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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/810,337	07/27/2015	Gabor T. Bartha	44168-702.401	1008
21971 7590 02/28/2019 WILSON, SONSINI, GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050			EXAMINER ZHANG, KAIJIANG	
			ART UNIT 1639	PAPER NUMBER
			NOTIFICATION DATE 02/28/2019	DELIVERY MODE 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):

patentdocket@wsgr.com

Notice of Allowability	Application No. 14/810,337	Applicant(s) Bartha et al.	
	Examiner KAIJIANG ZHANG	Art Unit 1639	AIA Status No

-- 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 the IDS filed on 2/12/2019 and the amendment filed on 2/14/2019.
☐ 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 31-39,41-47 and 49 . 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 2/12/2019. | 6. ☐ Examiner's Statement of Reasons for Allowance |
| 3. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material _____. | 7. ☒ Other <u>PTO-271</u> . |
| 4. ☐ Interview Summary (PTO-413),
Paper No./Mail Date. _____. | |

/KAIJIANG ZHANG/
Primary Examiner, Art Unit 1639

Electronically Filed On: February 14, 2019

PATENT
Attorney Docket No. 44168-702.401

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application	)	
Inventors: Gabor T. BARTHA, <i>et al.</i>	)	Confirmation No.: 1008
Application No.: 14/810,337	)	Art Unit: 1639
Filed: July 27, 2015	)	Examiner: Kaijiang ZHANG
Title: METHODS AND SYSTEMS FOR GENETIC ANALYSIS	)	Customer No. 021971

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AFTER ALLOWANCE UNDER 37 C.F.R. § 1.312

Dear Commissioner:

This Amendment under 37 C.F.R. § 1.312 is submitted after the Notice of Allowance mailed January 18, 2019. Entry of the following amendment under 37 C.F.R. § 1.312 is respectfully requested.

Amendments to the Claims begin on page **2** of this paper.

Remarks begin on page **5** of this paper.

REMARKS

This Amendment under 37 C.F.R. § 1.312 is submitted after the Notice of Allowance mailed January 18, 2019, and before payment of the Issue Fee.

Claims 31-39, 41-47 and 49 have been allowed. Claims 42 and 46 are herein amended for antecedent basis and typographical purposes. No new matter has been added by this amendment. Accordingly, Applicant respectfully requests entry of the amendment.

CONCLUSION

In light of the foregoing remarks, Applicant respectfully requests entry of the abovementioned amendments. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned. The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit account No. 23-2415 (Attorney Docket No. 44168-702.401).

Respectfully submitted,

Date: February 14, 2019

By: /Jacqueline Stroncek/
Jacqueline Stroncek, Reg. No. 72,619

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1050
Phone: (650) 493-9300
Customer No. 021971

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in this application. Applicant reserves the right to pursue any subject matter of any canceled claims in this or any other appropriate patent application. Support for these claims is provided in the remarks following the listing of claims.

Listing of the Claims

1-30. **(Canceled)**

31. **(Previously Presented)** A method for analyzing a nucleic acid sample, comprising:

- a. producing two or more subsets of nucleic acid molecules from a nucleic acid sample, wherein the two or more subsets differ by one or more genomic features selected from the group consisting of: genomic regions, mean GC content, mean molecular size, methylation state, insertion or deletion, and single nucleotide variant (SNV), with the aid of pulldown probes that selectively enrich for the one or more genomic features in at least a first subset or a second subset of the two or more subsets of nucleic acid molecules as compared to another genomic feature(s) in the at least the first subset or the second subset;
- b. combining at least two of the two or more subsets of nucleic acid molecules to produce a first combined pool of nucleic acid molecules; and
- c. conducting one or more assays on the first combined pool of nucleic acid molecules, wherein at least one of the one or more assays comprises a sequencing reaction.

32. **(Previously Presented)** The method of claim 31, wherein the nucleic acid molecules are DNA.

33. **(Previously Presented)** The method of claim 31, wherein the genomic regions are selected from the group consisting of alternative sequences, entire exome, a set of genes, and a set of regulatory elements.

34. **(Previously Presented)** The method of claim 33, wherein the set of genes is selected from the group consisting of a set of genes with Mendelian traits, a set of genes with disease traits, a set of genes with known drug traits, and a set of genes with biomedically interpretable variants.

35. **(Previously Presented)** The method of claim 33, wherein the alternative sequences are selected from the group consisting of one or more small insertions, small deletions, structural variant junctions, variable length tandem repeats, and flanking sequences.
36. **(Previously Presented)** The method of claim 31, wherein the two or more subsets of nucleic acid molecules differ by mean molecular size.
37. **(Previously Presented)** The method of claim 31, further comprising producing a unified assessment of a genetic state of the nucleic acid sample at each locus addressed by the one or more assays.
38. **(Previously Presented)** The method of claim 31, wherein conducting the one or more assays further comprises conducting one or more amplification reactions.
39. **(Previously Presented)** The method of claim 38, wherein conducting the one or more amplification reactions comprises polymerase chain reaction-based amplification.
40. **(Canceled)**
41. **(Previously Presented)** The method of claim 31, wherein producing two or more subsets of nucleic acid molecules from a nucleic acid sample with the aid of pulldown probes comprises conducting one or more hybridization reactions.
42. **(Currently Amended)** The method of claim 31, wherein producing the two or more subsets further comprises differential amplification of ~~the two~~ of the two or more subsets based on the one or more genomic features.
43. **(Previously Presented)** The method of claim 31, wherein conducting one or more assays comprises conducting two or more assays, and further comprising (d) combining results from the two or more assays.
44. **(Previously Presented)** The method of claim 31, further comprising producing one or more biomedical reports after conducting the one or more assays, wherein the one or more biomedical reports comprise biomedical information of a subject from which the nucleic acid sample was derived.
45. **(Previously Presented)** The method of claim 44, wherein the biomedical information of the subject is indicative of one or more biomedical features selected from the group consisting of disease state, genetic risk of a disease, reproductive risk, genetic risk to a fetus, risk of an adverse drug reaction, efficacy of a drug therapy, prediction of optimal drug dosage, and transplant tolerance.

