In order to make changes to the information of record, an ADS must be properly signed and properly marked up relative to the current information of record.

Proper signature: The ADS must be signed with a handwritten signature or proper S-signature by:

- A patent practitioner, with the practitioner's registration number accompanying the signature (e.g., immediately below or adjacent to the signature), or
- The applicant, if the applicant is an individual other than the inventor(s) and no power of attorney has been appointed, or
- All of the inventors, if no other applicant has been established and no power of attorney has been appointed.

A proper S-signature consists of only letters and/or Arabic numerals, with appropriate spaces and commas, periods, apostrophes, or hyphens for punctuation contained between a first single forward slash mark before, and a second single forward slash mark after, the S-signature.

Proper markings: The ADS must identify the changes being made with underlining for insertions and strike-through or brackets for text removed relative to the information of record. No other markings or indications are acceptable. Where an ADS providing corrected or updated information does not contain all of the sections of the ADS, the entire section (including the heading) in which changes are being made must be included in the ADS. Information of record can generally be found on the latest filing receipt.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at (571) 272-4000 or (571) 272-4200 or 1-888-786-0101.

/rmohamed/



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NOTICE OF ALLOWANCE AND FEE(S) DUE

45200 7590 08/07/2024
K&L Gates LLP-Orange County
1 Park Plaza
Twelfth Floor
Irvine, CA 92614

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/07/2024

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025

TITLE OF INVENTION: METHOD FOR PRODUCING RECOMBINANT HYALURONIDASE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$480	\$0.00	\$0.00	\$480	11/07/2024

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025
TITLE OF INVENTION: METHOD FOR PRODUCING RECOMBINANT HYALURONIDASE				

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$480	\$0.00	\$0.00	\$480	11/07/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
FRONDA, CHRISTIAN L	1652	435-201000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025
45200	7590	08/07/2024	EXAMINER	
K&L Gates LLP-Orange County 1 Park Plaza Twelfth Floor Irvine, CA 92614			FRONDA, CHRISTIAN L	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 08/07/2024				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. 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 30 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. 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.

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. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).

<https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf>

Routine uses of the information in this record may include disclosure to:

- 1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
- 2) a federal, state, local, or international agency, in response to its request;
- 3) a contractor of the USPTO having need for the information in order to perform a contract;
- 4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
- 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
- 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
- 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
- 8) 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));
- 9) the Office of Personnel Management (OPM) for personnel research purposes; and
- 10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 17/907,538	Applicant(s) PARK et al.	
	Examiner CHRISTIAN L FRONDA	Art Unit 1652	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Request for Continued Examination dated 07/22/2024.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ 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.

3. ☒ The allowed claim(s) is/are 1-7,9-13 and 17-19. As a result of the allowed claim(s), 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.

4. ☒ 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)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>07/22/2024</u> . 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____. 4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.	5. ☐ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____.
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/CHRISTIAN L FRONDA/ Primary Examiner, Art Unit 1652	
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Notice of Allowability

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 07/22/2024 has been entered.

2. Claims 1-7, 9-13, and 17-19 are pending in the instant application.

3. The IDS filed 07/22/2024 has been considered and a signed copy is attached to the instant action.

4. Claims 1-7, 9-13, and 17-19 are allowed.

5. The prior art neither teaches nor suggests the claimed method for producing a recombinant protein wherein sialylation of N-glycan of the produced recombinant protein is 1 to 38%, and wherein the produced recombinant protein has a hyaluronidase enzymatic activity at 10,000 units/mL or higher.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272 0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM-5:00PM.

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

Art Unit: 1652

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, Robert Mondesi can be reached on (408)918-7584. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit:

<https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHRISTIAN L FRONDA/
Primary Examiner, Art Unit 1652

AMENDMENTS TO THE CLAIMS

1. (Previously Presented) A method for producing a recombinant protein, the method comprising:

first culturing host animal cells expressing the recombinant protein until an integral viable cell density of the host animal cells reaches 20×10^6 to 120×10^6 cells $\times$ day/mL, wherein first culturing is performed within a first temperature range from 35°C to 38°C; and

subsequently second culturing at least part of the host animal cells from first culturing for 2 to 18 days, which produces the recombinant protein, wherein second culturing is performed within a second temperature range from 28°C to 34°C,

wherein the second culturing maintains (a) a residual glucose concentration within a range from 0.001 g/L to 4.5 g/L and/or (b) pH within a range from 6.8 to 7.2 in a culture medium therefor, wherein sialylation of N-glycan of the produced recombinant protein is 1 to 38%, and

wherein the produced recombinant protein has a hyaluronidase enzymatic activity at 10,000 units/mL or higher.

2. (Previously Presented) The method according to claim 1, wherein galactosylation of N-glycan is 1 to 68%, and mannosylation of N-glycan is 40 to 63%.

3. (Previously Presented) The method according to claim 1, wherein sialylation of N-glycan is 1 to 30%.

4. (Currently Amended) The method according to claim 1, wherein the ~~variant recombinant~~ protein has a specific enzymatic activity as hyaluronidase at least 10% higher than a specific enzymatic activity of a wild human PH20.

