PTO/AIA/40 (04-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
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REQUEST FOR CORRECTION IN A PATENT APPLICATION RELATING TO INVENTORSHIP OR AN INVENTOR NAME, OR ORDER OF NAMES, OTHER THAN IN A REISSUE APPLICATION (37 CFR 1.48)

☐ 2. This request is to correct or update the name of the inventor or a joint inventor, or the order of names of joint inventors, in a **nonprovisional** application (**under 37 CFR 1.48(f)**) and includes:

☐ An application data sheet in accordance with 37 CFR 1.76(c) identifying the complete inventive entity, including the corrected or updated name of the inventor, or the new order of names shown with markings (*e.g.*, underlining for insertions, strikethrough for deletions). See the MPEP 601.05(a) for information about filing an ADS in an application filed on/after September 16, 2012. For information about filing a Supplemental ADS in an application filed before September 16, 2012, see MPEP 601.05(b).

☐ The processing fee set forth in 37 CFR 1.17(i). $ _____

For a provisional application:

☐ This request is to change or correct the inventorship, or correct or update the name of the inventor or a joint inventor, in a **provisional** application (**under 37 CFR 1.48(d)**) and includes:

☐ **Attached hereto** is a document that is signed by a party set forth in 37 CFR 1.33(b) and identifies each inventor by his or her legal name, in the preferred order. Note: the document may be an application data sheet in accordance with 37 CFR 1.76(c) that identifies the changes with markings (underlining for insertions, strikethrough for deletions).

☐ The processing fee set forth in 37 CFR 1.17(q). $ _____

Fee Payment Information:

☐ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 50-6075.

☒ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ Applicant*

☒ attorney or agent of record
Registration number 67162

☐ attorney or agent acting under 37 CFR 1.34
Registration number _____

Signature /Tianran Yan/

Typed or printed name Tianran Yan

Date 5-3-2021

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. *Juristic entities must be represented by a patent practitioner (See 37 CFR 1.31, applicable to any paper filed on or after September 16, 2012 that is presented on behalf of a juristic entity, regardless of application filing date). Submit multiple forms if more than one signature is required, see below**.

☒ ** Total of 1 forms are submitted.

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.

Electronic Patent Application Fee Transmittal

Application Number:	16934407
Filing Date:	21-Jul-2020
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Filer:	Anton John Bokal/Angela McGowan
Attorney Docket Number:	N.012.US.32

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
PROCESSING FEE, EXCEPT PROV. APPLS.	1830	1	140	140
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
CORRECTION OF INVENTORSHIP ON MERITS	1819	1	640	640
		Total in USD ($)		**780**

Electronic Acknowledgement Receipt

EFS ID:	42671224
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	07-MAY-2021
Filing Date:	21-JUL-2020
Time Stamp:	18:51:45
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$780
RAM confirmation Number	E202157I52081178
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	02_N012US32_ADS_SIGNED.pdf	1228619 9235597ba2402a6ea38427e7bfad39654eff68a6	no	16
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
2	Oath or Declaration filed	03_N012US32_Declaration_BANER_SIGNED.pdf	558042 f7152977952c91835a9d7aedf7af883051823957	no	1
Warnings:					
Information:					
3	Oath or Declaration filed	04_N012US32_Declaration_BANJEVIC_SIGNED.pdf	125897 f92da0d10dc9ff1c9e56beeadc070f3eeb21aa92	no	2
Warnings:					
Information:					
4	Oath or Declaration filed	05_N012US32_Declaration_DEMKO_SIGNED.pdf	120111 726f0e24f6ca089101b8b50da561537471f9af5e	no	2
Warnings:					
Information:					
5	Oath or Declaration filed	06_N012US32_Declaration_RYAN_SIGNED.pdf	45929 f183bebbcf5d3a5374d99a944185d86be44c21ce	no	1
Warnings:					
Information:					
6	Request under Rule 48 correcting inventorship	01_N012US32_Request_for_Correction_Relating_to_Inventorship_SIGNED.pdf	173584 6662109c92b9060dc9c08291c65d7fd9c5b27278	no	3
Warnings:					

Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	32391 3a0b10dc773a9e021b65a504a3d4c475e34b4d3a	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	2284573	

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

New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

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

Secrecy Order 37 CFR 5.2:

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

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Joshua~~ Matthew		~~BABIARZ~~ RABINOWITZ	

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

City	~~Castro Valley~~ San Francisco	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	201 Industrial Road
Address 2	Suite 410

City	San Carlos	State/Province	CA
Postal Code	94070	Country i	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Tudor~~ Matthew	~~Pompiliu~~ Micah	~~CONSTANTIN~~ HILL	

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

City	~~Berkeley~~ Belmont	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	201 Industrial Road
Address 2	Suite 410

City	San Carlos	State/Province	CA
Postal Code	94070	Country i	US

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Lane~~ Bernhard	~~A.~~	EUBANK ~~ZIMMERMANN~~	

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

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

City	~~San Carlos~~ Manteca	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	State/Province	CA
Postal Code	94070	Country i	US

Inventor 4 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~George~~ Johan		~~GEMELOS~~ BANER	

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

City	~~Portland~~ San Francisco	State/Province	~~OR~~ CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	State/Province	CA
Postal Code	94070	Country i	US

Inventor 5 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Matthew~~ George	~~Micah~~	~~Hilt~~ GEMELOS	

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

City	~~Belmont~~ Portland	State/Province	~~CA~~ OR	Country of Residence	US

Mailing Address of Inventor:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	State/Province	CA
Postal Code	94070	Country i	US

Inventor 6 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Huseyin~~ Milena	~~Eser~~	~~KIRKIZLAR~~ BANJEVIC	

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

City	~~Los Angeles~~ Los Altos Hills	State/Province	CA	Country of Residence	US

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Mailing Address of Inventor:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	**State/Province**	CA
Postal Code	94070	**Country**	US

Inventor 7 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Matthew~~ Allison		~~RABINOWITZ~~ RYAN	

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

City	~~San Francisco~~ Belmont	**State/Province**	CA	**Country of Residence**	US

Mailing Address of Inventor:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	**State/Province**	CA
Postal Code	94070	**Country**	US

Inventor 8 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Onur~~ Styrmir		~~SAKARYA~~ SIGURJONSSON	

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

City	~~Redwood City~~ San Jose	**State/Province**	CA	**Country of Residence**	US

Mailing Address of Inventor:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	**State/Province**	CA
Postal Code	94070	**Country**	US

Inventor 9 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Styrmir~~ Zachary		~~SIGURJONSSON~~ DEMKO	

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

City	~~San Jose~~ San Francisco	**State/Province**	CA	**Country of Residence**	US

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Mailing Address of Inventor:			
Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	State/Province	CA
Postal Code	94070	Country i	US

Inventor 10 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	~~Bernhard~~		~~ZIMMERMANN~~	

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

City	~~Manteca~~	State/Province	~~CA~~	Country of Residence	~~US~~

Mailing Address of Inventor:			
Address 1	~~201 Industrial Road~~		
Address 2	~~Suite 410~~		
City	~~San Carlos~~	State/Province	~~CA~~
Postal Code	~~94070~~	Country i	~~US~~

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

Correspondence Information:

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

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

Customer Number	110711		
Email Address	IP@Natera.com	Add Email	Remove Email

Application Information:

Title of the Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI		
Attorney Docket Number	N.012.US.32	Small Entity Status Claimed	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	58	Suggested Figure for Publication (if any)	

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Filing By Reference:

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

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

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

Publication Information:

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

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

Representative Information:

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

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	110711		

Domestic Benefit/National Stage Information:

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

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	16743724	2020-01-15

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16743724	Continuation of	16399268	2019-04-30	10538814	2020-01-21

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16399268	Continuation of	16140298	2018-09-24

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16140298	Continuation of	14918544	2015-10-20	10316362	2019-06-11

Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14918544	Continuation in part of	14877925	2015-10-07

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14918544	Continuation in part of	14692703	2015-04-21	10179937	2019-01-15

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14918544	Continuation in part of	14538982	2014-11-24	9677118	2017-06-13

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14918544	Claims benefit of provisional	62148173	2015-04-15

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14918544	Claims benefit of provisional	62147377	2015-04-14

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14918544	Claims benefit of provisional	62146188	2015-04-10

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14918544	Claims benefit of provisional	62066514	2014-10-21
Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14877925	Continuation in part of	14225356	2014-03-25
Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14877925	Continuation in part of	13780022	2013-02-28
Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14877925	Continuation of	13683604	2012-11-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	62148173	2015-04-15
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	62147377	2015-04-14
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	62146188	2015-04-10
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	62066514	2014-10-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	61994791	2014-05-16

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	61987407	2014-05-01
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14692703	Claims benefit of provisional	61982245	2014-04-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14538982	Claims benefit of provisional	62066514	2014-10-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14538982	Claims benefit of provisional	61994791	2014-05-16
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14538982	Claims benefit of provisional	61987407	2014-05-01
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14538982	Claims benefit of provisional	61982245	2014-04-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
14225356	Continuation of	PCTUS2012058578	2012-10-03
Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13780022	Continuation in part of	13683604	2012-11-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13780022	Continuation in part of	PCTUS201258578	2012-10-03

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13780022	Continuation in part of	13335043	2011-12-22	10113196	2018-10-30
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13780022	Continuation in part of	13300235	2011-11-18	10017812	2018-07-10
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13780022	Continuation in part of	13110685	2011-05-18	8825412	2014-09-02
Prior Application Status	Expired			Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
13780022	Claims benefit of provisional	61634431	2012-02-29		
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13683604	Continuation in part of	13300235	2011-11-18	10017812	2018-07-10
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13683604	Continuation in part of	13110685	2011-05-18	8825412	2014-09-02
Prior Application Status	Expired			Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
13683604	Claims benefit of provisional	61675020	2012-07-24		
Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
PCTUS201258578	Continuation in part of	13300235	2011-11-18	10017812	2018-07-10
Prior Application Status	Expired			Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
PCTUS201258578	Claims benefit of provisional	61683331	2012-08-15		
Prior Application Status	Expired			Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
PCTUS201258578	Claims benefit of provisional	61542508	2011-10-03		

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13335043	Continuation in part of	13300235	2011-11-18	10017812	2018-07-10
Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13335043	Continuation in part of	13110685	2011-05-18	8825412	2014-09-02
Prior Application Status	Expired				Remove
Application Number	Continuity Type	Prior Application Number			Filing or 371(c) Date (YYYY-MM-DD)
13335043	Claims benefit of provisional	61426208			2010-12-22
Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13300235	Continuation in part of	13110685	2011-05-18	8825412	2014-09-02
Prior Application Status	Expired				Remove
Application Number	Continuity Type	Prior Application Number			Filing or 371(c) Date (YYYY-MM-DD)
13300235	Claims benefit of provisional	61542508			2011-10-03
Prior Application Status	Expired				Remove
Application Number	Continuity Type	Prior Application Number			Filing or 371(c) Date (YYYY-MM-DD)
13300235	Claims benefit of provisional	61571248			2011-06-23
Prior Application Status	Expired				Remove
Application Number	Continuity Type	Prior Application Number			Filing or 371(c) Date (YYYY-MM-DD)
13110685	Claims benefit of provisional	61516996			2011-04-12
Prior Application Status	Expired				Remove
Application Number	Continuity Type	Prior Application Number			Filing or 371(c) Date (YYYY-MM-DD)
13110685	Claims benefit of provisional	61448547			2011-03-02
Prior Application Status	Expired				Remove
Application Number	Continuity Type	Prior Application Number			Filing or 371(c) Date (YYYY-MM-DD)
13110685	Claims benefit of provisional	61462972			2011-02-09

Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13110685	Claims benefit of provisional	61398159	2010-06-21
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13110685	Claims benefit of provisional	61395850	2010-05-18
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.			

Foreign Priority Information:

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

			Remove
Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)
Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.			

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

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

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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Authorization or Opt-Out of Authorization to Permit Access:

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

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

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

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

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

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

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

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

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

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

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

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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Applicant Information:

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

Applicant 1

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

Clear

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

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

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Natera, Inc.

Mailing Address Information For Applicant:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	**State/Province**	CA
Country US		Postal Code	94070
Phone Number	650-249-9091	Fax Number	
Email Address	IP@Natera.com		

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

Assignee Information including Non-Applicant Assignee Information:

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

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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

Assignee 1

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

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

Organization Name	Natera, Inc.

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1	201 Industrial Road		
Address 2	Suite 410		
City	San Carlos	**State/Province**	CA
Country i	US	Postal Code	94070
Phone Number	650-249-9091	Fax Number	
Email Address	IP@Natera.com		

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

Signature:

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

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

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

Signature	/Tianran Yan/			Date (YYYY-MM-DD)	2021-05-03
First Name	Tianran	Last Name	Yan	Registration Number	67162

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

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Supplemental Application Data Sheet 37 CFR 1.76	Attorney Docket Number	N.012.US.32
	Application Number	16/934,407
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

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

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

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

Title of Invention	METHODS FOR PREIMPLANTATION GENETIC DIAGNOSIS BY SEQUENCING

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [■] The attached application, or
- [ ] United States application or PCT international application number _____

  filed on _____.

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

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

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

WARNING:

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

LEGAL NAME OF INVENTOR

Inventor: Johan Baner Date (Optional): 1/8/2014

Signature: _____

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

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

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

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

Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 16/934,407 filed on Jul 21, 2020.

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

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

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

WARNING:

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LEGAL NAME OF INVENTOR

Inventor: Milena BANJEVIC Date (Optional) :

Signature:

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

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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.

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

Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 16/934,407

filed on Jul 21, 2020.

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

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

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

WARNING:

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

LEGAL NAME OF INVENTOR

Inventor: Zachary DEMKO Date (Optional) :_____

Signature: _____

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

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

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

Title of Invention	METHODS FOR PREIMPLANTATION GENETIC DIAGNOSIS BY SEQUENCING

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [x] The attached application, or
- [ ] United States application or PCT international application number _____ filed on _____.

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

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

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LEGAL NAME OF INVENTOR

Inventor: Allison Ryan Date (Optional): 1/7/14

Signature: _____

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

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16/934,407
	Filing Date	Jul 21, 2020
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

U.S. PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

U.S. PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns, Lines where Relevant Passages or Relevant Figures Appear	T[5]
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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.
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CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (1).

OR

☒ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (2).

☐ See attached certification statement.

☒ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ None

The submission of this Information Disclosure Statement does not constitute an admission that a search was made, does not constitute an admission that any information cited is prior art, and does not constitute an admission that no other or better art exists.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2021-04-16
Name/Print	Tianran Yan	Registration Number	67,162

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	Attorney Docket Number	N.012.US.32

U.S. PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16/934,407
	Filing Date	Jul 21, 2020
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☒ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (1).

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SIGNATURE

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Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2021-04-16
Name/Print	Tianran Yan	Registration Number	67,162

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
16/934,407	**04/16/2021 05:16:35 PM ET**	**N.012.US.32**

Title of Invention

METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2396	FILED BY	Angela McGowan
PATENT CENTER #	60178173	FILING DATE	07/21/2020
CUSTOMER #	110711	FIRST NAMED INVENTOR	Joshua BABIARZ
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Anton Bokal

Documents

TOTAL DOCUMENTS: 59

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
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Digest

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SCHUBERT_2004_1pg_NPL.pdf	B1DE0B2D035A4D6D966A0F09D250CC3E753F9CDA2B4BBC241F5253CA58337E7331521F88B148AA0A1D022EA5FE174D1EBF8CA88DD980409C4B42074656C80A46
SHENDURE_2007_p18_NPL.pdf	564638302CEF682FDAD97F688E9312B85954AD607BDEE96C70A6BD0F8D6B83EC53FC3091DF74F0556E41EAC4332AD9DB5D0EE6ED9B2FF76307EC38A8D11C6E51
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SHOKRALLA_2014_p892_NPL.pdf	5751DD0CCB3A819A9F27014C33F3132C1EFAFA735C9BC4E9468A51D3FAAF1340EFC7AFEC207D2543FD6E81C489E6A6EB82CCE7E1967C703F9F6A95117078D200
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STEWART_2018_p169_NPL.pdf	3A9EBEE21CE02AA848F21F1BD3A6B8BC91C559D1D0E9004BCBE13E223849F03F96DA9CB0F34F8BED157498CF447BAFA60DE18860796FEE93DFFB98E75E5E09CB
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WEI_2001_p336_NPL.pdf	B49C399C9CCDF80E28BA71DC090D735B3ADF84E103644CBBA50BFFB55CCC9396EE4B68B0A457D6207CA1DA159A2940C2

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WO2001057269A2.pdf	64A5207ACD77516ED197F238FB7BD70797A65423850E1C391D5BEE641664F6FD59062DA4AA14E4F8906FBD6DA20FCBDF3FB70873B25D4A628C8EBF0D61F20C47
WO2002070751A1.pdf	B906F2FC4E2A39867060A117792E541989CBF37954CBC7386254FA3C2441A567C7B6B976D4C9C4713598B05ABCFA7DA6B229C914E70580491EB035CDDA30D290
WO2007052006A1.pdf	7F82D2A83F9131D2C3F94C923AFDE97581BA69EBCA0FDE84725CDA057095476A2BF5F246829486A58D8C99E733C1EF5AD59A93B09D67E9C9F9D2224680CE452C
WO2008061213A2.pdf	3A6E0053A0B4A9B072AD21E09834BF099EB72EBAF7A8D8EA2AB77611F801B40AE1A85C86554A68B24392BB0792A32E3ACF99E4794AE6DA331DADE9873A9C8128
WO2013123220A1.pdf	7C03040E24E196DDF9C6575FB1B7B64C56D873A9E33527DB66C92D6587E9B61BD75FF874AE550E2A9EF148F2ED547C817356B36775F24F25242851E8930C90EE
WO2013138510A1.pdf	2ACC5C5FD0CE02BBD592F77AA55F9278C626DC5727E4FF13881C97E9B338CB533BB36C0420C19C9F3502F0E0FE48BF23B2F3AA61DAD89FAC9672A3AA294DE18E
WO2019118926A1.pdf	EE5768423C6A4CA98D2D2E3B1D712590E262B47F9A2B443F10B4F7A4B2F1E9B9168CE16BA4006661D8C53FD3B929D9E96A63DEFBFB951E95C42A2F57F8ECA5EA

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

New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

Electronic Acknowledgement Receipt

EFS ID:	42478968
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	16-APR-2021
Filing Date:	21-JUL-2020
Time Stamp:	17:17:51
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$260
RAM confirmation Number	E20214FH18121329
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Fee Worksheet (SB06)	fee-info.pdf	30600 ded1c8012f3c5bc6fa3b431da607424eb7942e82	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	30600		

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

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
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If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

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

NOTICE OF ALLOWANCE AND FEE(S) DUE

110711 7590 04/09/2021

Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

EXAMINER
MUMMERT, STEPHANIE KANE

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/09/2021

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32	2396

TITLE OF INVENTION: METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	07/09/2021

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.