46. **(Currently Amended)** The method of claim 31, wherein ~~[[a]]~~the first subset of nucleic acid molecules and ~~[[a]]~~the second subset of nucleic acid molecules of the two or more subsets of nucleic acid molecules are complementary with respect to the one or more genomic features selected from the group consisting of genomic regions, mean GC content and mean molecular size.
47. **(Previously Presented)** The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ at least by mean GC content.
48. **(Canceled)**
49. **(Previously Presented)** The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by at least mean GC content and mean molecular size.
50. **(Canceled)**



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NOTICE OF ALLOWANCE AND FEE(S) DUE

21971 7590 01/18/2019
WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER

ZHANG, KAIJIANG

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 01/18/2019

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/810,337	07/27/2015	Gabor T. Bartha	44168-702.401	1008

TITLE OF INVENTION: METHODS AND SYSTEMS FOR GENETIC ANALYSIS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1000	\$0.00	\$0.00	\$1000	04/18/2019

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 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity 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 and an extra copy of the form should be submitted. 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 EFS-Web.

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 including the Patent, advance orders and notification of maintenance fees 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.

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

21971 7590 01/18/2019
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650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

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 EFS-Web 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.
14/810,337	07/27/2015	Gabor T. Bartha	44168-702.401	1008

TITLE OF INVENTION: METHODS AND SYSTEMS FOR GENETIC ANALYSIS

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EXAMINER	ART UNIT	CLASS-SUBCLASS
ZHANG, KAIJIANG	1639	435-006100

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/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-09 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,

(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.

1 _____
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) ☐ Advance Order - # of Copies _____

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

☐ Electronic Payment via EFS-Web ☐ 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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650 PAGE MILL ROAD			ART UNIT	PAPER NUMBER
PALO ALTO, CA 94304-1050			1639	

DATE MAILED: 01/18/2019

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

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

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

<i>Notice of Allowability</i>	Application No. 14/810,337	Applicant(s) Bartha et al.	
	Examiner KAIJIANG ZHANG	Art Unit 1639	AIA Status No

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☐ 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 31-39,41-47 and 49 . 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)).

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☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

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2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 10/8/2018.	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. _____.	

/KAIJIANG ZHANG/ Primary Examiner, Art Unit 1639	
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DETAILED ACTION

Terminal Disclaimer

1. The terminal disclaimer filed on 10/8/2018 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 9,745,626 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Response to Amendments and Arguments

2. Applicant's amendments and arguments filed 10/8/2018 have been fully considered. In view of applicant's amendments to the claims as well as the terminal disclaimer filed, all the rejections from the previous Office action have been withdrawn. Since claims 34-36, 47 and 49, previously withdrawn due to an election of species requirement, depend from and thus require all the limitations of allowable claim 31, they have been rejoined. Accordingly, claims 31-39, 41-47 and 49 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAIJIANG ZHANG whose telephone number is (571)272-5207. The examiner can normally be reached on Monday - Friday, 8:30 am - 5 pm.

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, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KAIJIANG ZHANG/
Primary Examiner, Art Unit 1639



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/810,337	07/27/2015	Gabor T. Bartha	44168-702.401	1008
21971 7590 10/11/2018 WILSON, SONSINI, GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050			EXAMINER ZHANG, KAIJIANG	
			ART UNIT 1639	PAPER NUMBER
			NOTIFICATION DATE 10/11/2018	DELIVERY MODE 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):

patentdocket@wsgr.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 14/810,337		Applicant(s) Bartha et al.	
	Examiner KAIJIANG ZHANG		Art Unit 1639	AIA Status No

All participants (applicant, applicants representative, PTO personnel):

(1) KAIJIANG ZHANG. (3) Ali Alemozafar.

(2) Jacqueline Stroncek. (4) Nicholas Tiee.

Date of Interview: 05 October 2018.

Type: ☒ Telephonic ☐ Video Conference
 ☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
 If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☒102 ☐103 ☒Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: 31.

Identification of prior art discussed: Craig et al. (of record).

Substance of Interview
 (For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Applicant's representative, Jacqueline Stroncek, initiated the telephone interview (which was joined by Ali Alemozafar and Nicholas Tiee who are also applicant's representatives) to discuss proposed amendment to claim 31 (see attached interview agenda). The examiner pointed out that amended claim 31, as currently proposed, would not distinguish over Craig et al. because the amplification primers used by Craig et al. could be reasonably interpreted as "probes" as currently recited in the claim. During the interview, possible ways to further amend claim 31 to distinguish over Craig et al. were discussed, but no specific agreement on the final claim language was reached..