5. (Previously Presented) The method according to claim 1, wherein at least one of the first culturing or the second culturing are performed by one or more methods selected from the group consisting of batch culture, repeated batch culture, fed-batch culture, repeated fed-batch culture, continuous culture, and perfusion culture.

6. (Previously Presented) The method according to claim 1, wherein at least one of the first culturing or the second culturing are performed under one or more conditions selected from the group consisting of:

- (i) a condition in which an ammonia concentration is maintained at 5 mM or higher in a culture medium thereof;
- (ii) a condition in which one or more substances is added to the culture medium thereof, wherein the one or more substances are selected from the group consisting of glutamine, glucosamine, uridine, glucosamine, and sodium butyrate; and
- (iii) a condition in which galactose and manNAc are not added to the culture medium thereof.

7. (Currently Amended) The method according to claim 1, wherein the ~~variant recombinant protein~~ comprises substitution of one or more amino acid residues when compared to an amino acid sequence of a wild human PH20.

8. (Previously Canceled)

9. (Previously Presented) The method according to claim 1, further comprising separating and purifying the produced recombinant protein.

10. (Currently Amended) The method according to claim 9, wherein separating and purifying ~~the separation and purification of~~ the produced recombinant protein are performed using ionic bond and/or hydrophobic interaction characteristics thereof, rather than affinity binding.

11. (Currently Amended) The method according to claim 10, wherein separating and purifying ~~the separation and purification of~~ the recombinant protein are performed using hydrophobic interaction chromatography and ion exchange chromatography, rather than affinity chromatography.

12. (Currently Amended) The method according to claim 9, wherein purifying ~~the purification~~ further comprises removing at least part of acidic recombinant protein.

13. (Currently Amended) The method according to claim 12, wherein ~~the removal of~~ removing the acidic recombinant protein uses ion exchange chromatography.
14. (Previously Canceled)
15. (Previously Canceled)
16. (Previously Canceled)
17. (Currently Amended) The method according to claim 7, wherein the ~~variant recombinant~~ protein further comprises truncation of at least one amino acid residue of N-terminus when compared to an amino acid sequence of a wild human PH20.
18. (Currently Amended) The method according to claim 7, wherein the ~~variant recombinant~~ protein further comprises truncation of at least one amino acid residue of C-terminus when compared to an amino acid sequence of a wild human PH20.
19. (Currently Amended) The method according to claim 7, wherein the ~~variant recombinant~~ protein further comprises truncation of at least one amino acid residue of N-terminus and at least one amino acid residue of C-terminus when compared to an amino acid sequence of a wild human PH20.

REMARKS

Applicant has amended the application as set forth above. No new matter is added by the amendments. Applicant files a request for continued examination (RCE) along with this paper. Applicant respectfully requests entry of the amendments in view of the RCE and reconsideration of the application in view of the above amendments and the following remarks.

Claims Allowed

Applicant notes that Claims 1-7, 9-13 and 17-19 were allowed in the Notice of Allowance dated April 24, 2024.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Application No.: 17/907,538
Filing Date: September 27, 2022

CONCLUSION

Applicant respectfully requests consideration of the claim amendments and remarks herein and entry of them into the file history for the application. If there are any questions which may be answered by telephone, the Examiner is invited to call the undersigned directly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 02-1818

Respectfully submitted,

K&L GATES, LLP

Dated: July 22, 2024

By: /Mincheol Kim/
Mincheol Kim
Registration No. 51,306
Attorney of Record
Customer No. 45,200
(949) 623-3611



UNITED STATES PATENT AND TRADEMARK OFFICE

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NOTICE OF ALLOWANCE AND FEE(S) DUE

45200 7590 04/24/2024
K&L Gates LLP-Orange County
1 Park Plaza
Twelfth Floor
Irvine, CA 92614

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/24/2024

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025

TITLE OF INVENTION: METHOD FOR PRODUCING RECOMBINANT HYALURONIDASE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$480	\$0.00	\$0.00	\$480	07/24/2024

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025

TITLE OF INVENTION: METHOD FOR PRODUCING RECOMBINANT HYALURONIDASE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$480	\$0.00	\$0.00	\$480	07/24/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
FRONDA, CHRISTIAN L	1652	435-201000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025
45200	7590	04/24/2024	EXAMINER	
K&L Gates LLP-Orange County 1 Park Plaza Twelfth Floor Irvine, CA 92614			FRONDA, CHRISTIAN L	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 04/24/2024				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. 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 30 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. 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.

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. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).

<https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf>

Routine uses of the information in this record may include disclosure to:

- 1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
- 2) a federal, state, local, or international agency, in response to its request;
- 3) a contractor of the USPTO having need for the information in order to perform a contract;
- 4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
- 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
- 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
- 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
- 8) 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));
- 9) the Office of Personnel Management (OPM) for personnel research purposes; and
- 10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 17/907,538	Applicant(s) PARK et al.	
	Examiner CHRISTIAN L FRONDA	Art Unit 1652	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendment dated 04/15/2024.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ 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.

3. ☒ The allowed claim(s) is/are 1-7,9-13 and 17-19. As a result of the allowed claim(s), 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.

4. ☒ 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)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)	5. ☐ Examiner's Amendment/Comment
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.	6. ☒ Examiner's Statement of Reasons for Allowance
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.	7. ☐ Other _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.	