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Exhibit 1003 Page 573

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)

110711 7590 04/09/2021

Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

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.
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32	2396

TITLE OF INVENTION: METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	07/09/2021

EXAMINER	ART UNIT	CLASS-SUBCLASS
MUMMERT, STEPHANIE KANE	1637	435-006120

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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Exhibit 1003 Page 574

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32	2396

110711 7590 04/09/2021

Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/09/2021

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.

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Exhibit 1003 Page 575

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.

Notice of Allowability	Application No. 16/934,407	Applicant(s) BABIARZ et al.	
	Examiner STEPHANIE K MUMMERT	Art Unit 1637	AIA (FITF) Status Yes

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

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

1. ☑ This communication is responsive to 3/3/21.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3. ☑ The allowed claim(s) is/are 1-15 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

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

   Certified copies:

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

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

   * Certified copies not received: _____ .

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

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

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

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

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 1/5/21 and 3/3/21.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☐ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☑ Other 2323 Form.

/STEPHANIE K MUMMERT/
Primary Examiner, Art Unit 1637

DETAILED ACTION

Notice of Pre-AIA or AIA Status

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

Applicant's response filed on March 3, 2021 is acknowledged and has been entered. Claims 1-15 are pending. Claim 1 is amended.

Claims 1-15 are discussed in this Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 5, 2021 and March 3, 2021 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Allowable Subject Matter

Claims 1-15 are allowed.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: The amendment to the claim requires the claimed method excludes samples of cell free nucleic acid obtained from a pregnant female and that the plural 25-2000 loci are associated with cancer. The amendment is sufficient to overcome the rejection of record and over any other references in the prior art which are focused on multiplex amplification and sequencing of 25 to 2000 SNP targets in a sample.

The prior art which is focused on combined amplification and sequencing of cell-free or circulating nucleic acid targets neither teach or suggest each of the claimed features of the method. Therefore, the claims are novel and non-obvious over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE KANE MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F 9:00-5:30.

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, Gary Benzion can be reached on 571-272-0782. 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 https://ppair-my.uspto.gov/pair/PrivatePair. Should you have questions on access to

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/STEPHANIE K MUMMERT/
Primary Examiner, Art Unit 1637

AFCP 2.0 Decision	Application No.	Applicant(s)	
	16/934,407	BABIARZ et al.	
	Examiner	Art Unit	AIA (FITF) Status
	STEPHANIE K MUMMERT	1637	Yes

This is in response to the After Final Consideration Pilot request filed 03 March 2021.

1. **Improper Request** – The AFCP 2.0 request is improper for the following reason(s) and the after final amendment submitted with the request will be treated under pre-pilot procedure.

   ☐ An AFCP 2.0 request form PTO/SB/434 (or equivalent document) was not submitted.

   ☐ A non-broadening amendment to at least one independent claim was not submitted.

   ☐ The request is not the first proper AFCP 2.0 request submitted in response to the most recent final rejection.

   ☐ Other: _____

2. **Proper Request**

   A. After final amendment submitted with the request will not be treated under AFCP 2.0.
   The after final amendment cannot be reviewed and a search conducted within the guidelines of the pilot program.

   ☐ The after final amendment will be treated under pre-pilot procedure.

   B. Updated search and/or completed additional consideration.
   The examiner performed an updated search and/or completed additional consideration of the after final amendment within the time authorized for the pilot program. The result(s) of the updated search and/or completed additional consideration are:

   ☑ 1. All of the rejections in the most recent final Office action are overcome and a Notice of Allowance is issued herewith.

   ☐ 2. The after final amendment would not overcome all of the rejections in the most recent final Office action . See attached interview summary for further details.

   ☐ 3. The after final amendment was reviewed, and it raises a new issue(s). See attached interview summary for further details.

   ☐ 4. The after final amendment raises new issues, but would overcome all of the rejections in the most recent final Office action. A decision on determining allowability could not be made within the guidelines of the pilot. See attached interview summary for further details, including any newly discovered prior art.

   ☐ 5. Other: _____

   Examiner Note: Please attach an interview summary when necessary as described above.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
inventor search - all names searched - PALM	08/31/2020	SKM
search Google/Scholar	09/03/2020	SKM
searched PE2E tool	09/03/2020	SKM
searched Google/Scholar	09/04/2020	SKM
searched using PE2E tool	01/01/2021	SKM
searched Google/Scholar	01/01/2021	SKM
considered 9/10/20 IDS and 12/2/20 IDS	01/01/2021	SKM
reviewed IDS	03/26/2021	SKM
search claims using PE2E search tool	03/26/2021	SKM

NeoGenomics
Exhibit 1003 Page 582

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
n/a	search claims using PE2E	03/26/2021	SKM

NeoGenomics
Exhibit 1003 Page 583

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

CPC						
Symbol					Type	Version
C12Q	/	1	/	6883	F	2013-01-01
C12Q	/	1	/	6811	I	2013-01-01
C12Q	/	1	/	6848	I	2013-01-01
C12Q	/	1	/	6809	I	2013-01-01
C12Q	/	1	/	6851	I	2013-01-01
C12Q	/	1	/	6844	I	2013-01-01
C12Q	/	1	/	6869	I	2013-01-01
C12Q	/	1	/	6855	I	2013-01-01
C12Q	/	1	/	6874	I	2013-01-01
C12Q	/	2600	/	156	A	2013-01-01

CPC Combination Sets								
Symbol					Type	Set	Ranking	Version
C12Q	/	1	/	6848	I	1	1	2013-01-01
C12Q	/	2527	/	107	I	1	2	2013-01-01
C12Q	/	2537	/	143	I	1	3	2013-01-01
C12Q	/	1	/	6809	I	2	1	2013-01-01
C12Q	/	2527	/	107	I	2	2	2013-01-01
C12Q	/	2537	/	143	I	2	3	2013-01-01
C12Q	/	1	/	6851	I	3	1	2013-01-01
C12Q	/	2531	/	113	I	3	2	2013-01-01
C12Q	/	2535	/	122	I	3	3	2013-01-01
C12Q	/	2537	/	143	I	3	4	2013-01-01
C12Q	/	2563	/	159	I	3	5	2013-01-01

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/STEPHANIE K MUMMERT/ Primary Examiner, Art Unit 1637	26 March 2021	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office

Part of Paper No.: 20210326

NeoGenomics
Exhibit 1003 Page 584

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

INTERNATIONAL CLASSIFICATION					
CLAIMED					
C12Q	/	1	/	68	
NON-CLAIMED					
	/		/		

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS
435	6.12

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					
435	91.2					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/STEPHANIE K MUMMERT/ Primary Examiner, Art Unit 1637	26 March 2021	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

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NeoGenomics
Exhibit 1003 Page 585

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

☑ Claims renumbered in the same order as presented by applicant ☐ CPA ☑ T.D. ☐ R.1.47

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/STEPHANIE K MUMMERT/ Primary Examiner, Art Unit 1637	26 March 2021	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

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NeoGenomics
Exhibit 1003 Page 586

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Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	16934407
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First Named Inventor	Joshua BABIARZ
Art Unit	1637
Examiner Name	Stephanie Kane Mummert
Attorney Docket Number	N.012.US.32

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5976790		1999-11-02	PINKEL, et al.	
	2	6335167	B1	2002-01-01	PINKEL, et al.	
	3	7790418	B2	2010-09-07	MAYER	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20040067493	A1	2004-04-08	MATSUZAKI, et al.	
	2	20040185495	A1	2004-09-23	SCHUELER, et al.	
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	Attorney Docket Number	N.012.US.32

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	14	20200407798	A1	2020-12-31	BABIARZ, et al.	

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	1	98/44151	WO		1998-10-08	GLAXO WELCOME PLC		
	2	00/18957	WO		2000-04-06			
	3	02/44411	WO	A1	2002-06-06	ROSETTA INPHARMATICS, INC.		
	4	03/000919	WO	A2	2003-01-03	UNIVERSITY OF GENEVA		
	5	03/020974	WO	A3	2003-03-13	THE CHINESE UNIVERSITY OF HONG KONG		
	6	2005/039389	WO	A3	2005-05-06	454 CORPORATION		
	7	2007/092473	WO	A2	2007-08-16	THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIO		
	8	2007/147073	WO	A2	2007-12-21	LIVING MICROSYSTEMS, INC.		
	9	2010/033639	WO	A2	2010-03-25	SEQUENOM, INC.		

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	10	2020/247263	WO	A1	2020-12-10	NATERA, INC.		

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	Filing Date	2020-07-21
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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	Examiner Name	Stephanie Kane Mummert
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EXAMINER SIGNATURE

Examiner Signature	/STEPHANIE K MUMMERT/	Date Considered	03/26/2021

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	Examiner Name	Stephanie Kane Mummert
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CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

✓ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2021-01-05
Name/Print	Tianran Yan	Registration Number	67162

This collection of information is required by 37 CFR 1.97 and 1.98. 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 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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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 inspections or an issued patent.

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

OK TO ENTER: /S.K.M/

03/26/2021

Atty. Dkt. No. N.012.US.32

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Joshua BABIARZ
Title:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
Application No.:	16/934,407
Filing Date:	7/21/2020
Examiner:	MUMMERT, STEPHANIE KANE
Art Unit:	1637
Conf. No.:	2396

AMENDMENT AND REPLY UNDER 37 CFR 1.116

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

Commissioner:

This communication is responsive to the final Office Action mailed January 6, 2021, concerning the above-referenced patent application. This response is submitted with a request under AFCP 2.0.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this document.

Remarks begin on page 4 of this document.

NeoGenomics
Exhibit 1003 Page 597

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.K.M/ 03/26/2021

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	16934407
Filing Date	2020-07-21
First Named Inventor	Joshua BABIARZ
Art Unit	1637
Examiner Name	Stephanie Kane Mummert
Attorney Docket Number	N.012.US.32

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	8703652	B2	2014-04-22	QUAKE, et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	1	CANICK, J. A., et al., "The impact of maternal plasma DNA fetal fraction on next generation sequencing tests for common fetal aneuploidies", Prenatal Diagnosis, 2013, 667-674	
	2	CHITTY, L. S., et al., "Noninvasive Prenatal Screening for Genetic Diseases Using Massively Parallel Sequencing of Maternal Plasma DNA", Cold Spring Harbor Perspectives in Medicine, 2015, 20 pages	
	3	DING, C. , et al., "MS analysis of single-nucleotide differences in circulating nucleic acids: Application to noninvasive prenatal diagnosis", PNAS, 20 JUL 2004, 10762-10767	
	4	LANDEGREN, U. , et al., "Padlock and proximity probes for in situ and array-based analyses: tools for the post-genomic era", Comparative and Functional Genomics, 2003, 525-530	
	5	MATSUZAKI, H. , et al., "Genotyping over 100,000 SNPs on a pair of oligonucleotide arrays", Nature Methods, NOV 2004, 109-111	
	6	MORRIS, J. K., et al., "Trends in Down's syndrome live births and antenatal diagnoses in England and Wales from 1989 to 2008: analysis of data from the National Down Syndrome Cytogenetic Register", BMJ Online, OCT 2009, 5 pages	
	7	NILSSON, M. , et al., "Padlock Probes: Circularizing Oligonucleotides for Localized DNA Detection", Science, 10 SEPT 1994, 2085-2088	
	8	PARAMESWARAN, P. , et al., "A pyrosequencing-tailored nucleotide barcode design unveils opportunities for large-scale sample multiplexing", Nucleic Acids Research, 11 OCT 2007, 9 pages	
	9	SYVANEN, A.C. , "Toward genome-wide SNP genotyping", Nature Genetics Supplement, JUN 2005, S5-S10	
	10	WU, T.L. , et al., "Cell-free DNA: measurement in various carcinomas and establishment of normal reference range", Clinica Chimica Acta, 2002, 77-87	
	11	YARON, Y. , "The implications of non-invasive prenatal testing failures: a review of an under-discussed phenomenon", Prenatal Diagnosis, 2016, 391-396	

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	Attorney Docket Number	N.012.US.32

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/STEPHANIE K MUMMERT/	Date Considered	03/26/2021

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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	Application Number	16934407
	Filing Date	2020-07-21
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Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2021-03-03
Name/Print	Tianran Yan	Registration Number	67162

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OK TO ENTER: /S.K.M/ 03/26/2021

Doc Code: A.NE.AFCP
Document Description: After Final Consideration Pilot Program Request

PTO/SB/434 (05-13)

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0

Practitioner Docket No.:	Application No.:	Filing Date:
N.012.US.32	16/934,407	7/21/2020
First Named Inventor:	**Title:**	
Joshua BABIARZ	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.

1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (*e.g.*, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c).
2. The above-identified application contains an outstanding final rejection.
3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect.
4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection.
5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response.
6. This certification and request is being filed electronically using the Office's electronic filing system (EFS-Web).
7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.]
8. By filing this certification and request, applicant acknowledges the following:
    - Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0.
    - The examiner will verify that the AFCP 2.0 submission is compliant, *i.e.*, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions:
        - The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, by mailing an advisory action.
        - If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview.
            - The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate.
            - If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116.

Signature	Date
/Tianran Yan/	3-3-2021
Name (Print/Typed) Tianran Yan	**Practitioner Registration No.** 67,162

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

☑ * Total of 1 forms are submitted.