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/KAIJIANG ZHANG/ Primary Examiner, Art Unit 1639	
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Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) 1.133 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiners responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicants correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,-
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicants record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiners version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, Interview Record OK on the paper recording the substance of the interview along with the date and the examiners initials.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in this application. Applicant reserves the right to pursue any subject matter of any canceled claims in this or any other appropriate patent application. Support for these claims is provided in the remarks following the listing of claims.

Listing of the Claims

1-30. **(Canceled)**

31. **(Currently amended)** A method for analyzing a nucleic acid sample, comprising:
- producing two or more subsets of nucleic acid molecules from a nucleic acid sample, wherein the two or more subsets differ by one or more genomic features selected from the group consisting of: genomic regions, mean GC content, mean molecular size, subset preparation method, methylation state, insertion or deletion, and single nucleotide variant (SNV) combination thereof, with the aid of pulldown probes that selectively enrich for the one or more genomic features in at least a first subset or a second subset of the two or more subsets of nucleic acid molecules as compared to another genomic feature(s) in the at least the first subset or the second subset;
 - combining at least two of the two or more subsets of nucleic acid molecules to produce a first combined pool of nucleic acid molecules; and
 - conducting one or more assays on the first combined pool of nucleic acid molecules, wherein at least one of the one or more assays comprises a sequencing reaction.

32. **(Previously Presented)** The method of claim 31, wherein the nucleic acid molecules are DNA.

33. **(Currently Amended)** The method of claim 31, wherein the genomic regions are selected from the group consisting of high GC content, low GC content, low complexity, low mappability, known single nucleotide variations (SNVs), known indels, [[known]] alternative sequences, entire genome, entire exome, a set of genes, and a set of regulatory elements, and methylation state.

34. **(Currently Amended)** The method of claim 33, wherein the set of genes is selected from the group consisting of a set of genes with **[[known]]** Mendelian traits, a set of genes with

[[known]] disease traits, a set of genes with known drug traits, and a set of genes with [[known]] biomedically interpretable variants.

35. **(Currently amended)** The method of claim 33, wherein the [[known]] alternative sequences are selected from the group consisting of one or more small insertions, small deletions, structural variant junctions, variable length tandem repeats, and flanking sequences.

36. **(Previously Presented)** The method of claim 31, wherein the two or more subsets of nucleic acid molecules differ by mean molecular size.

37. **(Previously Presented)** The method of claim 31, further comprising producing a unified assessment of a genetic state of the nucleic acid sample at each locus addressed by the one or more assays.

38. **(Currently Amended)** The method of claim 31, wherein conducting the one or more assays further comprises conducting one or more amplification reactions.

39. **(Previously Presented)** The method of claim 38, wherein conducting the one or more amplification reactions comprises polymerase chain reaction-based amplification.

40. **(Canceled)**

41. **(Currently amended)** The method of claim ~~31~~[[40]], wherein producing two or more subsets of nucleic acid molecules from a nucleic acid sample with the aid of pulldown probes~~conducting the enrichment reaction~~ comprises conducting one or more hybridization reactions.

42. **(Currently Amended)** The method of claim ~~31~~[[40]], wherein producing the two or more subsets ~~further conducting the enrichment reaction~~ comprises differential amplification of ~~at least the~~ two of the two or more subsets based on the one or more genomic ~~region~~ features.

43. **(Currently Amended)** The method of claim 31, wherein conducting one or more assays comprises conducting two or more assays, and ~~wherein (c) further compris~~[[es]]ing (d) combining results from the two or more assays.

44. **(Currently Amended)** The method of claim 31, further comprising producing one or more biomedical reports after conducting the one or more assays, wherein the one or more biomedical reports comprise biomedical information of a subject [[of]] from which the nucleic acid sample was derived.

45. **(Currently Amended)** The method of claim 44, wherein the biomedical information of the subject ~~predicts, prognoses, or diagnoses~~ is indicative of one or more biomedical features selected from the group consisting of disease state, genetic risk of a disease, reproductive risk, genetic risk to a fetus, risk of an adverse drug reaction, efficacy of a drug therapy, prediction of optimal drug dosage, and ~~transplant tolerance, and a combination thereof.~~

46. **(Previously Presented)** The method of claim 31, wherein a first subset of nucleic acid molecules and a second subset of nucleic acid molecules of the two or more subsets of nucleic acid molecules are complementary ~~[[in]]~~ with respect to the one or more genomic features selected from the group consisting of genomic regions, mean GC content and mean molecular size.

47. **(Currently Amended)** The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ at least by mean GC content.

48. **(Canceled)**

49. **(Currently Amended)** The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by at least mean GC content and mean molecular size.

50. **(Canceled)**

AMENDMENTS TO THE DRAWINGS

The Office action dated April 9, 2018 objects to the drawings in Figures 2-15 for allegedly containing text that is illegible due to poor resolution. Applicant attaches herewith replacement sheets for Figure 2-15 that Applicant believes address the issues raised by the Office. Accordingly, Applicant respectfully requests that this object be withdrawn.

SUMMARY OF THE INTERVIEW

Applicant is appreciative of Primary Examiner Zhang for extending the courtesy of a telephonic interview to Applicant's representatives, Ali Alemozafar, Jacqueline Stroncek, and Nicholas Tiee, on October 5, 2018. During the interview, amendments and arguments consistent with those detailed herein were discussed.

REMARKS

Claims 31-47, 49 and 50 were pending. Claims 40 and 50 are canceled without prejudice. Claims 31, 33, 34, 38, 41-45, 47, and 49 are amended. No new matter is added by any of these amendments. Accordingly, upon entry, claims 31-39, 41-47, and 49 will be pending.