/CHRISTIAN L FRONDA/ Primary Examiner, Art Unit 1652	
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Notice of Allowability

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

1. Claims 1-7, 9-13, 17-19 are pending in the instant application.
2. In view of the claim amendment and arguments filed 11/03/2023 all previous claim rejections have been withdrawn.
3. Claims 1-7, 9-13, 17-19 are allowed.
4. The prior art neither teaches nor suggests the method for producing a recombinant protein that comprises at least one of hyaluronidase PH20 or a variant thereof as recited in the claims.
5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272 0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM-5:00PM.

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, Robert Mondesi can be reached on (408)918-7584. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about

Application/Control Number: 17/907,538
Art Unit: 1652

Page 3

filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHRISTIAN L FRONDA/
Primary Examiner, Art Unit 1652

OK TO ENTER: /C.L.F/

1959690.00014/ALTEO.12A

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor	:	Soon Jae PARK
App. No.	:	17/907,538
Filed	:	September 27, 2022
Examiner	:	CHRISTIAN L FRONDA
Art Unit	:	1652
Conf. No.	:	2025

AMENDMENT AND RESPONSE TO OFFICE ACTION**Mail Stop Amendment**

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Dear Sir:

This is in response to the Office Action dated February 15, 2024 in the above-identified application. Applicant submits the following items for consideration in connection with the application.

Amendments to the Claims**Remarks**

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for producing a recombinant protein that comprises at least one of hyaluronidase PH20 or a variant thereof, ~~the method having hyaluronidase enzymatic activity~~, comprising:

~~first (1) culturing host animal cells expressing the recombinant protein hyaluronidase PH20 or the variant thereof having hyaluronidase enzymatic activity at a culture temperature of 35°C to 38°C until an integral viable cell density of the host animal cells reaches 20x10⁶ to 120x10⁶ cells x day/mL, wherein first culturing is performed within a first temperature range from 35°C to 38°C; and~~

~~subsequently (2) decreasing the culture temperature to 28°C to 34°C and then second culturing at least part of the host animal cells from first culturing for 2 to 18 days, which produces the recombinant protein, wherein second culturing is performed within a second temperature range from 28°C to 34°C, while maintaining the culture temperature;~~

~~(a) wherein the second culturing maintains (a) a residual glucose concentration within a range from 0.001 g/L to 4.5 g/L and/or (b) pH within a range from 6.8 to 7.2 in a culture medium therefor, the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or (b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2;~~

~~wherein a sialylation content of an N-glycan of the produced recombinant protein PH20 or variant thereof is 1 to 38%, and~~

~~wherein the produced recombinant protein has a hyaluronidase enzymatic activity in the culture medium is at 10,000 units/mL or more higher.~~

2. (Currently Amended) The method according to claim 1, wherein ~~a galactosylation content of N-glycan is 1 to 68%, the sialylation content is 1 to 38%, and a mannosylation of N-glycan content is 40 to 63% of the N-glycan of the produced PH20 or the variant thereof, respectively.~~

3. (Currently Amended) The method according to claim 1, wherein ~~the sialylation content of N-glycan is 1 to 30% of the N-glycan of the produced PH20 or the variant thereof.~~

4. (Currently Amended) The method according to claim 1, wherein the variant has a specific enzymatic activity as hyaluronidase ~~a specific activity of the produced PH20 or the variant thereof~~ is at least 10% higher than a specific enzymatic activity of the ~~a~~ wild human PH20.
5. (Currently Amended) The method according to claim 1, wherein at least one of the first culturing or the second culturing are ~~the culture of the host cells in step (1) and/or step (2)~~ is performed by one or more methods selected from the group consisting of batch culture, repeated batch culture, fed-batch culture, repeated fed-batch culture, continuous culture, and perfusion culture.
6. (Currently Amended) The method according to claim 1, wherein at least one of the first culturing or the second culturing are ~~the culture of the host cells in step (1) and/or step (2)~~ is performed under one or more conditions selected from the group consisting of:
- (i) a condition in which an ammonia concentration ~~in the medium~~ is maintained to at 5 mM or more higher in a culture medium thereof;
 - (ii) a condition in which one or more substances is added to the culture medium thereof, wherein the one or more substances are selected from the group consisting of glutamine, glucosamine, uridine, glucosamine, and sodium butyrate ~~to the medium;~~ and
 - (iii) a condition in which galactose and manNAc are not added to the culture medium thereof.
7. (Currently Amended) The method according to claim 1, wherein the variant comprises substitution ~~PH20 variant comprises substitutions of one or more amino acid residues, and optionally comprises truncation of one or more amino acid residues of N terminus and/or C terminus in~~ when compared to an amino acid sequence of a wild human PH20.
8. (Previously Canceled)
9. (Currently Amended) The method according to claim 1, further comprising separating and purifying the produced recombinant protein. ~~PH20 or a variant thereof.~~

10. (Currently Amended) The method according to claim 49, wherein the separation and purification of the produced recombinant protein PH20 or a variant thereof are performed using ionic bond and/or hydrophobic interaction characteristics of the ~~PH20 or the variant thereof~~, rather than affinity binding.