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Bibliographic Data

Application No: 16/934,407

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☑ No ☐ Met After Allowance

Verified and Acknowledged: /STEPHANIE K MUMMERT/ (Examiner's Signature) | (Initials)

Title: METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
07/21/2020	435	1637	N.012.US.32
RULE			

APPLICANTS

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Onur SAKARYA, Redwood City, CA, UNITED STATES

Styrmir SIGURJONSSON, San Jose, CA, UNITED STATES

Bernhard ZIMMERMANN, Manteca, CA, UNITED STATES

CONTINUING DATA

This application is a CON of 16743724 01/15/2020 PAT 10731220

16743724 is a CON of 16399268 04/30/2019 PAT 10538814

16399268 is a CON of 16140298 09/24/2018

16140298 is a CON of 14918544 10/20/2015 PAT 10316362

14918544 is a CIP of 14877925 10/07/2015ABN

14918544 is a CIP of 14692703 04/21/2015 PAT 10179937

14692703 has PRO of 62148173 04/15/2015

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14692703 has PRO of 62146188 04/10/2015

14918544 has PRO of 62146188 04/10/2015

14918544 is a CIP of 14538982 11/24/2014 PAT 9677118

14692703 has PRO of 62066514 10/21/2014

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14538982 has PRO of 61982245 04/21/2014

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14877925 is a CIP of 14225356 03/25/2014ABN

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13780022 is a CIP of 13683604 11/21/2012ABN

13780022 is a CIP of PCT/US2012/058578 10/03/2012

14225356 is a CON of PCT/US2012/058578 10/03/2012

PCT/US2012/058578 has PRO of 61683331 08/15/2012

13683604 has PRO of 61675020 07/24/2012

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13780022 is a CIP of 13335043 12/22/2011 PAT 10113196

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PCT/US2012/058578 is a CIP of 13300235 11/18/2011 PAT 10017812

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13300235 has PRO of 61542508 10/03/2011

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13300235 has PRO of 61571248 06/23/2011

13300235 is a CIP of 13110685 05/18/2011 PAT 8825412

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13110685 has PRO of 61516996 04/12/2011

13110685 has PRO of 61448547 03/02/2011

13110685 has PRO of 61462972 02/09/2011

13335043 has PRO of 61426208 12/22/2010

13110685 has PRO of 61398159 06/21/2010

13110685 has PRO of 61395850 05/18/2010

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

07/27/2020

STATE OR COUNTRY

UNITED STATES

ADDRESS

Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070
UNITED STATES

FILING FEE RECEIVED

$7,860

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	92	(multiplex SAME tagg$3 SAME barcode SAME universal)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L2	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L3	0	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3 SAME "cell free")	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L4	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3),clm.	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L5	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail) SAME sequenc$3)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L6	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail)) AND sequenc$3	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L7	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequenc$3	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L8	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequencing	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L9	3	(multiplex SAME (universal NEAR tail)) AND tagged AND barcode AND sequencing	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/08/31 10:08 AM
L10	3711884	(universal adaptor) multiplex AND sequencing AND "cell free" AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 10:09 PM
L11	527	(universal SAME adaptor) AND multiplex AND sequencing AND "cell free" AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 10:09 PM

L12	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 10:09 PM
L13	0	(universal SAME adaptor) AND (multiplex NEAR sequencing NEAR "cell free") AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L14	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L15	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L16	12948	"L19" NOT L14	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L17	26547	"L15" NOT L14	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L18	0	L15 NOT L14	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L19	472	(universal SAME adaptor) AND (multiplex SAME sequencing) AND "cell free" AND tagging	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/02 11:09 PM
L20	580	(universal SAME adaptor) AND (sequencing) AND "cell free" AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/03 09:09 PM
L21	22	((universal SAME adaptor) SAME sequencing SAME "cell free") AND tagging AND barcode	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2020/09/03 09:09 PM
L22	9	("universal tail" SAME "SNP" AND "cell free")	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 04:01 PM
L23	0	("universal tail" SAME "SNP" SAME "cell free")	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 04:01 PM
L24	107	("universal tail" AND "SNP" AND "cell free")	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 04:01 PM

L25	107	("universal tail" AND "SNP" AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 04:01 PM
L26	67	(L25) AND @ay<2010	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 05:01 PM
L27	1	("universal tail" AND ("SNP" NEAR (plurality OR multiplex)) AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 05:01 PM
L28	197	(((tail OR adaptor) NEAR universal) AND ("SNP" NEAR (plurality OR multiplex)) AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 05:01 PM
L29	8	((((tail OR adaptor) NEAR universal) SAME ("SNP" NEAR (plurality OR multiplex))) AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 05:01 PM
L30	8	((((tail OR adaptor) NEAR universal) SAME (("SNP" OR polymorphism) NEAR (plurality OR multiplex))) AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 05:01 PM
L31	2	((tagged SAME (("SNP" OR polymorphism) NEAR (plurality OR multiplex))) AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 06:01 PM
L32	170	((tagged SAME ("SNP" OR polymorphism) SAME (plurality OR multiplex)) AND "cell free" AND sequencing)	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 06:01 PM
L33	16	(L32) AND @ay<2010	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 06:01 PM
L34	0	((tagged SAME ("SNP" OR polymorphism) SAME (plurality OR multiplex)) AND "cell free" AND sequencing).clm.	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 07:01 PM
L35	0	(((tail OR adaptor) NEAR universal) AND ("SNP" NEAR (plurality OR multiplex)) AND "cell free" AND sequencing).clm.	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/01/01 07:01 PM

L36	0	((tagged SAME ("SNP" OR polymorphism) SAME (plurality OR multiplex)) AND "cell free" AND sequencing).clm.	(US-PGPUB ; USPAT ; USOCR ; FIT (CN , FR , WO) ; FPRS ; EPO ; JPO ; DERWENT ; IBM_TDB)	OR	ON	ON	2021/03/26 07:03 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	16934407
Filing Date	2020-07-21
First Named Inventor	Joshua BABIARZ
Art Unit	1637
Examiner Name	Stephanie Kane Mummert
Attorney Docket Number	N.012.US.32

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	8703652	B2	2014-04-22	QUAKE, et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16934407
	Filing Date	2020-07-21
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

	1	CANICK, J. A., et al., "The impact of maternal plasma DNA fetal fraction on next generation sequencing tests for common fetal aneuploidies", Prenatal Diagnosis, 2013, 667-674	
	2	CHITTY, L. S., et al., "Noninvasive Prenatal Screening for Genetic Diseases Using Massively Parallel Sequencing of Maternal Plasma DNA", Cold Spring Harbor Perspectives in Medicine, 2015, 20 pages	
	3	DING, C. , et al., "MS analysis of single-nucleotide differences in circulating nucleic acids: Application to noninvasive prenatal diagnosis", PNAS, 20 JUL 2004, 10762-10767	
	4	LANDEGREN, U. , et al., "Padlock and proximity probes for in situ and array-based analyses: tools for the post-genomic era", Comparative and Functional Genomics, 2003, 525-530	
	5	MATSUZAKI, H. , et al., "Genotyping over 100,000 SNPs on a pair of oligonucleotide arrays", Nature Methods, NOV 2004, 109-111	
	6	MORRIS, J. K., et al., "Trends in Down's syndrome live births and antenatal diagnoses in England and Wales from 1989 to 2008: analysis of data from the National Down Syndrome Cytogenetic Register", BMJ Online, OCT 2009, 5 pages	
	7	NILSSON, M. , et al., "Padlock Probes: Circularizing Oligonucleotides for Localized DNA Detection", Science, 10 SEPT 1994, 2085-2088	
	8	PARAMESWARAN, P. , et al., "A pyrosequencing-tailored nucleotide barcode design unveils opportunities for large-scale sample multiplexing", Nucleic Acids Research, 11 OCT 2007, 9 pages	
	9	SYVANEN, A.C. , "Toward genome-wide SNP genotyping", Nature Genetics Supplement, JUN 2005, S5-S10	
	10	WU, T.L. , et al., "Cell-free DNA: measurement in various carcinomas and establishment of normal reference range", Clinica Chimica Acta, 2002, 77-87	
	11	YARON, Y. , "The implications of non-invasive prenatal testing failures: a review of an under-discussed phenomenon", Prenatal Diagnosis, 2016, 391-396	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	16934407
	Filing Date	2020-07-21
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16934407
	Filing Date	2020-07-21
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☑ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

✓ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2021-03-03
Name/Print	Tianran Yan	Registration Number	67162

This collection of information is required by 37 CFR 1.97 and 1.98. 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 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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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.

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Electronic Patent Application Fee Transmittal

Application Number:	16934407
Filing Date:	21-Jul-2020
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Filer:	Anton John Bokal/Angela McGowan
Attorney Docket Number:	N.012.US.32

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
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Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
		Total in USD ($)		**260**

Electronic Acknowledgement Receipt	
EFS ID:	42083019
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	03-MAR-2021
Filing Date:	21-JUL-2020
Time Stamp:	19:39:36
Application Type:	Utility under 35 USC 111(a)

Payment information:

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1	After Final Consideration Program Request	01_N012US32_AFCP_2_0_Request_SIGNED.pdf	227417 30ff621e264261480bec3ee73f6f1282439c806a	no	2
Warnings:					
Information:					
2		02_N012US32_Response_to_Final_Office_Action_dated_06JAN2021_SIGNED.pdf	49486 f933e0be5cce6794d3f817111c3aa84b5ef81cd4	yes	7
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Response After Final Action		1	1	
	Claims		2	3	
	Applicant Arguments/Remarks Made in an Amendment		4	7	
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	03_N012US32_SB08_SIGNED.pdf	1036086 e43420c8474256250414422ec59c4d99878e0e2d	no	5
Warnings:					
Information:					
4	Non Patent Literature	CANICK_2013_p667_NPL.pdf	1050983 aff5a4b4488185ff5fed9b696cc41c50bcd55c40	no	8
Warnings:					
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5	Non Patent Literature	CHITTY_2015_20pgs_NPL.pdf	785852 609e0cada692b50cef6274879629e7243fc60ea8	no	20

Warnings:					
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6	Non Patent Literature	LANDEGREN_2003_p525_NPL.pdf	138810 3e174f70cbf185edaf84196fcd1c2e8c38cae75d	no	6
Warnings:					
Information:					
7	Non Patent Literature	MATSUZAKI_2004_p109_NPL.pdf	333716 db9365917c198a2ecd6322b0d6b9dfabf5b99998	no	3
Warnings:					
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8	Non Patent Literature	MORRIS_2009_5pgs_NPL.pdf	110576 77f1d9fd49f1e981088212ecc6a70b462ff376fc	no	5
Warnings:					
Information:					
9	Non Patent Literature	NILSSON_1994_p2085_NPL.pdf	3126445 f2b00ba996b0f158327caf73fc34633ed097aa70	no	4
Warnings:					
Information:					
10	Non Patent Literature	PARAMESWARAN_2007_9pgs_NPL.pdf	1432604 5747ff9b9ec27c4d90defa37526a80447df41660	no	9
Warnings:					
Information:					
11	Non Patent Literature	SYVANEN_2005_p55_NPL.pdf	1063631 4e307462d22a8ecddc2db44dfb6c4423339d72b6	no	6
Warnings:					
Information:					
12	Non Patent Literature	WU_2002_p77_NPL.pdf	707422 a8339926571b8b13746fb036e9e201fea3b9a8b0	no	11
Warnings:					
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13	Non Patent Literature	YARON_2016_P391_NPL.pdf	900436 2f41f2231fe1f7c140b327f5f86aac2430f6661e	no	6
Warnings:					
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14	Non Patent Literature	DING_2004_p10762_NPL.pdf	336755 5f24dd961846a285e6090a9e8225fe2adb161b93	no	7
Warnings:					
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15	Fee Worksheet (SB06)	fee-info.pdf	30600 1c130b8e4ca193de67e00dcb80bd44797e03c639	no	2
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<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: A.NE.AFCP
Document Description: After Final Consideration Pilot Program Request

PTO/SB/434 (05-13)

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0

Practitioner Docket No.:	Application No.:	Filing Date:
N.012.US.32	16/934,407	7/21/2020
First Named Inventor:	**Title:**	
Joshua BABIARZ	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI	

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.

1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (*e.g.*, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c).
2. The above-identified application contains an outstanding final rejection.
3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect.
4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection.
5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response.
6. This certification and request is being filed electronically using the Office's electronic filing system (EFS-Web).
7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.]
8. By filing this certification and request, applicant acknowledges the following:
    - Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0.
    - The examiner will verify that the AFCP 2.0 submission is compliant, *i.e.*, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions:
        - The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, by mailing an advisory action.
        - If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview.
            - The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate.
            - If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116.

Signature	Date
/Tianran Yan/	3-3-2021
Name (Print/Typed) Tianran Yan	Practitioner Registration No. 67,162

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

[✓] * Total of 1 forms are submitted.

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Joshua BABIARZ
Title:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
Application No.:	16/934,407
Filing Date:	7/21/2020
Examiner:	MUMMERT, STEPHANIE KANE
Art Unit:	1637
Conf. No.:	2396

AMENDMENT AND REPLY UNDER 37 CFR 1.116

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

Commissioner:

This communication is responsive to the final Office Action mailed January 6, 2021, concerning the above-referenced patent application. This response is submitted with a request under AFCP 2.0.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this document.

Remarks begin on page 4 of this document.

Amendments to the Claims:

This listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

1. (**Currently Amended**) A method for amplifying and sequencing DNA, comprising:

tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject who is not a pregnant women;

amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplification steps comprises targeted amplification of a plurality of single nucleotide polymorphism (SNP) loci in a single reaction volume, wherein one of the amplifying steps introduces a barcode and one or more sequencing tags; and

sequencing the plurality of SNP loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of SNP loci comprises 25-2,000 loci associated with cancer.

2. (Previously Presented) The method of claim 1, wherein tagging the cell free DNA comprises ligating the one or more universal tail adaptors to the cell free DNA.

3. (Original) The method of claim 2, wherein the one or more universal tail adaptors each comprise a first strand and a second strand, wherein a first end of each of the universal tail adaptors comprises a double-stranded section comprising the 5' portion of the first strand and the 3' portion of the second strand, wherein the first end is ligated to the cell free DNA.

4. (Previously Presented) The method of claim 3, wherein amplifying the tagged products comprises a first amplifying step and a second amplifying step, wherein the first amplifying step comprises using a first target-specific primer that specifically anneals to a target sequence and a first adaptor primer having a nucleotide sequence identical to a first portion of the first strand to generate a first amplification product.

5. (Previously Presented) The method of claim 4, wherein the second amplifying step comprises using a second target-specific primer that specifically anneals to the first amplification product and a second adaptor primer having a nucleotide sequence identical to a second portion of the first strand to generate the final amplification product.

6. (Original) The method of claim 5, wherein the second adaptor primer is nested relative to the first adaptor primer.

7. (Original) The method of claim 6, wherein the second target-specific primer comprises an index tag.

8. (Previously Presented) The method of claim 7, wherein the second amplifying step further comprises using an index primer comprising a sequence complementary to the index tag.

9. (Original) The method of claim 8, wherein the index primer comprises the barcode and a first sequencing tag.

10. (Original) The method of claim 1, wherein the one or more universal tail adaptors comprise a second barcode.

11. (Original) The method of claim 1, wherein the one or more universal tail adaptors comprise a second sequencing tag.

12. (Original) The method of claim 1, wherein the one or more universal tail adaptors comprise a first universal tail adaptor and a second universal tail adaptor.

13. (Previously Presented) The method of claim 12, wherein tagging the cell free DNA comprises amplifying the cell free DNA with a first primer comprising the first universal tail adaptor and a second primer comprising the second universal tail adaptor.

14. (Previously Presented) The method of claim 12, wherein amplifying the tagged products comprises a single amplifying step.

15. (Previously Presented) The method of claim 14, wherein amplifying the tagged products comprises using a third primer and a fourth primer, wherein the third primer comprises a first sequencing tag and wherein the fourth primer comprises a second sequencing tag.

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

Status of Claims

Claims 1-15 were pending in the subject case. With this submission, claim 1 is amended to more clearly and particularly describe the claimed invention. Support for the amendments to claim 1 can be found in the published application at paragraphs 0041, 0082, 0388, 0397, 0450, 0956, and Examples 26-29. *See also* M.P.E.P. §2173.05(i) ("If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims."), citing *In re Johnson,* 558 F.2d 1008, 1019 (C.C.P.A. 1977) ("[the] specification, having described the whole, necessarily described the part remaining.").

No new matter has been introduced. Upon entry of the foregoing amendments, claims 1-15 will remain pending in this application.

AFCP 2.0 and Request for Interview

Applicant requests consideration of this response under AFCP 2.0. A transmittal form that identifies this response as an AFCP 2.0 submission and requests consideration under AFCP 2.0 is submitted herewith. The foregoing claim amendments include an amendment to at least one independent claim that does not broaden the scope of the independent claim in any aspect. Applicant is willing and available to participate in any interview initiated by the Examiner concerning the response. Thus, the requirements for AFCP 2.0 are believed to be satisfied.

Applicant also respectfully requests an interview with the Examiner if any issue remains after consideration and entry of this paper, prior to issuance of any paper other than a Notice of Allowance.

Claim Rejection under 35 U.S.C. 102

Claims 1-5 and 10-15 are rejected under 35 U.S.C. 102 for allegedly being anticipated by US 8,318,430 ("Chuu"). Applicant respectfully traverses this rejection.

For the sole purpose of expediting prosecution and without acquiescing to the rejections, Applicant has amended claim 1 to recite:

> 1. A method for amplifying and sequencing DNA, comprising:
> tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject who is not a pregnant women;
> amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplification steps comprises targeted amplification of a plurality of single nucleotide polymorphism (SNP) loci in a single reaction volume, wherein one of the amplifying steps introduces a barcode and one or more sequencing tags; and
> sequencing the plurality of SNP loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of SNP loci comprises 25-2,000 loci associated with cancer.

Chuu is directed to analysis of maternal plasma samples for detection of fetal aneuploidy, but fails to teach or suggest anything about amplifying and sequencing cell-free DNA isolated from a blood sample collected from a subject who is not a pregnant women. Moreover, Chuu fails to teach or suggest targeted amplification of 25-2,000 target loci associated with cancer in a single reaction volume.

Accordingly, so far as Chuu fails to disclose each and every limitation of the claimed invention, the anticipation rejection cannot be sustained. Applicant therefore respectfully requests reconsideration and withdrawal of the subject rejection.

Claim Rejection under 35 U.S.C. 103

Claim 6 is rejected under 35 U.S.C. 103 for allegedly being unpatentable over Chuu in view of Wright et al. 2009. Claims 7-9 are rejected under 35 U.S.C. 103 for allegedly being unpatentable over Chuu in view of Cronn et al. 2008. Applicant respectfully traverses these rejections.

The deficiencies of Chuu are explained in the foregoing section. Wright is merely cited in the Office Action for disclosing nested PCR, and the disclosure of Wright is limited to analysis of maternal plasma samples for detection of fetal abnormalities. Cronn is merely cited in the Office Action for disclosing index tags, and the disclosure of Cronn is limited to sequencing of plant chloroplast genome. Neither Wright nor Cronn could cure the aforementioned deficiencies of Chuu.

For at least these reasons, a person having ordinary skill in the art would not have found the amended claims obvious over the cited references. Applicant therefore respectfully requests reconsideration and withdrawal of the subject rejection.