Reconsideration and allowance is respectfully requested in light of the abovementioned amendments and the following remarks.

Claims amendments

Claims 31, 33, 34, 38, 41-45, 47, and 49 have been amended to clarify the claimed subject matter. These amendments are fully supported by the application as originally filed, U.S. Patent Application Serial No. 14/810,337, now U.S. Patent Publication No. US 20160017417 (hereinafter “Application”) at, for example, paragraphs [0004], [0020], [0139]-[0144], [0163] and [0285].

Drawings

The Office has objected to the drawings. Corrected drawing sheets in compliance with 37 C.F.R. 1.121(d) are submitted herewith. Accordingly, Applicant respectfully requests withdrawal of the objection.

35 U.S.C. § 112

Claim 33 stands rejected under 35 U.S.C. § 112 (pre-AIA), second paragraph.

Without conceding in the basis of rejection, and solely to expedite the prosecution of this application, Applicant has amended claim 33 to clarify the claimed subject matter. Accordingly, Applicant respectfully requests that the § 112 rejection of claim 33 be withdrawn.

35 U.S.C. § 102

Claims 31-33, 37-43 and 46 stand rejected under pre-AIA 35 U.S.C. 102(b) over Craig et al. (Nature Methods 2008, 5:887-893, with additional 10 pages of Supplementary Information, hereinafter “Craig”).

Without conceding in the basis of rejection, and solely to expedite the prosecution of this application, Applicant has amended claim 31 to clarify certain differences between the claimed

subject matter and Craig. Applicant submits that claim 31 is novel of Craig because this reference does not meet all of the elements of this claim.

In Craig, “[f]or each HapMap individual, the ENCODE regions were amplified by long-range PCR in a 25ul reaction volume using 75ng template DNA, 1X PfuUltraBuffer, 2mM dNTPs (total), 400nM each of the forward and reverse primers, and 0.5ul PfuUltraII HS DNA polymerase (Stratagene) per reaction.” See Craig, Supplementary Methods. According to Craig, “[l]ibraries were PCR-enriched using Phusion DNA polymerase PCR mix and adapter compatible primers 1.1 and 2.1 (Illumina).” Id.

However, nothing in Craig teaches or discloses “producing two or more subsets of nucleic acid molecules . . . with the aid of **pulldown probes** that selectively enrich for the one or more genomic features in at least a first subset or a second subset of the two or more subsets of nucleic acid molecules as compared to another genomic feature(s) in the at least the first subset or the second subset,” as recited in claim 31. The “primers” of Craig are not pulldown probes. For example, Craig nowhere teaches or discloses using probes for pulling down sequences from a solution for enrichment.

Accordingly, Applicant respectfully requests that the § 102 rejection of claim 31 be withdrawn.

Claims 32, 33, 37-39, 41-43 and 46 depend from and include all elements of claim 31 and recite additional elements of particular advantage and utility. Craig does not meet all the elements of claim 31, much less the combination of claims 32, 33, 37-39, 41-43, and 46. Accordingly, Applicant respectfully requests that the § 102 rejections of claims 32, 33, 37-39, 41-43, and 46 also be withdrawn.

Without conceding in the basis of rejection, Applicant submits that the § 102 rejections of claims 40 and 50 are moot in view of the cancellation of these claims.

35 U.S.C. § 103

Claims 44 and 45 stand rejected under pre-AIA 35 U.S.C. § 103(a) over Craig.

Claims 44 and 45 are not obvious over Craig for at least the reason that they depend from and include all elements of claim 31, and recite additional elements of particular advantage and utility. Craig does not meet all the elements of claim 31, much less the combination of claims 44 and 45.

Accordingly, Applicant respectfully requests that the §103 rejections of claims 44 and 45 be withdrawn.

Double patenting

Claims 31-33 and 37-46 are rejected on the ground of nonstatutory double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent No. 9,745,626 (“the ‘626 patent”).

Without conceding in the basis of rejection, and solely to expedite the prosecution of this application, Applicant submits herewith a terminal disclaimer over the ‘626 patent. Accordingly, Applicant respectfully requests that the double patenting rejections be withdrawn.

It shall be understood herein that any instance in which Applicant has addressed certain comments set forth by the Office shall not be construed as a concession to other comments or arguments advanced by the Office. Any circumstance in which Applicant has amended or cancelled a claim also does not mean that Applicant concedes to the arguments or positions advanced by the Office with respect to that claim or other claims pending herein.

CONCLUSION

In light of the remarks set forth above, Applicants believe that the pending claims are under condition for allowance. Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner have any question, the Examiner is encouraged to telephone the undersigned.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit account No. 23-2415 (Attorney Docket No. 44168-702.401).

Respectfully submitted,

Date: October 8, 2018

By: /Jacqueline Stroncek/
Jacqueline Stroncek, Reg. No. 72,619

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1050
Phone: (650) 493-9300
Customer No. 021971



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/810,337	07/27/2015	Gabor T. Bartha	44168-702.401	1008
21971 7590 04/09/2018 WILSON, SONSINI, GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050			EXAMINER ZHANG, KAIJIANG	
			ART UNIT	PAPER NUMBER
			1639	
			NOTIFICATION DATE	DELIVERY MODE
			04/09/2018	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):

patentdocket@wsgr.com

Office Action Summary	Application No. 14/810,337	Applicant(s) BARTHA ET AL.	
	Examiner Kaijiang Zhang	Art Unit 1639	AIA (First Inventor to File) Status No

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

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 2/23/2018.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 31-47,49 and 50 is/are pending in the application.
5a) Of the above claim(s) 34-36,47,49 and 50 is/are withdrawn from consideration.