11. (Currently Amended) The method according to claim 10, wherein the separation and purification of the recombinant protein PH20 or a variant thereof are performed using hydrophobic interaction chromatography and ion exchange chromatography, rather than affinity chromatography.

12. (Currently Amended) The method according to claim 9, wherein the purification further comprises removing at least part of acidic recombinant protein. H20 or a variant thereof is removed.

13. (Currently Amended) The method according to claim 12, wherein the removal of the acidic recombinant protein uses hyaluronidase PH20 or a variant thereof is performed using ion exchange chromatography.

14. (Canceled Herein)

15. (Canceled Herein)

16. (Canceled Herein)

17. (New) The method according to claim 7, wherein the variant further comprises truncation of at least one amino acid residue of N-terminus when compared to an amino acid sequence of a wild human PH20.

18. (New) The method according to claim 7, wherein the variant further comprises truncation of at least one amino acid residue of C-terminus when compared to an amino acid sequence of a wild human PH20.

Application No.: 17/907,538
Filing Date: September 27, 2022

19. (New) The method according to claim 7, wherein the variant further comprises truncation of at least one amino acid residue of N-terminus and at least one amino acid residue of C-terminus when compared to an amino acid sequence of a wild human PH20.

REMARKS

This paper is in response to the Office Action dated February 15, 2024. Applicant has amended the application as set forth above. No new matter is added by the amendments. Applicant respectfully requests entry of the amendments and reconsideration of the application in view of the above amendments and the following remarks. Applicant reserves the right to pursue the cancelled subject matter in this application or a related application.

Allowable Subject Matter

Applicant notes that Claims 1-7 and 9-13 are allowed.

Cancellation of Claims 14-16

Applicant has canceled Claims 14-16 without prejudice.

Claim Amendments

Applicant has amended Claims 1-7 and 9-13 and added Claims 17-19 to clarify the claimed subject matter.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Application No.: 17/907,538
Filing Date: September 27, 2022

CONCLUSION

Applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. In light of the above remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If there are any questions which may be answered by telephone, the Examiner is invited to call the undersigned directly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 02-1818

Respectfully submitted,

K&L GATES, LLP

Dated: April 15, 2024

By: /Mincheol Kim/
Mincheol Kim
Registration No. 51,306
Attorney of Record
Customer No. 45,200
(949) 623-3611



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	1959690.00014/ ALTEO.12NP	2025
45200	7590	02/15/2024	EXAMINER	
K&L Gates LLP-Orange County 1 Park Plaza Twelfth Floor Irvine, CA 92614			FRONDA, CHRISTIAN L	
			ART UNIT	PAPER NUMBER
			1652	
			NOTIFICATION DATE	DELIVERY MODE
			02/15/2024	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):

uspatentmail@klgates.com

DETAILED ACTION

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

1. Claims 1-7 and 9-16 are pending in the instant application. Claims 14-16 have been withdrawn from further consideration as being drawn to a nonelected invention.
2. Claims 1-7 and 9-13 are under consideration in this Office Action.
3. In view of the claim amendment and arguments filed 11/03/2023 all previous claim rejections have been withdrawn.

Conclusion

4. Claims 1-7 and 9-13 are allowed. Claims 14-16 have been withdrawn from further consideration as being drawn to a nonelected invention.
5. This application is in condition for allowance except for the presence of claims 14-16 which is directed to a non-elected invention.

Applicant is given **TWO MONTHS or THIRTY DAYS** from the date of this letter, whichever is longer, to cancel the noted claims or take other appropriate action (37 CFR 1.144). Failure to take action during this period will be treated as authorization to cancel the noted claims by Examiner's Amendment and pass the case to issue. Extensions of time under 37 CFR 1.136(a) will not be permitted since this application will be passed to issue. The prosecution of this case is closed except for consideration of the above matter.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272 0929.

The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM-5:00PM.

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, Robert Mondesi can be reached on (408)918-7584. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHRISTIAN L FRONDA/
Primary Examiner, Art Unit 1652

Section I (Amendments to the Claims)

Please amend claim 1 and cancel claim 8, as set out in the following listing of the claims 1-16 of the application, which hereby supersedes and replaces all prior listings and versions of the claims.

1. **(Currently amended)** A method for producing a recombinant hyaluronidase PH20 or a variant thereof having hyaluronidase enzymatic activity, comprising:

(1) culturing host animal cells expressing [[a]] the recombinant hyaluronidase PH20 or [[a]] the variant thereof having hyaluronidase enzymatic activity at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20×10^6 to 120×10^6 cells x day/mL; and

(2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature:

(a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or

(b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2;

wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and

wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more.

2. **(Original)** The method according to claim 1, wherein a galactosylation content is 1 to 68%, the sialylation content is 1 to 38%, and a mannosylation content is 40 to 63% of the N-glycan of the produced PH20 or the variant thereof, respectively.

3. **(Original)** The method according to claim 1, wherein the sialylation content is 1 to 30% of the N-glycan of the produced PH20 or the variant thereof.

4. **(Original)** The method according to claim 1, wherein a specific activity of the produced PH20 or the variant thereof is at least 10% higher than a specific activity of the wild human PH20.