Concluding Remarks

Applicant believes that the application is in condition for allowance. Favorable consideration is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-6075. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account No. 50-6075.

Respectfully submitted,

Date 3-3-3021

By /Tianran Yan/

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Attorney for Applicant

NeoGenomics
Exhibit 1003 Page 631

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32	2396

110711 7590 01/06/2021

Natera, Inc.
201 Industrial Road
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San Carlos, CA 94070

EXAMINER	
MUMMERT, STEPHANIE KANE	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
01/06/2021	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):

IP@natera.com

Office Action Summary	Application No. 16/934,407	Applicant(s) BABIARZ et al.	
	Examiner STEPHANIE K MUMMERT	Art Unit 1637	AIA (FITF) Status Yes

-- 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 12/2/20.

☐ 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) 1-15 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) 1-15 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 _____ 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 9/10/20;12/2/20.

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

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

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

Applicant's response filed on December 2, 2020 is acknowledged and has been entered. Claims 1-15 are pending. Claims 1-2, 4-5, 8, 13-15 are amended.

Claims 1-15 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This rejection is made FINAL.

Sequence Compliance - Notice to Comply - Withdrawn

This objection is overcome in view of the amendment to Figure 12 to include SEQ IDNOs.

Terminal Disclaimer

The terminal disclaimer filed on December 2, 2020 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 10,731,220, 10,538,814 and 10,557,172 have been reviewed and is accepted. The terminal disclaimer has been recorded.

New Grounds of Rejection As Necessitated by Amendment

Information Disclosure Statement

The information disclosure statement (IDS) submitted on September 10, 2020 and December 2, 2020 was filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 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 –
>
> (a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.
>
> (a)(2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

Claim(s) 1-5 and 10-15 is/are rejected under 35 U.S.C. 102(a)(1) as being anticipated by Chuu et al. (US Patent 8,318,430; November 2012).

With regard to claim 1, Chuu teaches a method for amplifying and sequencing DNA, comprising:

tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject (col. 1-4, where cell free DNA is amplified);

amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplifying steps introduces a barcode and one or more sequencing

tags (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught); and

sequencing a plurality of loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of loci comprises 25-2,000 loci (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 2, Chuu teaches a method of claim 1, wherein the tagging the cell free DNA comprises ligating the one or more universal tail adaptors to the cell free DNA (col. 1-4, where cell free DNA is amplified).

With regard to claim 3, Chuu teaches a method of claim 2, wherein the one or more universal tail adaptors each comprise a first strand and a second strand, wherein a first end of each of the universal tail adaptors comprises a double-stranded section comprising the 5' portion of the first strand and the 3' portion of the second strand, wherein the first end is ligated to the cell free DNA (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 4, Chuu teaches a method of claim 3, wherein the amplifying the tagged products comprises a first amplifying and a second amplifying, wherein the first amplifying comprises a first target- specific primer that specifically anneals to a target sequence and a first adaptor primer having a nucleotide sequence identical to a first portion of the first strand to generate a first amplification product (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 5, Fan teaches a method of claim 4, wherein the second amplifying comprises a second target- specific primer that specifically anneals to the first amplification

product and a second adaptor primer having a nucleotide sequence identical to a second portion of the first strand to generate the final amplification product (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 10, Chuu teaches a method of claim 1, wherein the one or more universal tail adaptors comprise a second barcode (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 11, Chuu teaches a method of claim 1, wherein the one or more universal tail adaptors comprise a second sequencing tag (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 12, Chuu teaches a method of claim 1, wherein the one or more universal tail adaptors comprise a first universal tail adaptor and a second universal tail adaptor(see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 13, Chuu teaches a method of claim 12, wherein the tagging the cell free DNA comprises amplifying the cell free DNA with a first primer comprising the first universal tail adaptor and a second primer comprising the second universal tail adaptor (see Figure 26, for example, where the primers with universal adaptors are added; see Example 4, where multiple PCR rounds are taught).

With regard to claim 14, Fan teaches a method of claim 12, wherein the amplifying the tagged products comprises a single amplifying (paragraph 76, where samples are amplified).

With regard to claim 15, Chuu teaches a method of claim 14, wherein the amplifying the tagged products comprises a third primer and a fourth primer, wherein the third primer comprises a first sequencing tag and wherein the fourth primer comprises a second sequencing tag (paragraph 76, where samples are amplified).

Claim Rejections - 35 USC § 103

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

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

This application currently names joint inventors. In considering patentability of the claims the examiner presumes that the subject matter of the various claims was commonly owned as of the effective filing date of the claimed invention(s) absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and effective filing dates of each claim that was not commonly owned as of the effective filing date of the later invention in order for the examiner to consider the applicability of 35 U.S.C. 102(b)(2)(C) for any potential 35 U.S.C. 102(a)(2) prior art against the later invention.

Claim 6 is/are rejected under 35 U.S.C. 103 as being unpatentable over Chuu et al. (US Patent 8,318,430; November 2012) as applied over claims 1-5 and 10-15 above and further in view of Wright et al. (Hum Reprod Updt, 2009, 15(1):139-151).

With regard to claim 6, Wright teaches a method of claim 5, wherein the second adaptor primer is nested relative to the first adaptor primer (Table 1, where nested amplification occurs, p. 141, col. 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Chuu to include a nested primer as taught by Wright to arrive at the claimed invention with a reasonable expectation for success. Wright teaches "A number of different types of PCR have been explored, of which the most popular is real-time quantitative PCR (Traeger-Synodinos, 2006), as it combines high sensitivity with a closed detection system, thereby minimiz-ing the risk of contamination. Nested PCR (Al-Yatama et al., 2001) and pyrophosphorolysis-activated polymerization PCR (Boon et al., 2007) have also been investigated in this context. Higher precision of measure-ment may be possible through the application of digital PCR, which allows the exact number of original template DNA molecules to be counted (Fan and Quake, 2007; Lo et al., 2007a)" (p. 141, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have adjusted the teachings of Chuu to include a nested primer as taught by Wright to arrive at the claimed invention with a reasonable expectation for success.

Claim 7-9 is/are rejected under 35 U.S.C. 103 as being unpatentable over Chuu et al. (US Patent 8,318,430; November 2012) as applied over claims 1-5 and 10-15 above and further in view of Cronn et al. (Nucleic Acids Research 2008, 36(19):e122).

With regard to claim 7, Cronn teaches a method of claim 6, wherein the second target-specific primer comprises an index tag (Abstract, p. 2 and p. 6).

With regard to claim 8, Cronn teaches a method of claim 7, wherein the second amplifying further comprises an index primer comprising a sequence complementary to the index tag (Abstract, p. 2 and p. 6).

With regard to claim 9, Cronn teaches a method of claim 8, wherein the index primer comprises the barcode and a first sequencing tag (Abstract, p. 2 and p. 6).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Chuu to include the index tag as taught by Cronn to arrive at the claimed invention with a reasonable expectation for success. Cronn teaches "To gain maximal access to the historical record contained within chloroplast genomes, we have adapted multiplex sequencing-by-synthesis (MSBS) to simultaneously sequence multiple genomes using the Illumina Genome Analyzer. We PCR-amplified ~120 kb plas-tomes from eight species (seven Pinus, one Picea)in 35 reactions. Pooled products were ligated to mod-ified adapters that included 3 bp indexing tags and samples were multiplexed at four genomes per lane. Tagged microreads were assembled by de novo and reference-guided assembly methods, using pre-viously published Pinus plastomes as surrogate references" (Abstract). Therefore, one of ordinary skill in the art at the time the invention was made would have adjusted the teachings of Chuu to include the index tag as taught by Cronn to arrive at the claimed invention with a reasonable expectation for success.

Response to Arguments

Applicant's arguments with respect to claim(s) 1-15 have been considered but are moot because the new ground of rejection does not rely on any reference applied in the prior rejection of record for any teaching or matter specifically challenged in the argument.

Conclusion

No claims are allowed. All claims stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE KANE MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F 9:00-5:30.

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, Gary Benzion can be reached on 571-272-0782. 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 https://ppair-my.uspto.gov/pair/PrivatePair. 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.

/STEPHANIE K MUMMERT/
Primary Examiner, Art Unit 1637

SKM

Notice of References Cited	Application/Control No. 16/934,407	Applicant(s)/Patent Under Reexamination BABIARZ et al.	
	Examiner STEPHANIE K MUMMERT	Art Unit 1637	Page 1 of 1

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	B					
	C					
	D					
	E					
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	H					
	I					
	J					
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	N					
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NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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	V	
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	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
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US Classification - Searched*			
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Search Notes		
Search Notes	Date	Examiner
inventor search - all names searched - PALM	08/31/2020	SKM
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searched PE2E tool	09/03/2020	SKM
searched Google/Scholar	09/04/2020	SKM
searched using PE2E tool	01/01/2021	SKM
searched Google/Scholar	01/01/2021	SKM
considered 9/10/20 IDS and 12/2/20 IDS	01/01/2021	SKM

NeoGenomics
Exhibit 1003 Page 644

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	Examiner	Art Unit
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Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns, Lines where Relevant Passages or Relevant Figures Appear	T[5]
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EXAMINER SIGNATURE

Examiner Signature	/STEPHANIE K MUMMERT/	Date Considered	01/01/2021

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Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (1).

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☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (2).

☐ See attached certification statement.

☒ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

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Name/Print	Tianran Yan	Registration Number	67,162

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	Attorney Docket Number	N.012.US.32

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EXAMINER SIGNATURE

Examiner Signature	/STEPHANIE K MUMMERT/	Date Considered	01/01/2021

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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[4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making

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reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (2).

☐ See attached certification statement.

☐ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2020-09-10
Name/Print	Tianran Yan	Registration Number	67,162

This collection of information is required by 37 CFR 1.97 and 1.98. 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 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	92	(multiplex SAME tagg$3 SAME barcode SAME universal)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:05 AM
L2	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:07 AM
L3	0	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3 SAME "cell free")	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:08 AM
L4	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3),clm.	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:08 AM
L5	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail) SAME sequenc$3)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:09 AM
L6	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail)) AND sequenc$3	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:09 AM
L7	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequenc$3	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:11 AM
L8	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequencing	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:11 AM
L9	3	(multiplex SAME (universal NEAR tail)) AND tagged AND barcode AND sequencing	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:12 AM
L10	3711884	(universal adaptor) multiplex AND sequencing AND "cell	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO;	OR	ON	ON	2020/09/02 10:54 PM

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Exhibit 1003 Page 754

		free" AND tagging AND barcode	DERWENT; IBM_TDB				
L11	527	(universal SAME adaptor) AND multiplex AND sequencing AND "cell free" AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 10:56 PM
L12	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 10:57 PM
L13	0	(universal SAME adaptor) AND (multiplex NEAR sequencing NEAR "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:02 PM
L14	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:02 PM
L15	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:11 PM
L16	12948	"L19" NOT L14	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:11 PM
L17	26547	"L15" NOT L14	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:11 PM
L18	0	L15 NOT L14	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:12 PM
L19	472	(universal SAME adaptor) AND (multiplex SAME sequencing) AND "cell free" AND tagging	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:12 PM
L20	580	(universal SAME adaptor) AND (sequencing) AND "cell free" AND tagging	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO;	OR	ON	ON	2020/09/03 09:11 PM

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Exhibit 1003 Page 755

		AND barcode	DERWENT; IBM_TDB				
L21	22	((universal SAME adaptor) SAME sequencing SAME "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/03 09:11 PM
L22	9	("universal tail" SAME "SNP" AND "cell free")	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 04:56 PM
L23	0	("universal tail" SAME "SNP" SAME "cell free")	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 04:56 PM
L24	107	("universal tail" AND "SNP" AND "cell free")	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 04:56 PM
L25	107	("universal tail" AND "SNP" AND "cell free" AND sequencing)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 04:57 PM
L26	67	(L25) AND @ay<2010	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 05:04 PM
L27	1	("universal tail" AND ("SNP" NEAR (plurality OR multiplex)) AND "cell free" AND sequencing)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 05:54 PM
L28	197	(((tail OR adaptor) NEAR universal) AND ("SNP" NEAR (plurality OR multiplex)) AND "cell free" AND sequencing)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 05:55 PM
L29	8	((((tail OR adaptor) NEAR universal) SAME ("SNP" NEAR (plurality OR multiplex))) AND "cell free" AND sequencing)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 05:56 PM
L30	8	((((tail OR adaptor) NEAR universal) SAME (("SNP" OR polymorphism) NEAR (plurality OR multiplex))) AND "cell free" AND	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 05:57 PM

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		sequencing)					
L31	2	((tagged SAME (("SNP" OR polymorphism) NEAR (plurality OR multiplex))) AND "cell free" AND sequencing)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 06:52 PM
L32	170	((tagged SAME ("SNP" OR polymorphism) SAME (plurality OR multiplex)) AND "cell free" AND sequencing)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 06:53 PM
L33	16	(L32) AND @ay<2010	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 06:53 PM
L34	0	((tagged SAME ("SNP" OR polymorphism) SAME (plurality OR multiplex)) AND "cell free" AND sequencing).clm.	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 07:07 PM
L35	0	(((tail OR adaptor) NEAR universal) AND ("SNP" NEAR (plurality OR multiplex)) AND "cell free" AND sequencing).clm.	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2021/01/01 07:07 PM

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Application Number	16934407
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First Named Inventor	Joshua BABIARZ
Art Unit	1637
Examiner Name	Stephanie Kane Mummert
Attorney Docket Number	N.012.US.32

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	1	5976790		1999-11-02	PINKEL, et al.	
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✓ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

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A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2021-01-05
Name/Print	Tianran Yan	Registration Number	67162

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

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

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

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Electronic Patent Application Fee Transmittal

Application Number:	16934407
Filing Date:	21-Jul-2020
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Filer:	Anton John Bokal/Angela McGowan
Attorney Docket Number:	N.012.US.32

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
		Total in USD ($)		**260**

Electronic Acknowledgement Receipt

EFS ID:	41564087
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	05-JAN-2021
Filing Date:	21-JUL-2020
Time Stamp:	20:25:42
Application Type:	Utility under 35 USC 111(a)

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RAM confirmation Number	E202115K26103465
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	01_N012US32_SB08_SIGNED.pdf	1039914 0ad4f0ba9b74a6883b9d9b2a4b050c980cf823c4	no	10
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3	Foreign Reference	WO2000018957A1.pdf	4474552 ae9cecaabcaebaba2c647c958ce326c62c3791e1	no	104
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12	Non Patent Literature	AVGIDOU_2005_p1761_NPL.pdf	1999124 1a1601f6066f260c1406df2f0d7900bd1beb175d	no	13
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13	Non Patent Literature	BARSKI_2007_p823_NPL.pdf	4558898 a4a16775a8deff579e192351e22efbe1a3808b20	no	16
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15	Non Patent Literature	BAXTER_2000_p195_NPL.pdf	611094 0a0659d7c2009f3c61ff8a594a94c9f0d2c0fee6	no	9
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19	Non Patent Literature	FALCON_2005_p151_NPL.pdf	1422394 0ca2af194b4d559849d873d5e6aeae65c1c2d3df	no	5
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22	Non Patent Literature	ILLUMINA_AutomatedGoldenGateGenotypingBeadstation_2004_NPL.pdf	1664121 a6d2eb0d43721985b92569ed6ad8a519f92dbeb4	no	2
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24	Non Patent Literature	ILLUMINA_2004_2pgs_NPL.pdf	100441 29a3dc73da312785c160f0f7f7b1bc4dbe04b411	no	2
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31	Non Patent Literature	JETT_2010_11pgs_NPL.pdf	532514 1b38e3e9c58ed25b469ea637e80d17b1f15830d7	no	11
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33	Non Patent Literature	KAMEL_2000_p110_NPL.pdf	3156044 ef7e9e5cb6b5e52049bc665ed5fc9f6fccda37ea	no	6
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35	Non Patent Literature	LAPIERRE_2000_p531_NPL.pdf	3921310 63896196878dbf4fb578e3217391eb6e30b71d02	no	10
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38	Non Patent Literature	LO_FetalDNAinMaternalPlasma_2000_p1903_NPL.pdf	5716079 c1075d6c514176dc26e4dd6647d461eaa7b1486b	no	4
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40	Non Patent Literature	NAGALLA_2007_p1245_NPL.pdf	7733226 738c485efed6ff20829cd6533b96b6048545e385	no	13
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44	Non Patent Literature	PAUNIO_1996_p1382_NPL.pdf	13099854 d2df87152672d64d5ec7c1af95803a76a2b4cb40	no	9
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45	Non Patent Literature	PHILIP_2004_p1164_NPL.pdf	12176330 64a8c5be6f56d6ac9f3f3fb77e925ecdf08a2975	no	10
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46	Non Patent Literature	ROBERTSON_2007_p651_NPL.pdf	452260 9ef8a0788c3642b3049c00fa2b4355fff89696802	no	8
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47	Non Patent Literature	ROMAN_1999_p236_NPL.pdf	2626739 86a8672c46a877ba0edfa431d5418e9b89492a87	no	3
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48	Non Patent Literature	RUANO_1990_p6296_NPL.pdf	1396279 0f10f23b1812c974284c2d887e3add9de54c038a	no	5
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49	Non Patent Literature	SAMURA_2001_p1622_NPL.pdf	313880 b311a9cac1c823a0b940d8bdbb8c83ad2f3b116a	no	5
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50	Non Patent Literature	SEPPO_2008_p815_NPL.pdf	4080483 69d5aed92a7f12c5dd6b947631cb9d72d65e0d8d	no	7
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Information:					
52	Non Patent Literature	SPENCER_2001_p270_NPL.pdf	911311 15d953867e2518969608973daf44566ea74ddfe0	no	4
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53	Non Patent Literature	SWINKELS_2003_p525_NPL.pdf	102753 1f784d5a3f0e3ad2f08efb5c5031311127efbc46	no	2
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54	Non Patent Literature	TSANGARIS_2006_p9236_NPL.pdf	9263094 12f0b29ec6f6933f5c59958875f52969cbd69053	no	10
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55	Non Patent Literature	VOGELSTEIN_1999_p9236_NPL.pdf	610258 2e6eb2884393f8020917649c119034692a11cdd4	no	6
Warnings:					
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56	Non Patent Literature	ZIMMERMANN_2002_p362_NPL.pdf	3091340 18fc3cd46a075f316ee247be0e53746ebbd5b1d3	no	2
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57	Non Patent Literature	ZIMMERMANN_2005_p1598_NPL.pdf	8791037 58e435886e6f4e8ee42f1eddd9a3a7504de96c3e	no	7
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60	Non Patent Literature	ZIMMERMANN_2008_p1087_NPL.pdf	4514026 76a0f2ededcb3971eca2251f6886800451b18657	no	7
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61	Fee Worksheet (SB06)	fee-info.pdf	30600 25db112b8cccca10d0727dba7d0a5e64a698f20c	no	2
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New Applications Under 35 U.S.C. 111