6) ☐ Claim(s) ____ is/are allowed.

7) ☒ Claim(s) 31-33 and 37-46 is/are rejected.

8) ☐ Claim(s) ____ is/are objected to.

9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☐ The specification is objected to by the Examiner.

11) ☒ The drawing(s) filed on 7/27/2015 and 10/6/2015 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some** c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
Paper No(s)/Mail Date See Continuation Sheet.

3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.

4) ☐ Other: ____.

Continuation of Attachment(s) 2). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date: 9/22/2015, 8/29/2016, 4/20/2017.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application is being examined under the pre-AIA first to invent provisions.

Election/Restrictions

2. The response filed on 2/23/2018 to the election of species requirement of 1/10/2018 has been received. For the first species election, applicant elected, without traverse, “genomic regions” as the “one or more features” that is/are differed between the two or more subsets of nucleic acid molecules (thus claims 36, 47, 49 and 50 are withdrawn as being drawn to non-elected species), and further elected “high GC content” listed in claim 33 as the *ultimate* sub-species regarding the “genomic regions” (thus claims 34 and 35 are withdrawn as being drawn to non-elected sub-species). For the second species election, although applicant elected the species of claim 41, both species of claims 41 and 42 are being examined because the non-elected species (i.e., the species of claim 42) is also taught in the prior art reference used in the 102 rejection below.
3. Claims 31-47, 49 and 50 are pending in the application. Claims 34-36, 47, 49 and 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 31-33 and 37-46 are currently under examination.

Drawings

4. The drawings are objected to because each of Figures 2-15 contains text that is illegible due to poor resolution. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double

Art Unit: 1639

patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(I)(1) - 706.02(I)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may

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be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

6. Claims 31-33 and 37-46 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 9,745,626.

Although the claims at issue are not identical, they are not patentably distinct from each other because claims 1-22 of U.S. Patent No. 9,745,626 teach or render obvious all the features as recited in instant claims 31-33 and 37-46. Specifically, claims 1 and 16 of U.S. Patent No. 9,745,626 disclose a method that is more specific than, and thus has all the features of, the method of instant claim 31. Furthermore, claims 2-22 of U.S. Patent No. 9,745,626 disclose or render obvious all the additional features as recited in instant claims 32, 33 and 37-46.

Claim Rejections - 35 USC § 112

7. The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

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

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 33 is rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

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Claim 33 recites “high GC content”, “low GC content”, “low complexity” and “low mappability” (lines 2-3, emphasis added). However, the terms “high” and “low” are relative terms which render the claim indefinite. The term “high” or “low” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In addition, claim 33 recites “known single nucleotide variations (SNVs)”, “known inDels” and “known alternative sequences” (lines 3-4, emphasis added). The term “known” renders the claim indefinite in that it does not provide a clear boundary of the scope of the claim, because the scope would change as new SNVs, inDels, or alternative sequences are discovered.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 31-33, 37-43 and 46 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Craig et al. (Nature Methods 2008, 5:887-893, with additional 10 pages of Supplementary Information).

Regarding claim 31

Craig et al. teach, throughout the whole document (particularly Figure 1), a method for analyzing a nucleic acid sample, comprising: a. producing two or more subsets of nucleic acid molecules (e.g., three subsets of nucleic acid molecules produced by amplifying “Region 1”, “Region 2” and “Region 3” respectively) from a nucleic acid sample (e.g., “Sample 1”, “Sample 2”, or “Sample 3”), wherein the two or more subsets differ by one or more features selected from genomic regions (e.g., “Region 1”, “Region 2” and “Region 3” are different genomic regions), mean GC content (e.g., since “Region 1”, “Region 2” and “Region 3” are *different* genomic regions, they would presumably have different mean GC content as well, absent evidence to the contrary), mean molecular size, subset preparation method (e.g., since each of the three subsets of nucleic acid molecules is produced by amplifying a *different* genomic region (i.e., “Region 1”, “Region 2” or “Region 3”) with primers *specific* to said *different* genomic region (see Supplementary Table 1), the three subsets of nucleic acid molecules are considered to be produced by three different preparation methods (i.e., *different* preparation methods involving the use of *different* sets of primers).), or combination thereof (Figure 1; paragraph spanning pages 887-888); b. combining at least two of the two or more subsets of nucleic acid molecules to produce a first combined pool of nucleic acid molecules (Figure 1; paragraph spanning pages 887-888); and c. conducting one or more assays on the first combined pool of nucleic acid molecules, wherein at least one of the one or more assays comprises a sequencing reaction (Figure 1; paragraph spanning pages 887-888).

Regarding claim 32

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The method according to Craig et al., wherein the nucleic acid molecules are DNA (Abstract).

Regarding claim 33

As discussed in the 112 rejection above, the term “high” or “low” as used in the claim is a relative term which is not defined. Thus, any genomic regions, including “Region 1”, “Region 2” and “Region 3” as used in the method of Craig et al., may be considered as genomic regions of high GC content or genomic regions of low GC content.

In addition, Craig et al. also teach that the genomic regions are regions with known single nucleotide variations or known alternative sequences (page 891, column 1: “**Genotyping individuals at known polymorphisms**”; Figure 4 caption: “Exact positions matching known polymorphisms are colored as red spheres”).