5. **(Original)** The method according to claim 1, wherein the culture of the host cells in step (1) and/or step (2) is performed by one or more methods selected from the group consisting of batch culture, repeated batch culture, fed-batch culture, repeated fed-batch culture, continuous culture,

and perfusion culture.

6. **(Original)** The method according to claim 1, wherein the culture of the host cells in step (1) and/or step (2) is performed under one or more conditions selected from the group consisting of:

(i) a condition in which an ammonia concentration in the medium is maintained to 5 mM or more;

(ii) a condition in which one or more substances is added selected from the group consisting of glutamine, glucosamine, uridine, glucosamine, and sodium butyrate to the medium; and

(iii) a condition in which galactose and manNAc are not added to the medium.

7. **(Original)** The method according to claim 1, wherein the PH20 variant comprises substitutions of one or more amino acid residues, and optionally comprises truncation of one or more amino acid residues of N-terminus and/or C-terminus in an amino acid sequence of wild PH20.

8. **(Canceled)**

9. **(Original)** The method according to claim 1, further comprising separating and purifying the produced PH20 or a variant thereof.

10. **(Original)** The method according to claim 1, wherein the separation and purification of the PH20 or a variant thereof are performed using ionic bond and/or hydrophobic interaction characteristics of the PH20 or the variant thereof, rather than affinity binding.

11. **(Original)** The method according to claim 10, wherein the separation and purification of the PH20 or a variant thereof are performed using hydrophobic interaction chromatography and ion exchange chromatography, rather than affinity chromatography.

12. **(Original)** The method according to claim 9, wherein acidic H20 or a variant thereof is removed.

13. **(Original)** The method according to claim 12, wherein the removal of the acidic

hyaluronidase PH20 or a variant thereof is performed using ion exchange chromatography.

14. **(Withdrawn)** PH20 or a variant thereof, in which a galactosylation content is 1 to 68%, a sialylation content is 1 to 38%, and a mannosylation content is 40 to 63% of N-glycan of PH20 or the variant thereof, respectively.

15. **(Withdrawn)** The PH20 or a variant thereof according to claim 14, wherein the sialylation content of the N-glycan is limited to 1 to 30%.

16. **(Withdrawn)** The PH20 or a variant thereof according to claim 14, wherein the PH20 or a variant thereof is produced by a method comprising:

(1) culturing host cells expressing a recombinant hyaluronidase PH20 or a variant thereof at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20×10^6 to 120×10^6 cells x day/mL; and

(2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature:

(a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or

(b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2;

wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and

wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more.

Section II (Remarks)

Submission of Second Supplemental Information Disclosure Statement and Accompanying Certification

A Second Supplemental Information Disclosure Statement is filed herewith, making of record information cited in the October 11, 2023 Office Action issued by the Japanese Patent Office in corresponding Japanese Patent Application 2022-559471.

The applicant correspondingly certifies that each item of information contained in such Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

Amendment of the Claims

Claim 1 has been amended herein in the preamble thereof to insert the indefinite article “a” before “recombinant hyaluronidase”, and the variant of the recombinant hyaluronidase PH20 has been further specified as a variant “having hyaluronidase enzymatic activity”, consistent with the disclosure at page 23, line 22 to page 24, line 7 (“‘PH20 variant’ ... is ... a variant which ... has hyaluronidase enzymatic activity”).

Claim 1 has also been amended in subparagraph (1) thereof to specify “culturing host animal cells expressing the recombinant hyaluronidase PH20 or the variant thereof having hyaluronidase enzymatic activity at a culture temperature ...”, for consistency with the amended preamble of the claim and to identify the host cells as “host animal cells”, consistent with the description at page 24, lines 8-10 of the specification (“host cells used herein for expression of the hyaluronidase proteins may include animal, yeast, actinomycetes and insect cells”) and consistent with the recital in now-canceled claim 8 (“wherein the host cells are animal, yeast, actinomycetes, or insect cells”).

Accordingly, the amendments of the claims herein do not introduce any new matter within the meaning of 35 USC §132.

The claims now pending and under examination are claims 1-7 and 9-13, claims 14-16 having been withdrawn pursuant to prior restriction requirement.

Rejection of Claims Under 35 USC §112(a) or 35 USC §112 (Pre-AIA), First Paragraph

In the August 3, 2023 Office Action, claims 1-13 as then pending were rejected under 35 USC §112(a) or 35 USC §112 (pre-AIA) first paragraph as failing to comply with the written description requirement.

In response, claim 1 has been amended to insert the limitation “having hyaluronidase enzymatic activity” after “a variant thereof” and the host cells of claim 1 have been limited to host animal cells. The applicant submits that the invention as now claimed in amended claim 1 is sufficiently supported and enabled by the description in the specification including experimental data relating to ExpiCHO cells.

The applicant further submits that based on the specification of the present application, the method as now claimed can be implemented based on the application disclosure to the full scope of recombinant hyaluronidase PH20 and variants thereof having hyaluronidase enzymatic activity, with the specification enabling one ordinarily skilled in the art to know and appreciate the meaning of PH20, variants thereof, and animal cells.

It correspondingly is requested that the §112(a)/¶1 rejection be withdrawn in respect of the amended claims 1-7 and 9-13.