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National Stage of an International Application under 35 U.S.C. 371

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New International Application Filed with the USPTO as a Receiving Office

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16/934,407
	Filing Date	Jul 21, 2020
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

U.S. PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		10774380	B2	2020-09-15	RYAN, A. et al.	
		10793912	B2	2020-10-06	BABIARZ, J. et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		20110015096	A1	2011-01-20	CHIU, K. P.	
		20150315657	A1	2015-11-05	RHODES, D. et al.	
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns, Lines where Relevant Passages or Relevant Figures Appear	T[5]
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		2010/127186	WO	A1	2010-11-04	CHEE, M. S.		
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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
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	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

		KUKITA, Y. et al., "High-fidelity target sequencing of individual molecules identified using barcode sequences: de nova detection and absolute quantitation of mutations in plasma cell-free DNA from cancer patients", DNA Research, Vol. 22, No. 4, 29 JUN 2015, 269-277	
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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

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	Attorney Docket Number	N.012.US.32

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[4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e) (2).

☐ See attached certification statement.

☒ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Tianran Yan/	Date (YYYY-MM-DD)	2020-12-02
Name/Print	Tianran Yan	Registration Number	67,162

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16/934,407
	Filing Date	Jul 21, 2020
	First Named Inventor	Joshua BABIARZ
	Art Unit	1637
	Examiner Name	Stephanie Kane Mummert
	Attorney Docket Number	N.012.US.32

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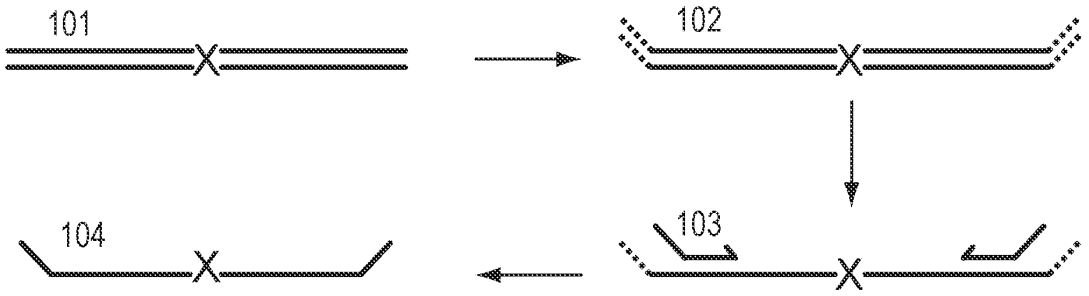