Regarding claim 37

The method according to Craig et al., further comprising producing a unified assessment of a genetic state of the nucleic acid sample at each locus (e.g., polymorphic site) addressed by the one or more assays (Abstract).

Regarding claims 38 and 39

The method according to Craig et al., wherein conducting the one or more assays comprises conducting one or more amplification reactions, wherein conducting the one or more amplification reactions comprises polymerase chain reaction-based amplification (paragraph spanning pages 887-888; Figure 1).

Regarding claims 40-42

The method according to Craig et al., wherein producing the two or more subsets of nucleic acid molecules comprises conducting an enrichment reaction (Figure 1: “Amplify regions”; page 887, column 2, last paragraph: “amplified multiple 5-kb regions.....by long-range PCR”), wherein conducting the enrichment reaction comprises conducting one or more hybridization reactions (i.e., PCR amplification would inherently involve one or more hybridization reactions), wherein conducting the enrichment reaction comprises differential amplification of at least two of the two or more subsets based on one or more genomic region features (i.e., different genomic regions have different genomic region features).

Regarding claim 43

The method according to Craig et al., wherein conducting one or more assays comprises conducting two or more assays, and wherein (c) further comprises combining results from the two or more assays (the method of Craig et al. meets the recited limitations in each of the following two ways: 1) conducting *multiple* sequencing assays, *simultaneously*, with the *combined* pool comprising all of the subsets of nucleic acid molecules, thus producing *combined* results from all of the *multiple* sequencing assays conducted simultaneously; or 2) the combined pool is enriched by “PCR amplification” and then “sequenced” (i.e., two assays. See page 897, column 2, last paragraph: “...we pooled samples from all individuals into a single sample (referred to as an indexed library), purified the samples, enriched them by PCR amplification **and** sequenced them on the Illumina GA”), wherein the sequencing results are considered as *combined* results from *all* the assays leading to such *final* sequencing results).

Regarding claim 46

The method according to Craig et al., wherein a first subset of nucleic acid molecules and a second subset of nucleic acid molecules of the two or more subsets of nucleic acid molecules (which are produced by amplifying “Region 1”, “Region 2” and “Region 3” respectively) are complementary in genomic regions (Figure 1; paragraph spanning pages 887-888).

Claim Rejections - 35 USC § 103

11. The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under pre-AIA 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of pre-AIA 35 U.S.C. 103(c) and potential pre-AIA 35 U.S.C. 102(e), (f) or (g) prior art under pre-AIA 35 U.S.C. 103(a).

13. Claims 44 and 45 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Craig et al. (Nature Methods 2008, 5:887-893, with additional 10 pages of Supplementary Information).

Craig et al. teach the method of claim 31 as discussed above. Craig et al. further teach using the method for discovering and genotyping polymorphisms (Abstract). According to Craig et al., such genetic polymorphisms or variants are associated with human diseases (page 887, column 1, paragraph 1). Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to further generate a biomedical report comprising biomedical information of a subject based on the disease-associated variants detected, because Craig et al. taught the association between the detected variants (page 887, column 1, paragraph 1) and human diseases and implicitly suggested using the detected variants in disease analysis/diagnosis. Detecting the disease-associated variants and using them in disease analysis/diagnosis would necessarily involve predicting or diagnosing biomedical features such as disease state or genetic risk of a disease. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

14. No claims are currently allowable.

The following prior art reference is made of record: Boers et al., PLoS ONE 2012, 7(7):e39630. Though this prior art reference is not relied upon, it is considered pertinent to applicant's disclosure because it anticipates at least claim 31 in a similar way as the Craig reference used in the 102 rejection above.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kaijiang Zhang whose telephone number is (571)272-5207. The examiner can normally be reached on Weekdays.

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, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kaijiang Zhang/
Primary Examiner, Art Unit 1639

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application	)	
	)	Examiner: Kaijiang Zhang
Inventor(s): Gabor T. Bartha, et al.	)	
	)	Art Unit: 1639
Application No. 14/810,337	)	
	)	Confirmation No.: 1008
Filed: July 27, 2015	)	
	)	Customer No.: 021971
Title: METHODS AND SYSTEMS FOR GENETIC	)	
ANALYSIS	)	

Mail Stop Amendment
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Sir:

This paper is filed in response to Requirement for Restriction/Species Election dated January 10, 2018. Reconsideration of the above-referenced application is respectfully requested in view of the following amendments and remarks.

Amendments to Claims begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

AMENDMENTS TO THE CLAIMS

1.-30. (Canceled)

31. (Previously Presented) A method for analyzing a nucleic acid sample, comprising:

- a. producing two or more subsets of nucleic acid molecules from a nucleic acid sample, wherein the two or more subsets differ by one or more features selected from genomic regions, mean GC content, mean molecular size, subset preparation method, or combination thereof;
- b. combining at least two of the two or more subsets of nucleic acid molecules to produce a first combined pool of nucleic acid molecules; and
- c. conducting one or more assays on the first combined pool of nucleic acid molecules, wherein at least one of the one or more assays comprises a sequencing reaction.

32. (Previously Presented) The method of claim 31, wherein the nucleic acid molecules are DNA.

33. (Currently Amended) The method of claim 31, wherein the genomic regions are selected from the group consisting of high GC content, low GC content, low complexity, low mappability, known single nucleotide variations (SNVs), known inDels, known alternative sequences, entire genome, entire exome, a set of genes, a set of regulatory elements, and methylation state.