Rejection of Claims Under 35 USC §103

In the August 3, 2023 Office Action, claims 1-13 as then pending were rejected under 35 USC §103 as unpatentable over EP 3037529 (“**EP529**”) in view of Chen et al., Constitutive expression of recombinant human hyaluronidase PH20 by Pichia pastoris, Journal of Bioscience and Bioengineering, 2016, Volume 122, Number 6, pp. 673-678 (“**Chen**”) and Frost et al., Recombinant human hyaluronidase (rHuPH20): an enabling platform for subcutaneous drug and fluid administration, Expert Opin. Drug Deliv., 2007, Volume 4, Number 4, pp. 427-440 (“**Frost**”).

Such rejection is traversed in respect of amended claims 1-7 and 9-13.

Amended claim 1, from which all other claims 2-7 and 9-13 under examination are directly or indirectly dependent, now specifies the method of the applicant's invention as follows:

1. A method for producing a recombinant hyaluronidase PH20 or a variant thereof having hyaluronidase enzymatic activity, comprising:

(1) culturing host animal cells expressing the recombinant hyaluronidase PH20 or the variant thereof having hyaluronidase enzymatic activity at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20×10^6 to 120×10^6 cells $\times$ day/mL; and

(2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature:

(a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or

(b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2;

wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and

wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more.

Each of **EP529**, **Chen**, and **Frost** fails to disclose the claimed features of the present invention.

EP529 fails to disclose or provide basis for deriving the step of “(2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days” and **EP529** fails to disclose or provide basis for deriving the limitations (a) and (b) specified in amended claim 1, *viz.*, “(a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L

during the culture period” and “(b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2” in such step (2).

Chen discloses the following empirical preparation and result:

A DNA fragment containing core domain of human PH20 gene was cloned into a constitutive expression plasmid (pGAPZ α C) of *Pichia pastoris* to produce a fusion protein with α factor signal in the N-terminus and 6 $\times$ His as well as c-Myc tags in the C-terminus. The resulting plasmid pGAPZ α C-PH20 was integrated into the genome of *P. pastoris* strain GS115. Functional recombinant human PH20 (rHuPH20) was successfully expressed and secreted by the recombinant *P. pastoris* transformant. Highest hyaluronidase activity of 2 mU/mL could be obtained at 3 day in an YPD culture.

Chen, Abstract, lines 2-7.

Chen, however, does not disclose or suggest

(2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature:

(a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or

(b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2;

as recited in amended claim 1.

According to Examples 2 to 5 of the present application, at pages 45-52 of the specification, it is sufficiently demonstrated that culture dependent on additives (Example 2), culturing duration (Example 3), controlled glucose concentration in culture medium (Example 4), and controlled pH

(Example 5) can affect the highest activity and the lowest sialylation level of the recombinant PH20 hyaluronidase or a variant thereof.

The claimed invention described in the present application correspondingly embodies and demonstrates the production of industrially useful hyaluronidase, which may be implemented for mass-producing wild PH20 hyaluronidase or a variant thereof using a recombinant method, to yield enzymes having greater industrial applicability as a result of the controlled sialylation level that is achieved in the applicant's inventive method disclosed and claimed in the present application.

It therefore is requested that the §112 and §103 rejections be reconsidered in respect of amended claims 1-7 and 9-13, and that such claims be allowed.

Respectfully submitted,

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/907,538	09/27/2022	Soon Jae PARK	4240-651	2025
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HULTQUIST IP P.O. BOX 14329 RESEARCH TRIANGLE PARK, NC 27709			EXAMINER FRONDA, CHRISTIAN L	
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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):

hip@hultquistip.com

DETAILED ACTION

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

1. Applicant's election without traverse of Invention I (claims 1-13) in the reply filed on 07/12/2023 is acknowledged. Claims 14-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-13 are under consideration in this Office Action.

Claim Rejections - 35 USC § 112

3. The following is a quotation 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 35 U.S.C. 112 (pre-AIA), first paragraph:

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.

4. Claims 1-13 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.

The claims are drawn to a broad and widely varying genus of methods for producing a genus of recombinant hyaluronidases PH20 or a genus of variants thereof, comprising: (1) culturing a genus of host cells expressing a recombinant hyaluronidase PH20 or a variant thereof at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells

reaches 20x10⁶ to 120x10⁶ cells x day/mL; and (2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature: (a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or (b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2; wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more, where the genus of variants of any amino acid sequence and structure includes PH20 variants comprising substitutions of one or more amino acid residues, and optionally comprises truncation of one or more amino acid residues of N-terminus and/or C-terminus in any amino acid sequence of wild PH20.

According to MPEP 2163:

“For each claim drawn to a genus: The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. See *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300, 111 USPQ2d 1780, 1790 (Fed. Cir. 2014)...”

According to MPEP 2163.02:

“The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).”