FIG. 1

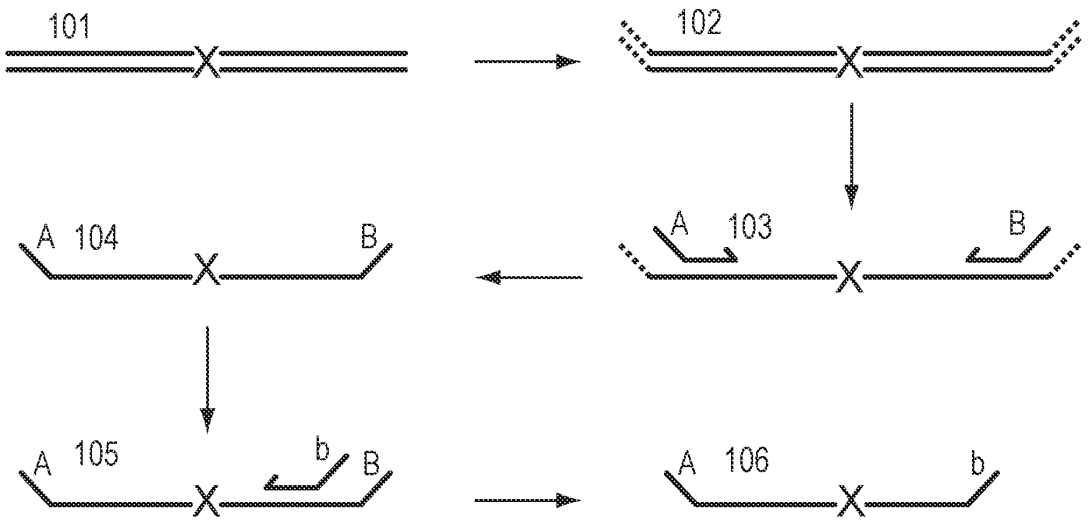


FIG. 2

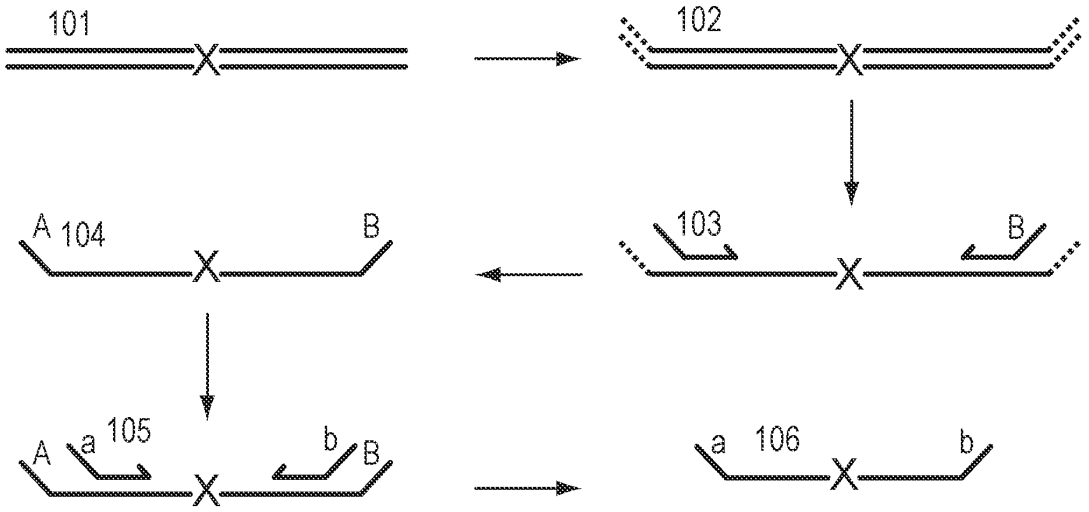

101
102
A 104
B
103
B
A
a 105
b
B
a 106
b

FIG. 3

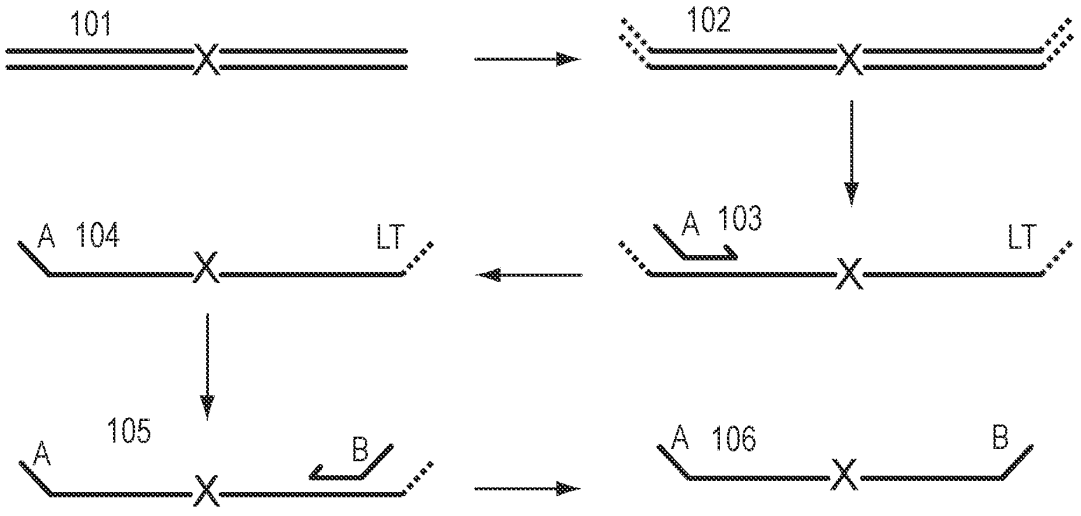

101
102
A 104
LT
A 103
LT
105
A
B
A 106
B

FIG. 4

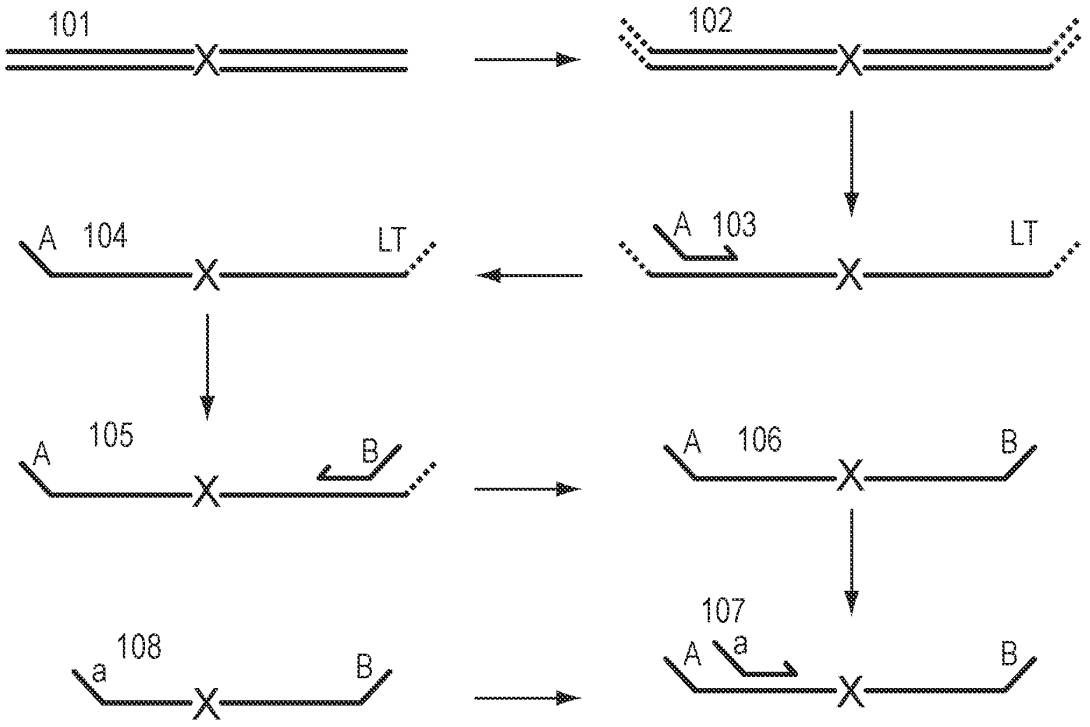

101
102
A 104
LT
A 103
LT
A 105
B
A 106
B
108
a
B
107
A
a
B

FIG. 5

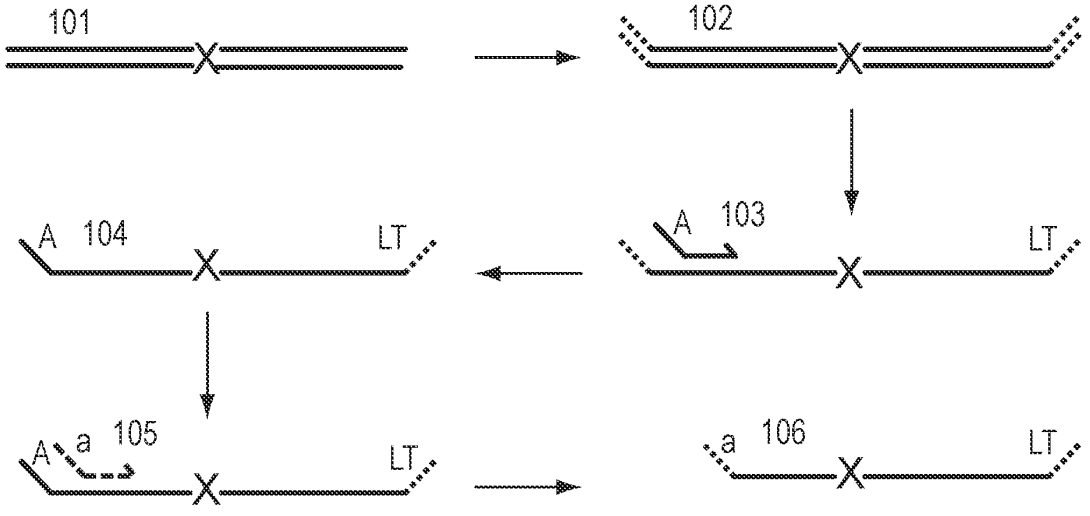

101
102
A 104
LT
A 103
LT
A
a 105
LT
a 106
LT

FIG. 6

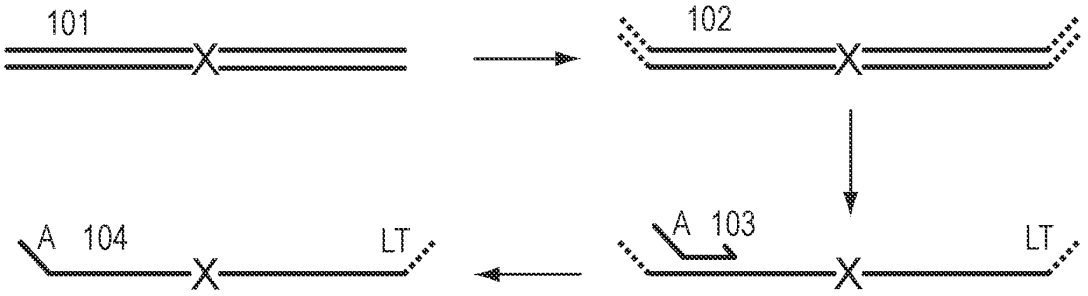


FIG. 7

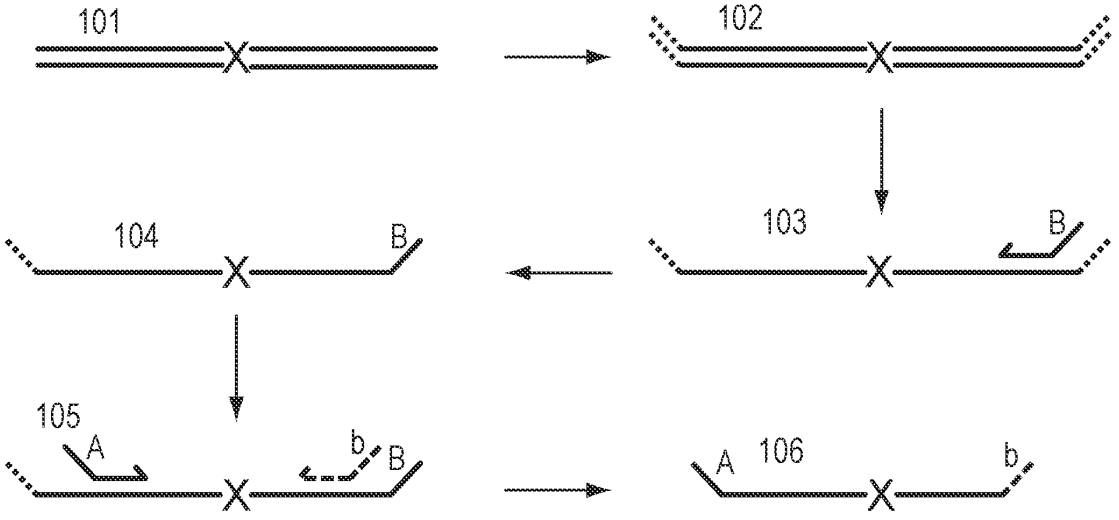


FIG. 8

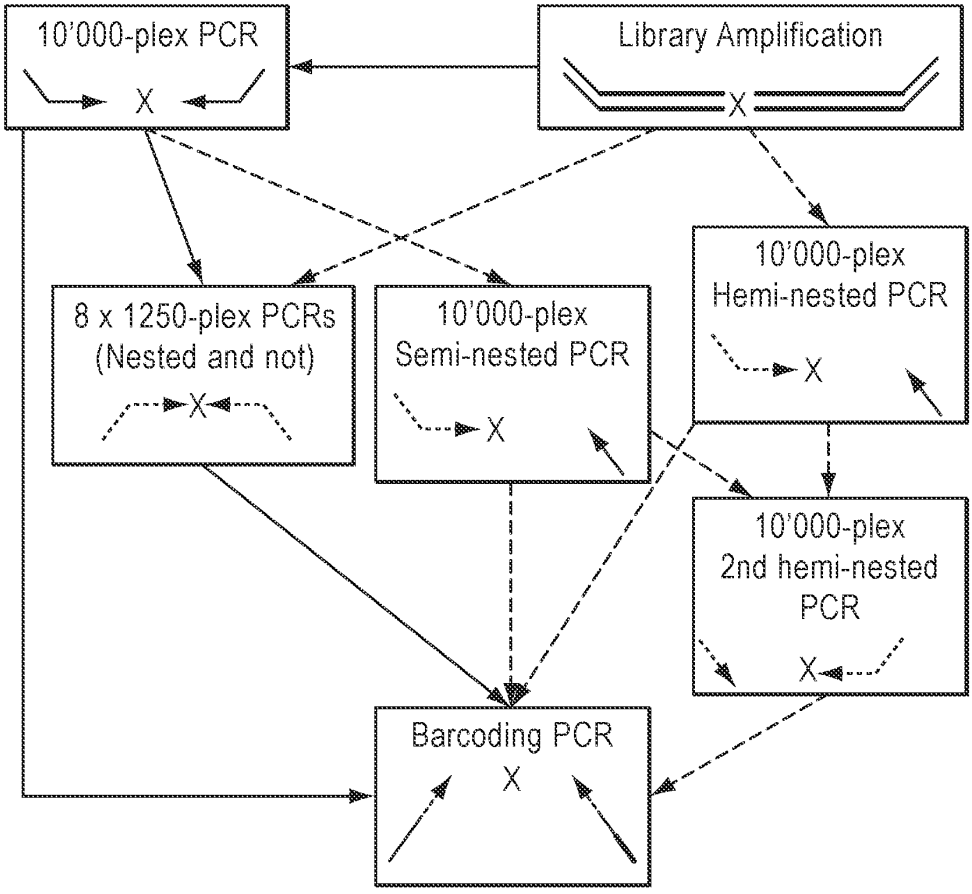

10'000-plex PCR
X
Library Amplification
X
8 x 1250-plex PCRs
(Nested and not)
X
10'000-plex
Semi-nested PCR
X
10'000-plex
Hemi-nested PCR
X
10'000-plex
2nd hemi-nested
PCR
X
Barcoding PCR
X

FIG. 9

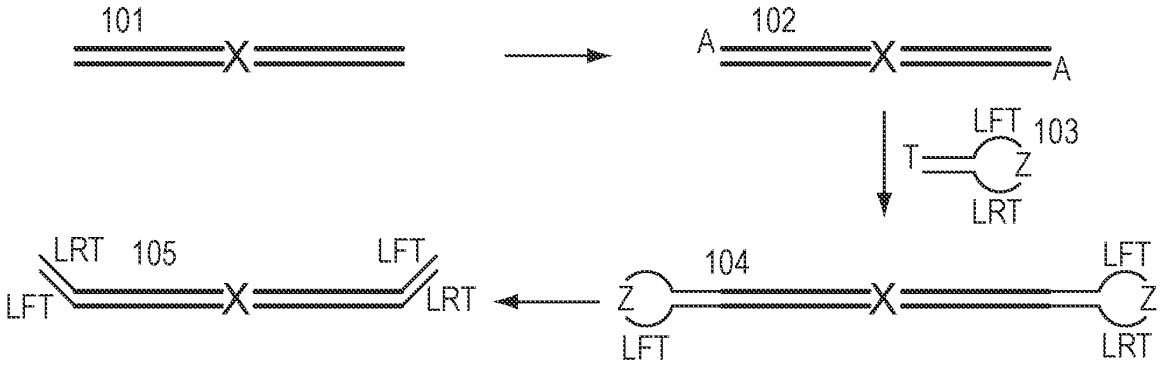

101
102
A
A
LFT
103
T
Z
LRT
LRT
105
LFT
LFT
LRT
104
Z
LFT
LFT
Z
LRT

FIG. 10

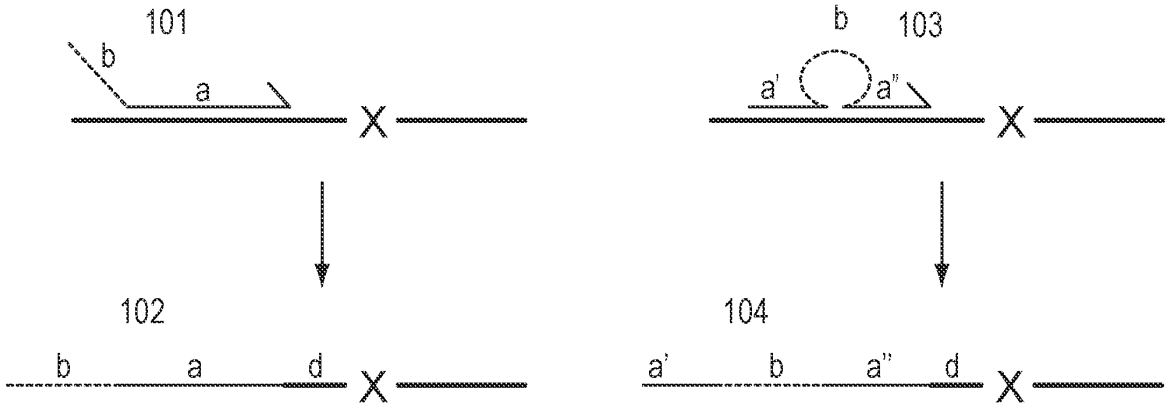


FIG. 11

			SEQ ID NO:
The sequencing-adaptor sequence is located inside the primer sequence and flanked by target specific sequence on both sides. 10 bases are target-specific at the 3'-end of each primer. Primers were tested successfully in real-time PCR. For sequencing this reduces the number of primer bases that need to be sequenced.			
rs8130564	int-tag 1.10	AACTCACATAGC*ACACGACGCTCTTCCGATCT*TGCAAGCACA	44611
rs2832093	int-tag 2.10	TCCTCTGTG*ACACGACGCTCTTCCGATCT*CCCTGCTCTT	44612
rs12011281	int-tag 3.10	tcctctctctACACGACGCTCTTCCGATCTcGGGCTGTCA	44613
rs6719561	int-tag 4.10	TACATCCTTGAGACACGACGCTCTTCCGATCTGCTGTGCAGT	44614
rs10187018	int-tag 5.10	tttgcttgagctACACGACGCTCTTCCGATCTcgggagtttc	44615
rs10460481	int-tag 6.10	gtcttatggtggACACGACGCTCTTCCGATCTcaaagccagt	44616
The sequencing-adaptor sequence is located inside the primer sequence and flanked by target specific sequence on both sides. The internal tag is formed into a hairpin structure by 10 complementary bases on either end. This brings the target-specific ends of the primer into close proximity and hinders unspecific binding to the "internal tag". 10 bases are target-specific at the 3'-end of each primer. Primers were tested successfully in real-time PCR.			
rs8130564	loop-int-tag 1.10	AACTCACATAGC*tgatcggtACACGACGCTCTTCCGATCT*TGCAAGCACA	44617
rs2832093	loop-int-tag 2.10	TCCTCTGTG*tgatcggtACACGACGCTCTTCCGATCT*CCCTGCTCTT	44618
rs12011281	loop-int-tag 3.10	tcctctcttgatcggtACACGACGCTCTTCCGATCTcGGGCTGTCA	44625
rs6719561	loop-int-tag 4.10	TACATCCTTGAGtgatcggtACACGACGCTCTTCCGATCTGCTGTGCAGT	44620
rs10187018	loop-int-tag 5.10	tttgcttgagcttgatcggtACACGACGCTCTTCCGATCTcgggagtttc	44621
rs10460481	loop-int-tag 6.10	gtcttatggtggtgatcggtACACGACGCTCTTCCGATCTcaaagccagt	44622

FIG. 12

NeoGenomics
Exhibit 1003 Page 793

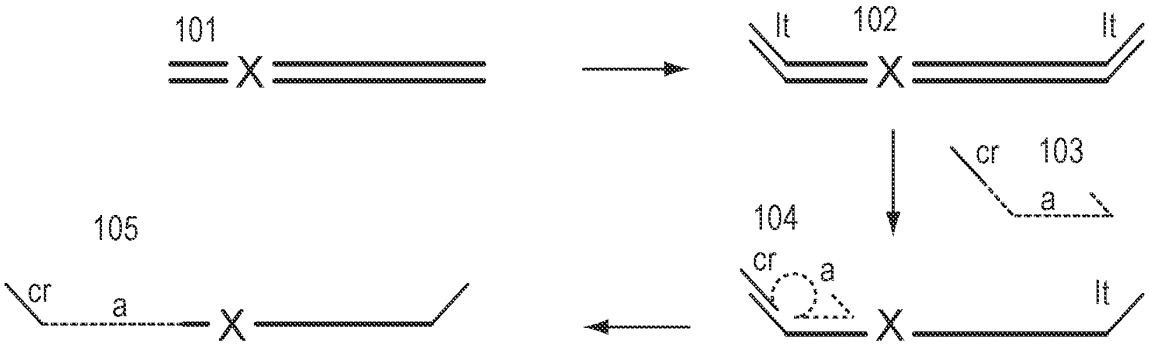

101
lt
102
lt
cr
103
a
104
cr
a
lt
105
cr
a

FIG. 13

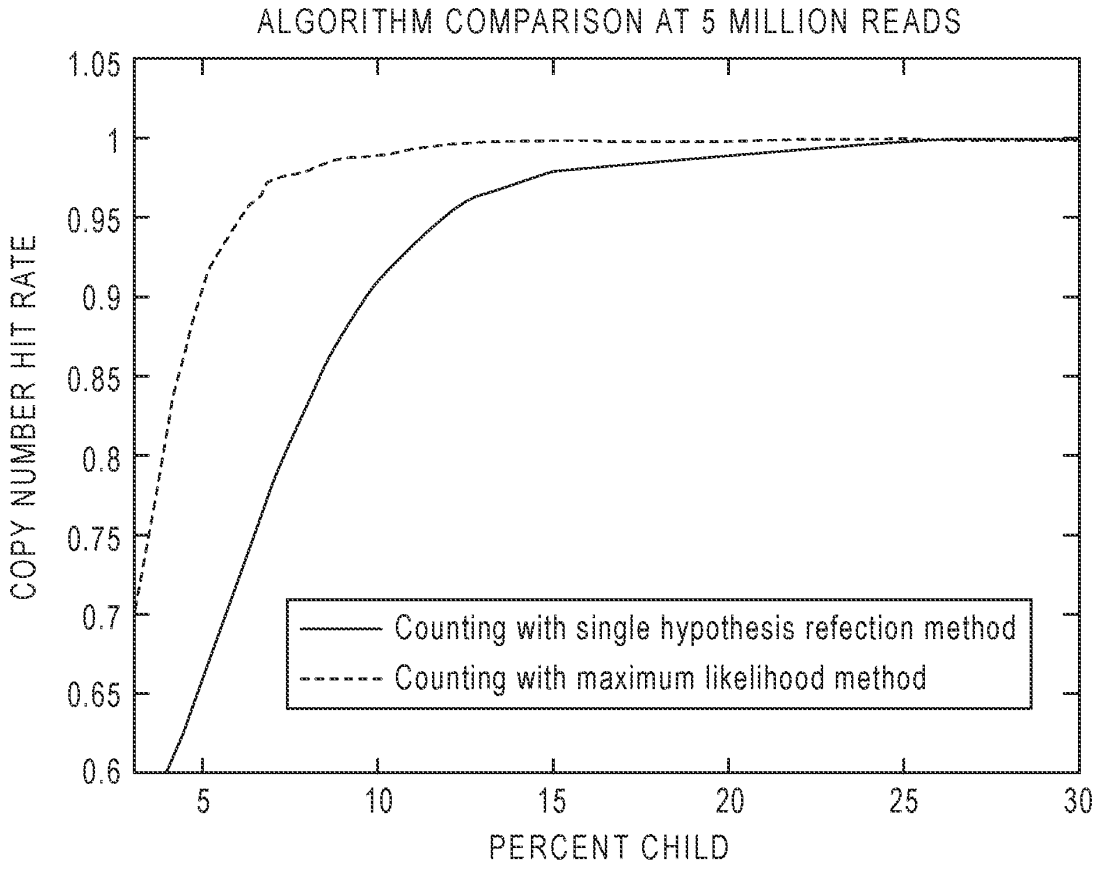

ALGORITHM COMPARISON AT 5 MILLION READS
COPY NUMBER HIT RATE
1.05
1
0.95
0.9
0.85
0.8
0.75
0.7
0.65
0.6
5
10
15
20
25
30
PERCENT CHILD
Counting with single hypothesis refection method
Counting with maximum likelihood method

FIG.14

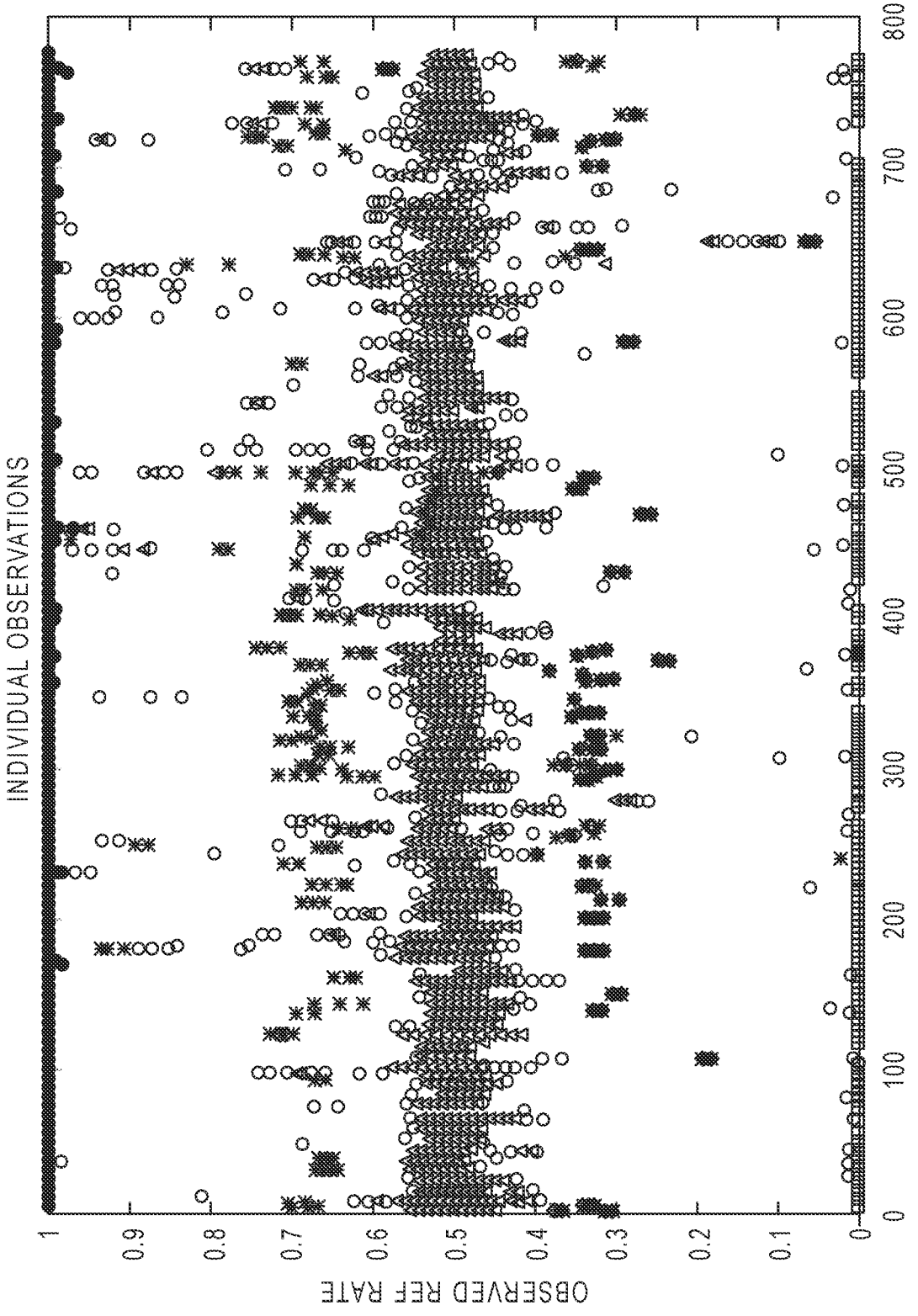

INDIVIDUAL OBSERVATIONS
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
OBSERVED REF RATE
0
100
200
300
400
500
600
700
800
SNP