34. (Currently Amended) The method of claim 33, wherein the set of genes is selected from the group consisting of a set of genes with known Mendelian traits, a set of genes with known disease traits, a set of genes with known drug traits, and a set of genes with known biomedically interpretable variants.

35. (Previously Presented) The method of claim 33, wherein the known alternative sequences are selected from the group consisting of one or more small insertions, small deletions, structural variant junctions, variable length tandem repeats, and flanking sequences.

36. (Previously Presented) The method of claim 31, wherein the two or more subsets of nucleic acid molecules differ by mean molecular size.
37. (Previously Presented) The method of claim 31, further comprising producing a unified assessment of a genetic state of the nucleic acid sample at each locus addressed by the one or more assays.
38. (Previously Presented) The method of claim 31, wherein conducting the one or more assays comprises conducting one or more amplification reactions.
39. (Previously Presented) The method of claim 38, wherein conducting the one or more amplification reactions comprises polymerase chain reaction-based amplification.
40. (Previously Presented) The method of claim 31, wherein producing the two or more subsets of nucleic acid molecules comprises conducting an enrichment reaction.
41. (Previously Presented) The method of claim 40, wherein conducting the enrichment reaction comprises conducting one or more hybridization reactions.
42. (Previously Presented) The method of claim 40, wherein conducting the enrichment reaction comprises differential amplification of at least two of the two or more subsets based on one or more genomic region features.
43. (Previously Presented) The method of claim 31, wherein conducting one or more assays comprises conducting two or more assays, and wherein (c) further comprises combining results from the two or more assays.
44. (Previously Presented) The method of claim 31, further comprising producing one or more biomedical reports after conducting the one or more assays, wherein the one or more biomedical reports comprise biomedical information of a subject of the nucleic acid sample.
45. (Previously Presented) The method of claim 44, wherein the biomedical information of the subject predicts, prognoses, or diagnoses one or more biomedical features selected from the group consisting of disease state, genetic risk of a disease, reproductive risk, genetic risk to a fetus, risk of an adverse drug reaction, efficacy of a drug therapy, prediction of optimal drug dosage, transplant tolerance, and a combination thereof.

46. (Previously Presented) The method of claim 31, wherein a first subset of nucleic acid molecules and a second subset of nucleic acid molecules of the two or more subsets of nucleic acid molecules are complementary in one or more features selected from the group consisting of genomic regions, mean GC content and mean molecular size.

47. (Currently Amended) The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by mean GC content.

48. (Canceled)

49. (Previously Presented) The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by mean GC content and mean molecular size.

50. (Previously Presented) The method of claim 31, wherein nucleic acid molecules of the two or more subsets are prepared to differ by one or more features selected from mean GC content and mean molecular size using a preparation protocol that includes enriching a first subset or second subset of the two or more subsets of nucleic acid molecules with a set of probes that provide a difference in mean GC content or mean molecular size between nucleic acid molecules of the first subset and the second subset.

REMARKS

Claims 31-50 are currently pending. Claim 48 is canceled. Claims 33, 34, and 47 are currently amended for antecedent basis purposes. No new matter is added by these amendments. Accordingly, claims 31-47, 49, and 50 are now pending.

Reconsideration and allowance is respectfully requested in light of the abovementioned amendments and the following remarks.

Species election

The Office has requested Applicant to make a species election from the following groups:

- 1) Elect a single species regarding the “one or more features” that is/are differed between the two or more subsets of nucleic acid molecules (see claim 31, step a). If the elected single species is (or includes) “genomic regions,” a further ultimate sub-species regarding the “genomic regions” must also be elected (please refer to claims 33-35).
- 2) Elect a single species regarding how “conducting the enrichment reaction” is done by electing claim 41 or 42.

Applicant elects, **without traverse**, 1) “genomic regions” (claim 31) and “high GC content” (claim 33) and 2) “one or more hybridization reactions” (claim 41). Claims 31-47, 49, and 50 encompass the elected species.

Applicant notes that upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim, as provided by 37 C.F.R. 1.141.

Serial No. 14/810,337
Restriction Requirement Dated January 10, 2018
Reply To Restriction Requirement Filed February 23, 2018

CONCLUSION

Applicant respectfully submits that this paper fully addresses the Requirement for Restriction/Election mailed January 10, 2018, and requests entry of the abovementioned amendment prior to examination of the present application. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned at 650-849-3293.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 44168-702.401).

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

Dated: February 23, 2018

By: /Jacqueline Stroncek/
Jacqueline Stroncek, Reg. No. 72,619

650 Page Mill Road
Palo Alto, CA 94304-1050
(650)565-3808
Customer No. 021971



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/810,337	07/27/2015	Gabor T. Bartha	44168-702.401	1008
21971 7590 01/10/2018 WILSON, SONSINI, GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050			EXAMINER ZHANG, KAIJIANG	
			ART UNIT 1639	PAPER NUMBER
			NOTIFICATION DATE 01/10/2018	DELIVERY MODE 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):

patentdocket@wsgr.com

Office Action Summary	Application No. 14/810,337	Applicant(s) BARTHA ET AL.	
	Examiner Kaijiang Zhang	Art Unit 1639	AIA (First Inventor to File) Status No

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

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 10/6/2015.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 31-50 is/are pending in the application.
5a) Of the above claim(s) ____ is/are withdrawn from consideration.

6) ☐ Claim(s) ____ is/are allowed.