The reference of Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teaches that the complexity of the structure/function relationship in enzymes has proven to be the factor limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships. The reference of Singh et al. (Curr Protein Pept Sci. 2017, 18, 1-11; PTO 892) reviews protein engineering methods including directed evolution, rational design, semi-rational design, and de-novo design; and states that despite the availability of a growing database of protein structures and highly sophisticated computational algorithms, protein engineering is still limited by the incomplete understanding of protein functions, folding, flexibility, and conformational changes (see entire publication especially Figs.1 and 3, and page 7, left column, lines 8-17). The reference teachings only provide guidance for searching and screening for the genus of recombinant hyaluronidases PH20 or a genus of variants thereof.

The specification as originally filed does not disclose a representative number of species encompassed by the claimed genus by actual reduction to practice including any host cells thereof other than CHO host cells. The specification as originally filed does not provide a correlation between function and structure to enable one of ordinary skill in the art to predict which amino acid sequences, structures, and specific substitution mutations correlate with increased hyaluronidase activity.

The specification discloses a method for producing recombinant hyaluronidase PH20 comprising the amino acid sequence of SEQ ID NO: 1 comprising culturing CHO host cells expressing said recombinant hyaluronidase PH20 comprising the amino acid sequence of SEQ ID NO: 1 at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20x10⁶ to 120x10⁶ cells x day/mL; and (2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature: (a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or (b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2; wherein a sialylation content of an N-glycan of the produced recombinant hyaluronidase PH20 is 1 to 38%, and wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more.

Hence, the specification does not provide sufficient written description to inform one of ordinary skill in the art that applicants were in possession at the time the application was filed of the claimed genus of methods for producing a genus of recombinant hyaluronidases PH20 or a genus of variants thereof, comprising: (1) culturing a genus of host cells expressing a recombinant hyaluronidase PH20 or a variant thereof at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20×10^6 to 120×10^6 cells $\times$ day/mL; and (2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature: (a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or (b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2; wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more, where the genus of variants of any amino acid sequence and structure includes PH20 variants comprising substitutions of one or more amino acid residues, and optionally comprises truncation of one or more amino acid residues of N-terminus and/or C-terminus in any amino acid sequence of wild PH20.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102 of this title, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1-13 are rejected under 35 U.S.C. 103 as being unpatentable over EP3037529 (06/29/2016; IDS filed 09/27/2022) in view of Chen et al. (Constitutive expression of recombinant human hyaluronidase PH20 by *Pichia pastoris*. Journal of Bioscience and Bioengineering. 2016, vol. 122, no. 6, pages 673-378; IDS filed 09/27/2022), Frost et al. (Recombinant human hyaluronidase (rHuPH20): an enabling platform for subcutaneous drug and

fluid administration. Expert Opin. Drug Deliv. 2007, vol. 4, no. 4, pages 427-440; IDS filed 09/27/2022).

EP3037529 teaches host cells expressing human-derived pH20 hyaluronidase are cultured in a medium at 37°C and pH 7.2 for 14 days; an integral cell density increases with the culture period; 25% of sialic acid is contained; and an enzymatic activity is 1600 units/mL (see entire publication and abstract especially paragraphs [0322], [0327], [0328] and [0358] and Tables 10, 11, 12 and 28). The teachings of the reference differ from the claims in that the reference does not teach the recited method steps of lowering the culture temperature to 28-34 °C and the activity in a culture solution of the enzyme, is 10,000 unit/mL or more.

Chen et al. teach constitutive expression of recombinant human hyaluronidase PH20 in *Pichia pastoris*. Chen et al. teach a DNA fragment containing core domain of human PH20 gene was cloned into a constitutive expression plasmid (pGAPZ α C) of *Pichia pastoris* to produce a fusion protein with α factor signal in the N-terminus and 6 $\times$ His as well as c-Myc tags in the C-terminus, where the resulting plasmid pGAPZ α C-PH20 was integrated into the genome of *P. pastoris* strain GS115. Chen et al. teach that functional recombinant human PH20 (rHuPH20) was successfully expressed and secreted by the recombinant *P. pastoris* transformant after incubation for 2 days at 30°C; the highest hyaluronidase activity of 2 mU/mL could be obtained at 3 day in an YPD culture; and after purified by phenylboronic acid resin adsorption, rHuPH20 with a specific activity of 230 mU/mg was obtained. See entire publication and abstract especially MATERIALS AND METHODS section, RESULTS AND DISCUSSION section, and pages 674-677.

Frost et al. teach recombinant human hyaluronidase (rHuPH20) where its cDNA was cloned into a well-characterized mammalian cell line. Frost et al. teach that a commercially acceptable expression vector containing the human PH20 cDNA encoding amino acids 1 – 482 (rHuPH20) followed by a cytomegalovirus-driven bicistronic vector with the dihydrofolate reductase (DHFR) selection marker was constructed to allow for positive selection in DHFR-deficient CHO cells previously adapted to grow in chemically defined media without any animal-derived materials. Frost et al. teach that transfectants were cloned in chemically defined

media and selected with increasing concentrations of methotrexate to produce a high level rHuPH20-secreting cell line. Frost et al. teach that a four-step column chromatographic downstream purification process was developed that resulted in a highly purified enzyme protein with a specific activity of over 100,000 USP Units/mg protein, where the process resulted in a 447 amino acid 61 kDa glycoprotein with a properly processed amino terminus and 6 N-linked glycosylation sites. See entire publication and abstract especially 2.2 Development of a manufacturing process for rHuPH20 section and pages 432-437.