FIG. 15

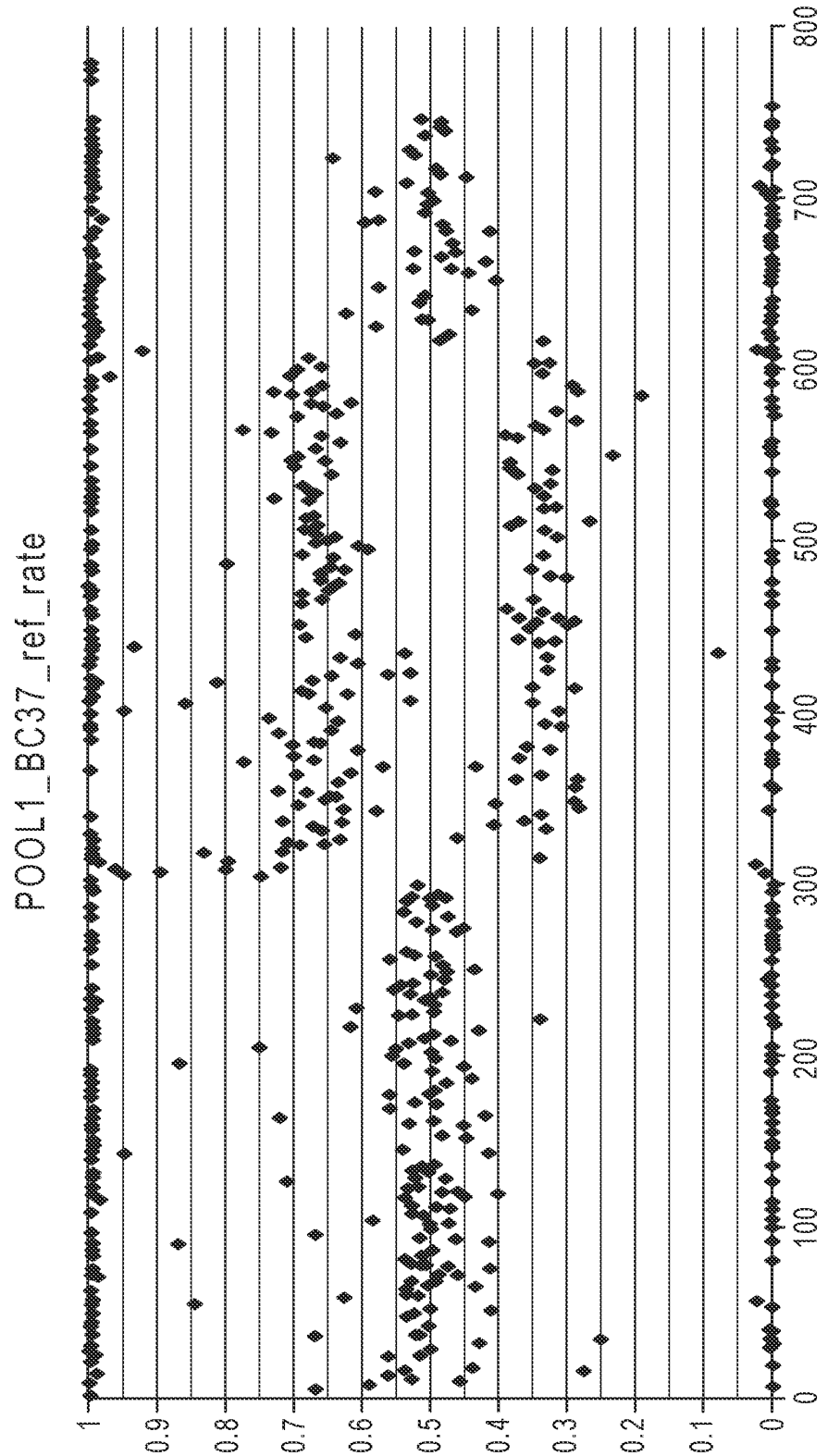

POOL1_BC37_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 16

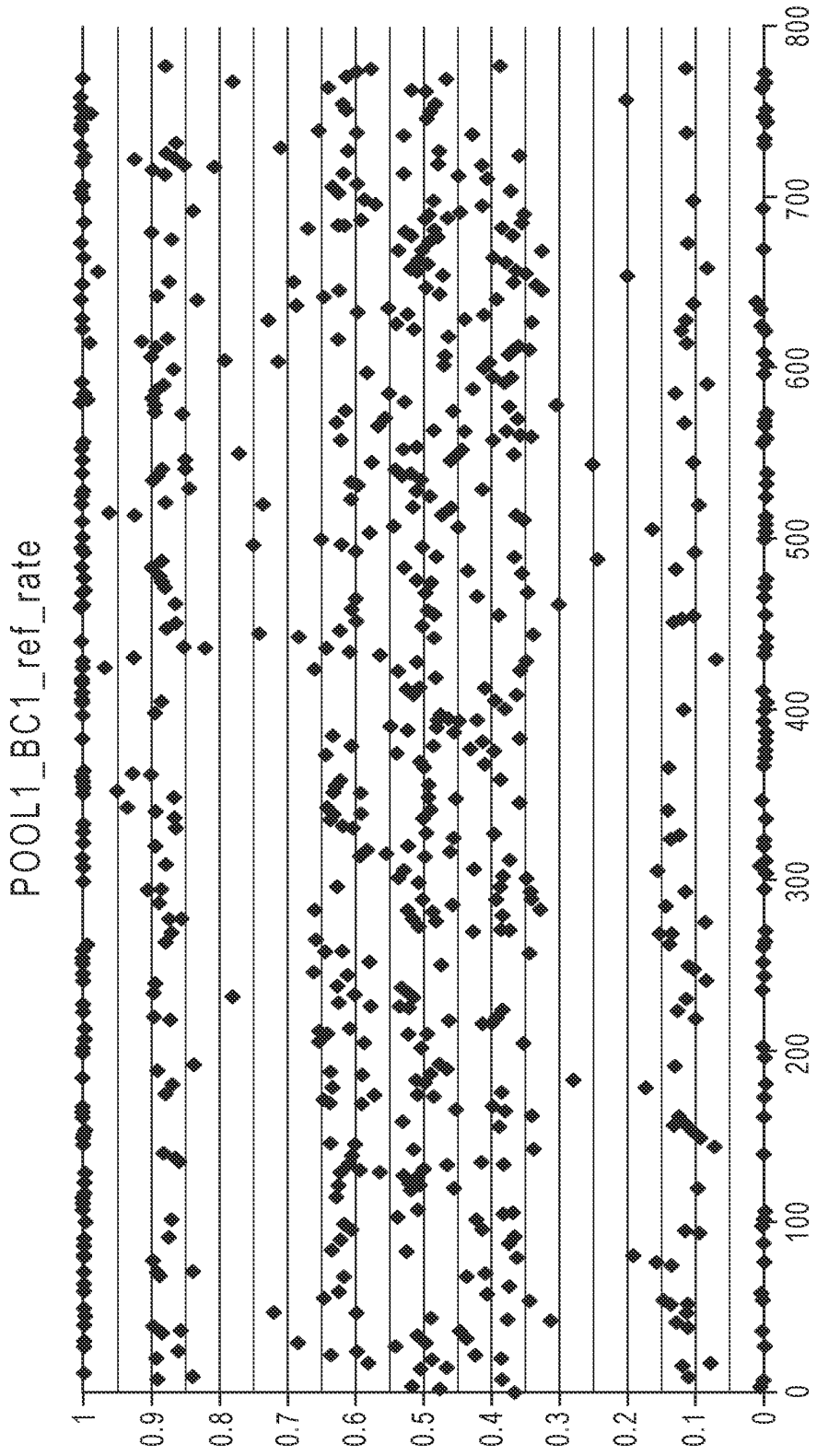

POOL1_BC1_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17A

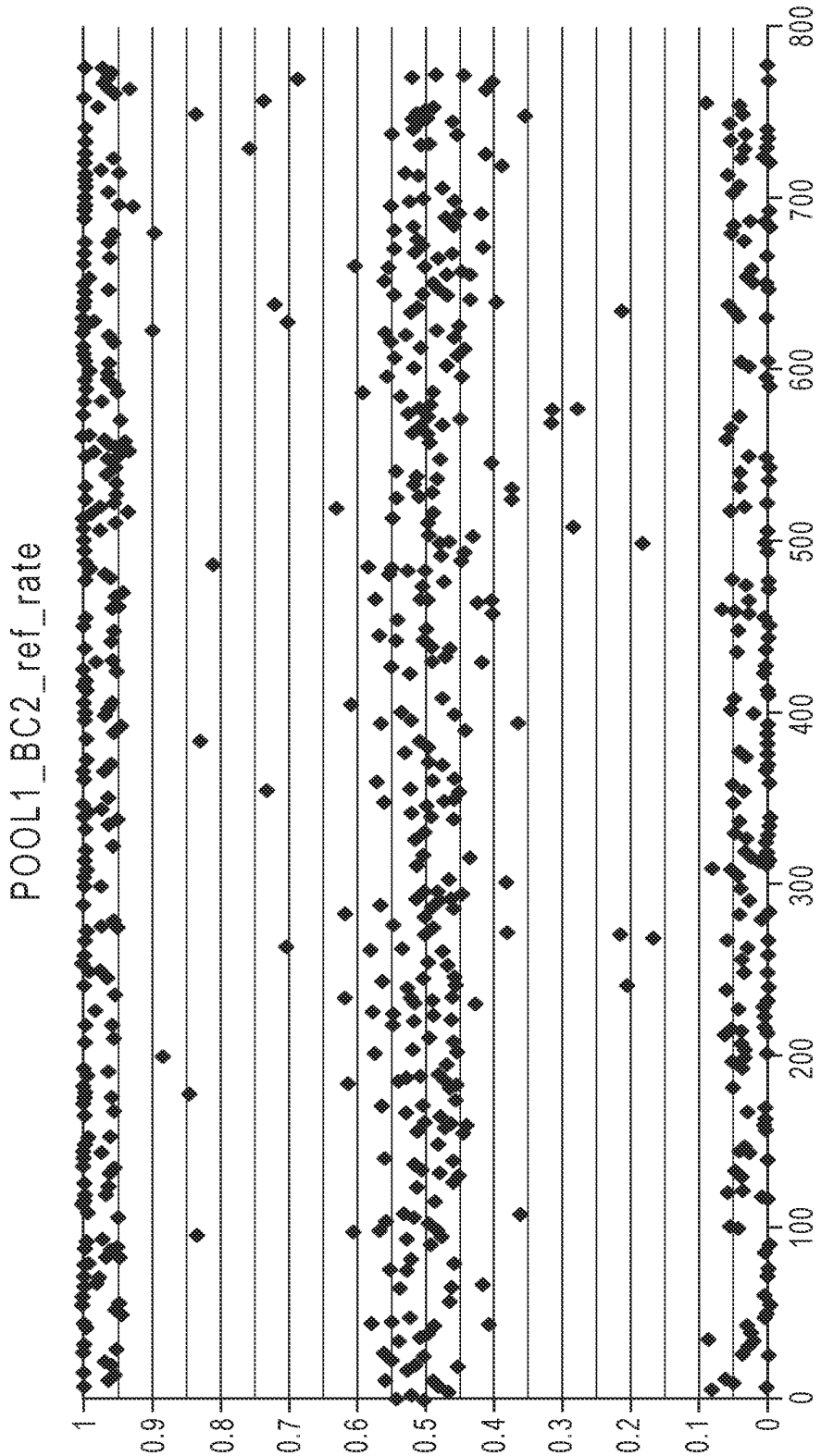

POOL1_BC2_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17B

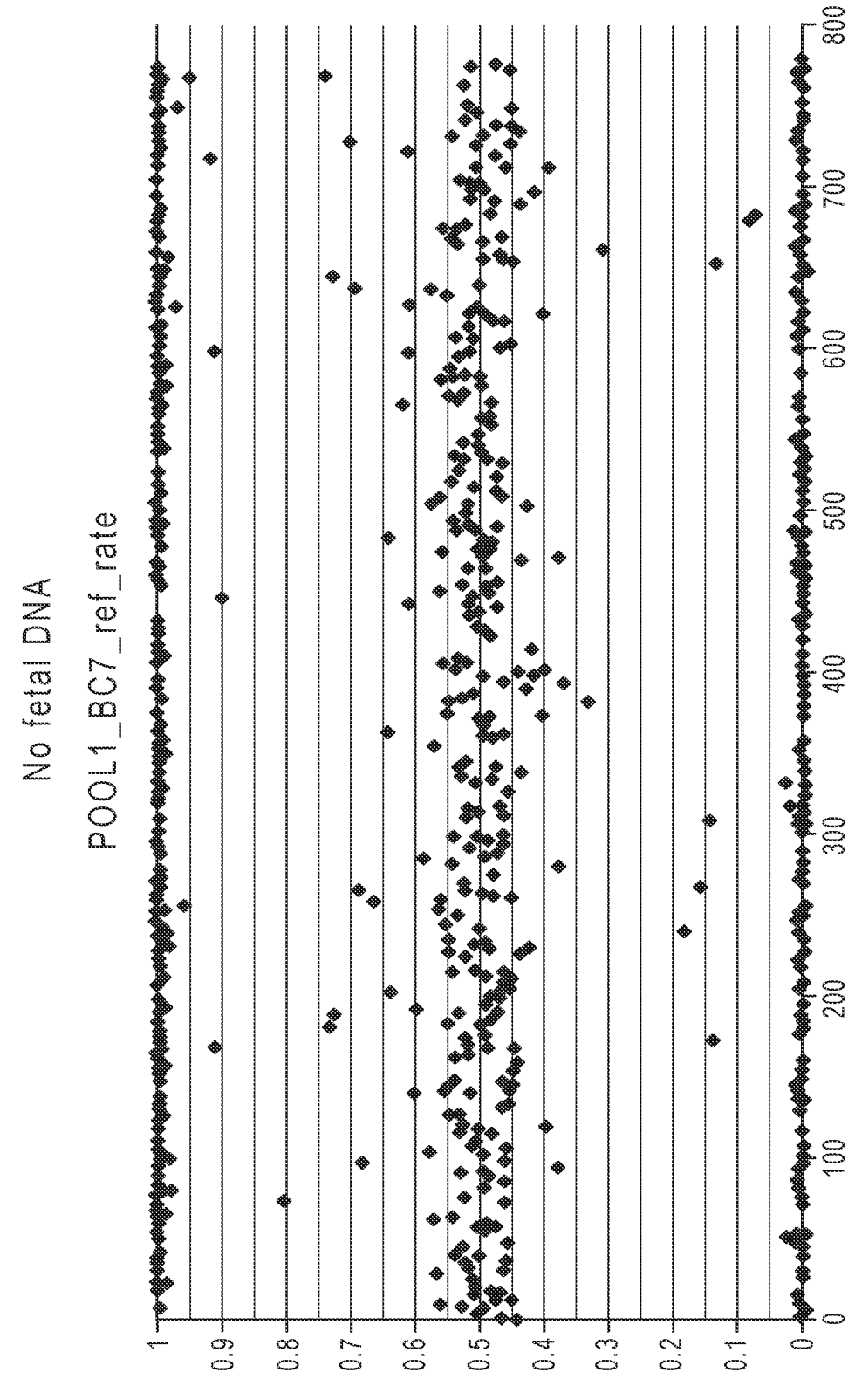

No fetal DNA
POOL1_BC7_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17C

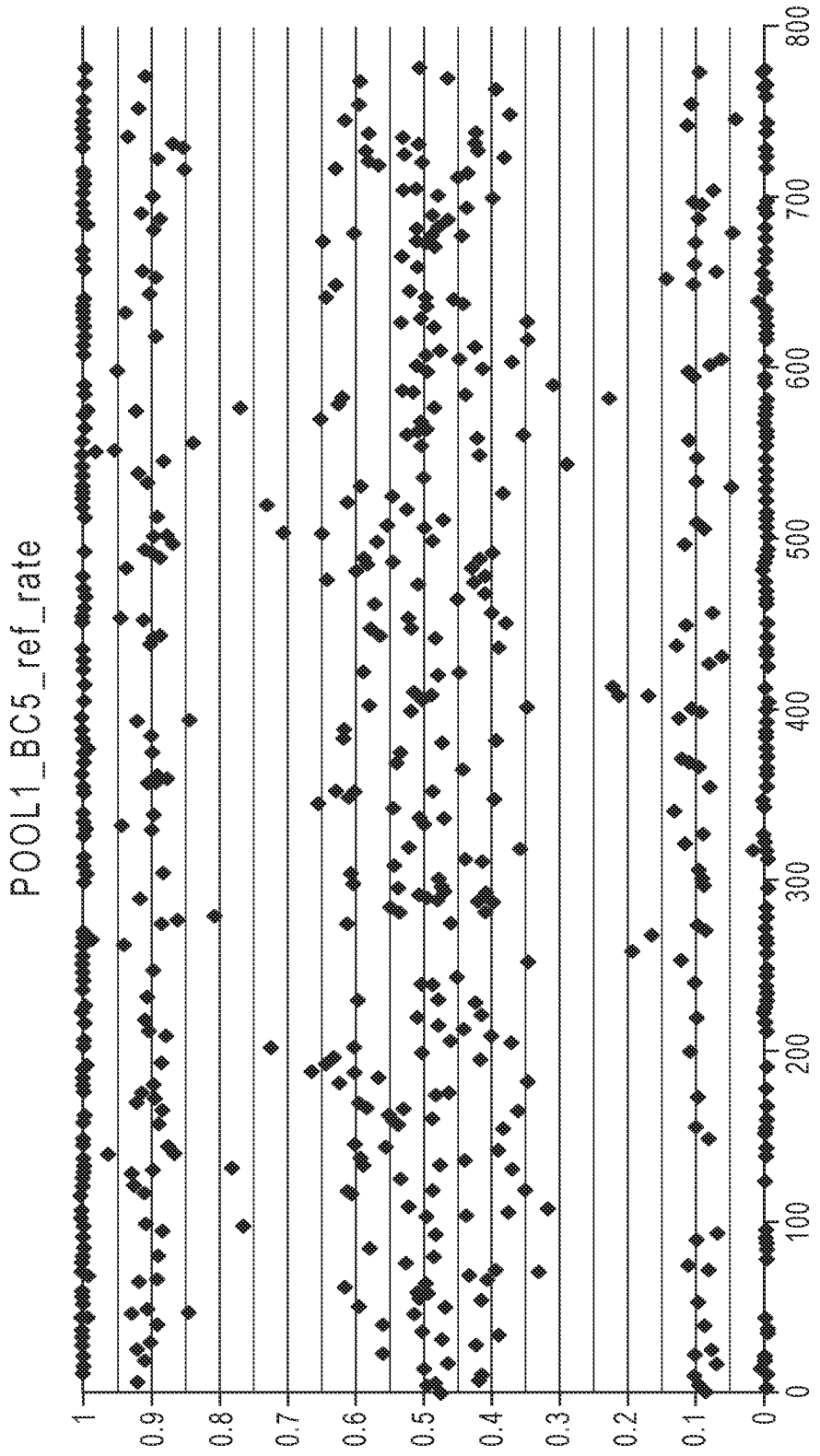

POOL1_BC5_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17D

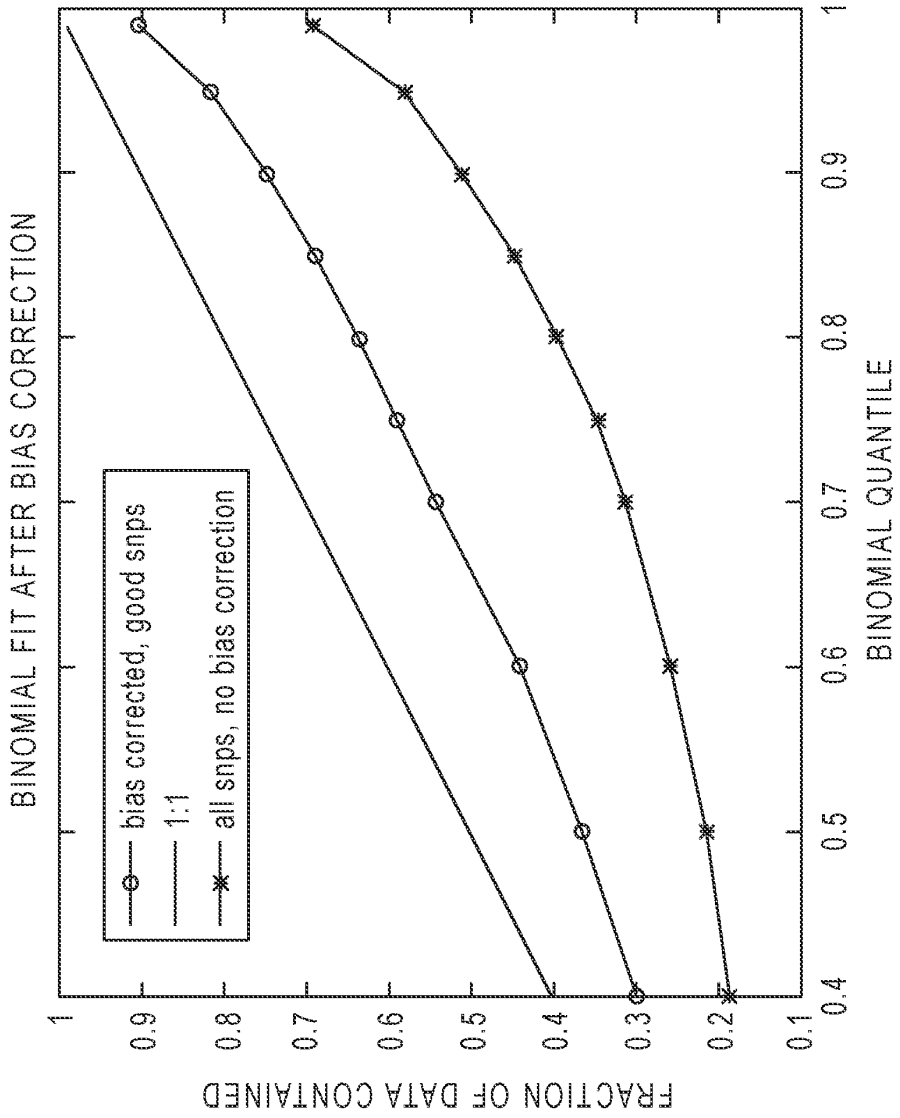