7) ☐ Claim(s) ____ is/are rejected.

8) ☐ Claim(s) ____ is/are objected to.

9) ☒ Claim(s) 31-50 are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some** c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
Paper No(s)/Mail Date ____.

3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.

4) ☐ Other: ____.

DETAILED ACTION

Election/Restrictions

Since this application contains claims directed to patentably distinct species, applicant is **required** to make the following species elections:

- 1) Elect a *single* species regarding the “one or more features” that is/are differed between the two or more subsets of nucleic acid molecules (see claim 31, step a). If the elected *single* species is (or includes) “genomic regions”, a further *ultimate* sub-species regarding the “genomic regions” **must** also be elected (please refer to claims 33-35).
- 2) Elect a *single* species regarding how “conducting the enrichment reaction” is done by electing claim 41 or 42.

For each of the species elections as discussed above, the species are independent or distinct because of their mutually exclusive characteristics. In addition, these species are not obvious variants of each other based on the current record.

Applicant is **required** under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is a search and/or examination burden for the patentably distinct species as set forth above because at least the following reason(s) apply:

- (a) the species require a different field of search (e.g., employing different search queries);

(b) the prior art applicable to one species would not likely be applicable to another species; and

(c) the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species or grouping of patentably indistinct species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species or grouping of patentably indistinct species.

Should applicant traverse on the ground that the species, or groupings of patentably indistinct species from which election is required, are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing them to be obvious variants or clearly admit on the record that this is the case. In either

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instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 or pre-AIA 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kaijiang Zhang whose telephone number is (571)272-5207. The examiner can normally be reached on Weekdays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit: 1639

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.

/Kaijiang Zhang/
Primary Examiner, Art Unit 1639

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in this application:

1.-30. (Canceled)

31. (New) A method for analyzing a nucleic acid sample, comprising:

- a. producing two or more subsets of nucleic acid molecules from a nucleic acid sample, wherein the two or more subsets differ by one or more features selected from genomic regions, mean GC content, mean molecular size, subset preparation method, or combination thereof;
- b. combining at least two of the two or more subsets of nucleic acid molecules to produce a first combined pool of nucleic acid molecules; and
- c. conducting one or more assays on the first combined pool of nucleic acid molecules, wherein at least one of the one or more assays comprises a sequencing reaction.

32. (New) The method of claim 31, wherein the nucleic acid molecules are DNA.

33. (New) The method of claim 31, wherein the genomic regions are selected from the group consisting of high GC content, low GC content, low complexity, low mappability, known single nucleotide variations (SNVs), known inDels, known alternative sequences, entire genome, entire exome, set of genes, set of regulatory elements, and methylation state.

34. (New) The method of claim 33, wherein the set of genes is selected from the group consisting of a set of genes with known Mendelian traits, set of genes with known disease traits, set of genes with known drug traits, and set of genes with known biomedically interpretable variants.

35. (New) The method of claim 33, wherein the known alternative sequences are selected from the group consisting of one or more small insertions, small deletions, structural variant junctions, variable length tandem repeats, and flanking sequences.

36. (New) The method of claim 31, wherein the two or more subsets of nucleic acid molecules differ by mean molecular size.

37. (New) The method of claim 31, further comprising producing a unified assessment of a genetic state of the nucleic acid sample at each locus addressed by the one or more assays.

38. (New) The method of claim 31, wherein conducting the one or more assays comprises conducting one or more amplification reactions.

39. (New) The method of claim 38, wherein conducting the one or more amplification reactions comprises polymerase chain reaction-based amplification.

40. (New) The method of claim 31, wherein producing the two or more subsets of nucleic acid molecules comprises conducting an enrichment reaction.

41. (New) The method of claim 40, wherein conducting the enrichment reaction comprises conducting one or more hybridization reactions.

42. (New) The method of claim 40, wherein conducting the enrichment reaction comprises differential amplification of at least two of the two or more subsets based on one or more genomic region features.

43. (New) The method of claim 31, wherein conducting one or more assays comprises conducting two or more assays, and wherein (c) further comprises combining results from the two or more assays.

44. (New) The method of claim 31, further comprising producing one or more biomedical reports after conducting the one or more assays, wherein the one or more biomedical reports comprise biomedical information of a subject of the nucleic acid sample.

45. (New) The method of claim 44, wherein the biomedical information of the subject predicts, prognoses, or diagnoses one or more biomedical features selected from the group consisting of disease state, genetic risk of a disease, reproductive risk, genetic risk to a fetus, risk of an adverse drug reaction, efficacy of a drug therapy, prediction of optimal drug dosage, transplant tolerance, and a combination thereof.

46. (New) The method of claim 31, wherein a first subset of nucleic acid molecules and a second subset of nucleic acid molecules of the two or more subsets of nucleic acid molecules are complementary in one or more features selected from the group consisting of genomic regions, mean GC content and mean molecular size.

47. (New) The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by mean GC.

48. (New) The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by mean molecular size.

49. (New) The method of claim 31, wherein nucleic acid molecules of the two or more subsets differ by mean GC content and mean molecular size.

50. (New) The method of claim 31, wherein nucleic acid molecules of the two or more subsets are prepared to differ by one or more features selected from mean GC content and mean molecular size using a preparation protocol that includes enriching a first subset or second subset of the two or more subsets of nucleic acid molecules with a set of probes that provide a difference in mean GC content or mean molecular size between nucleic acid molecules of the first subset and the second subset.