Therefore, it would have been obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to modify the teachings of EP3037529 to include the methods steps as taught and/or suggested by Chen et al. and Frost et al. for production of the human-derived pH20 hyaluronidase or any other PH20 variant including lowering the culture temperature to 28-34 °C. One of ordinary skill in the art before the effective filing date of the claimed invention would have been motivated to do this in order to obtain a simple method for producing rHuPH20. It would have been obvious to further modify the teachings of EP3037529 to incorporate the recited culturing steps and/or conditions, and purify the produced PH20 using chromatography recited in the claims as routine experimentation and/or as desired for efficient production of the PH20. One of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success because recombinantly producing PH20 is known in the art as shown by the above reference teachings. Hence, the claimed invention as a whole is prima facie obvious.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272 0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between

Art Unit: 1652

9:00AM 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (408)918-7584. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

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>.

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.

/CHRISTIAN L FRONDA/
Primary Examiner, Art Unit 1652

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States Patent Application of:	)	Docket No.: 4240-651
	)	
Applicant: ALTEOGEN INC.	)	Conf. No.: 2025
	)	
Application No.: 17/907,538	)	Art Unit: 1652
	)	
Date Filed: September 27, 2022	)	Examiner: Christian L. Fronda
	)	
Title: METHOD FOR PRODUCING RECOMBINANT HYALURONIDASE	)	Customer No.: 23448
	)	
	)	

CERTIFICATE OF EFS FILING

I hereby certify that this document is being filed via EFS in the United States Patent and
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/steven.j. hultquist/

**U.S. PATENT APPLICATION NO. 17/907,538
RESPONSE TO MAY 12, 2023 OFFICE ACTION**

Mail Stop: Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

This responds to the May 12, 2023 Office Action in the above-identified application, in which the Examiner has imposed a restriction requirement on pending claims 1-16, requiring election of one of the following Inventions 1 and 2:

Invention 1, claims 1-13, drawn to to a method for producing recombinant hyaluronidase PH20 or a variant thereof, comprising: (1) culturing host cells expressing a recombinant hyaluronidase PH20 or a variant thereof at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20x10⁶ to 120x10⁶ cells x day/mL; and (2) decreasing the culture temperature to 20°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature: (a) wherein the residual glucose concentration in the medium is

maintained at 0.01 g/L to 4.5 g/L during the culture period; and/or (b) wherein the pH of the culture medium is maintained at 6.8 ~7.2; wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more; and

Invention 2, claims 14-16, drawn to PH20 or variant thereof, in which a galactosylation content is 1 to 68%, a sialylation content is 1 to 38%, and mannosylation content is 40 to 63% of N-glycan of PH20 or the variant thereof, respectively.

In response, the applicant hereby elects Invention 1, and identifies claims 1-13 as readable thereon. Such election is without traverse.

It correspondingly is requested that examination of the application proceed, consistent with the foregoing election.

Respectfully submitted,

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

NOTIFICATION DATE	DELIVERY MODE
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05/12/2023

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):

hip@hultquistip.com

DETAILED ACTION

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Election/Restriction

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Invention 1 Claims 1-13 drawn to a method for producing recombinant hyaluronidase PH20 or a variant thereof, comprising: (1) culturing host cells expressing a recombinant hyaluronidase PH20 or a variant thereof at a culture temperature of 35°C to 38°C until an integral viable cell density of the host cells reaches 20x10⁶ to 120x10⁶ cells x day/mL; and (2) decreasing the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days; while maintaining the culture temperature: (a) wherein the residual glucose concentration in the medium is maintained at 0.001 g/L to 4.5 g/L during the culture period; and/or (b) wherein the pH of the culture medium is maintained at 6.8 ~ 7.2; wherein a sialylation content of an N-glycan of the produced PH20 or variant thereof is 1 to 38%, and wherein a hyaluronidase activity in the culture medium is 10,000 units/mL or more.

Invention 2 Claims 14-16, drawn to PH20 or a variant thereof, in which a galactosylation content is 1 to 68%, a sialylation content is 1 to 38%, and a mannosylation content is 40 to 63% of N-glycan of PH20 or the variant thereof, respectively.

The inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

EP3037529 (06/29/2016; IDS filed 09/27/2022) teaches host cells expressing human-derived pH20 hyaluronidase are cultured in a medium at 37°C and pH 7.2 for 14 days; an integral cell density increases with the culture period; 25% of sialic acid is contained; and an enzymatic activity is 1600 units/mL (see entire publication and abstract especially paragraphs [0322], [0327], [0328] and [0358] and Tables 10, 11, 12 and 28). It would have been obvious to modify the teachings of the reference to include all of the recited methods steps in the claims to produce the recombinant hyaluronidase PH20 or a variant thereof. Thus, the same or corresponding technical feature was known in the prior art and therefore cannot make a contribution over the prior art. Since the inventions lack the same or corresponding special technical feature, then the inventions listed above are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272 0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (408)918-7584. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

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

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encouraged to use the USPTO Automated Interview Request (AIR) at

<http://www.uspto.gov/interviewpractice>.

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.

/CHRISTIAN L FRONDA/

Primary Examiner, Art Unit 1652