BINOMIAL FIT AFTER BIAS CORRECTION
FRACTION OF DATA CONTAINED
BINOMIAL QUANTILE
bias corrected, good snps
1:1
all snps, no bias correction
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0.4
0.5
0.6
0.7
0.8
0.9
1

FIG. 18

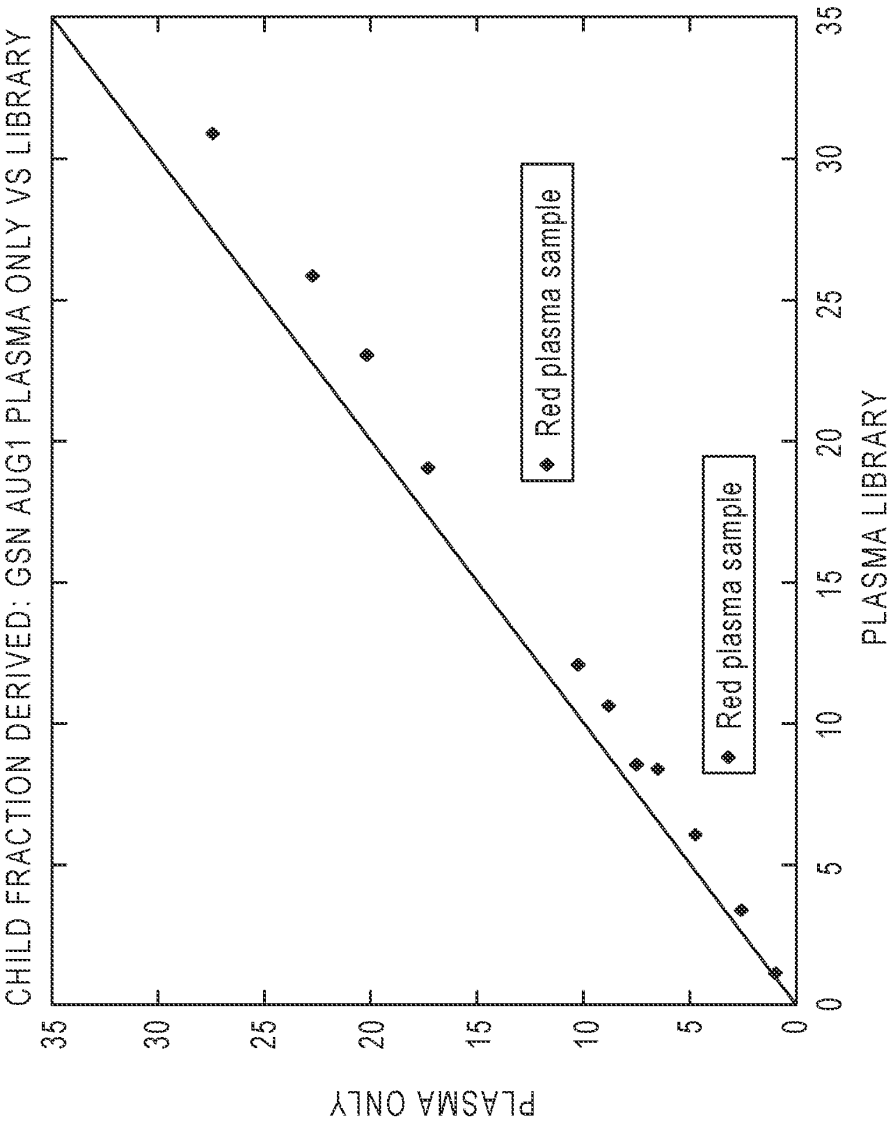

CHILD FRACTION DERIVED: GSN AUG1 PLASMA ONLY VS LIBRARY
PLASMA ONLY
PLASMA LIBRARY
0
5
10
15
20
25
30
35
Red plasma sample
Red plasma sample

FIG. 19

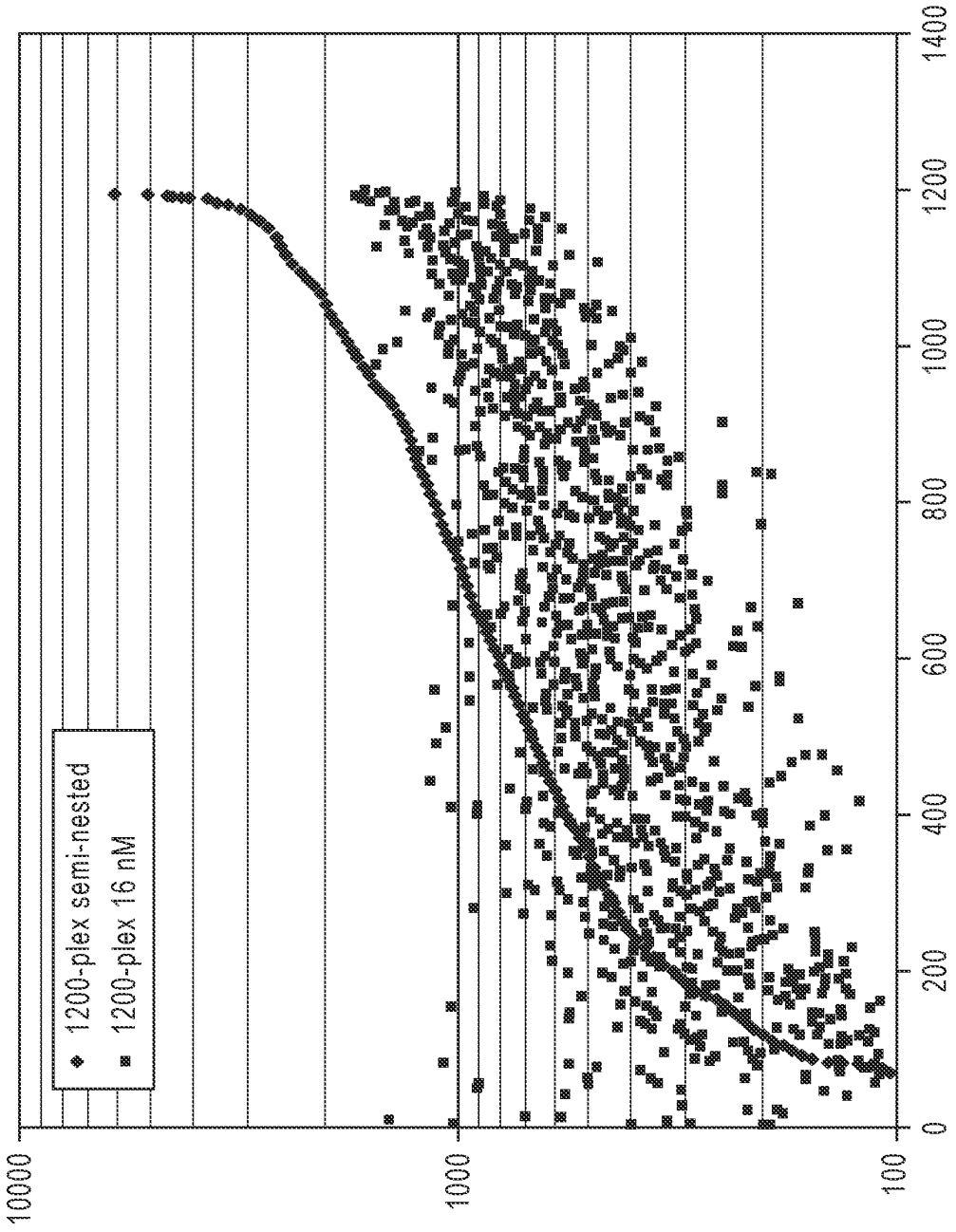

1200-plex semi-nested
1200-plex 16 nM
10000
1000
100
0
200
400
600
800
1000
1200
1400

FIG. 20

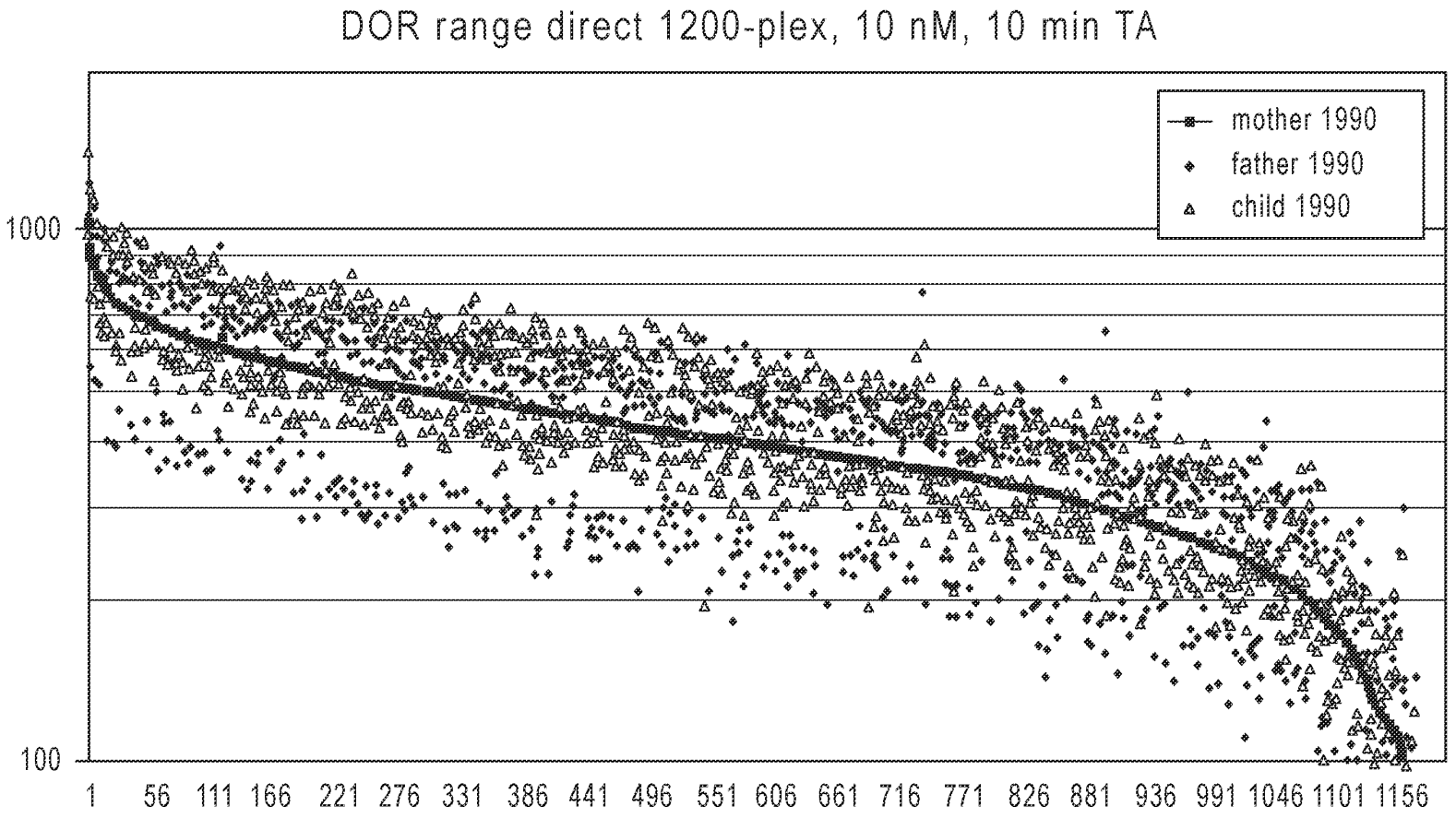


FIG. 21

NeoGenomics
Exhibit 1003 Page 804

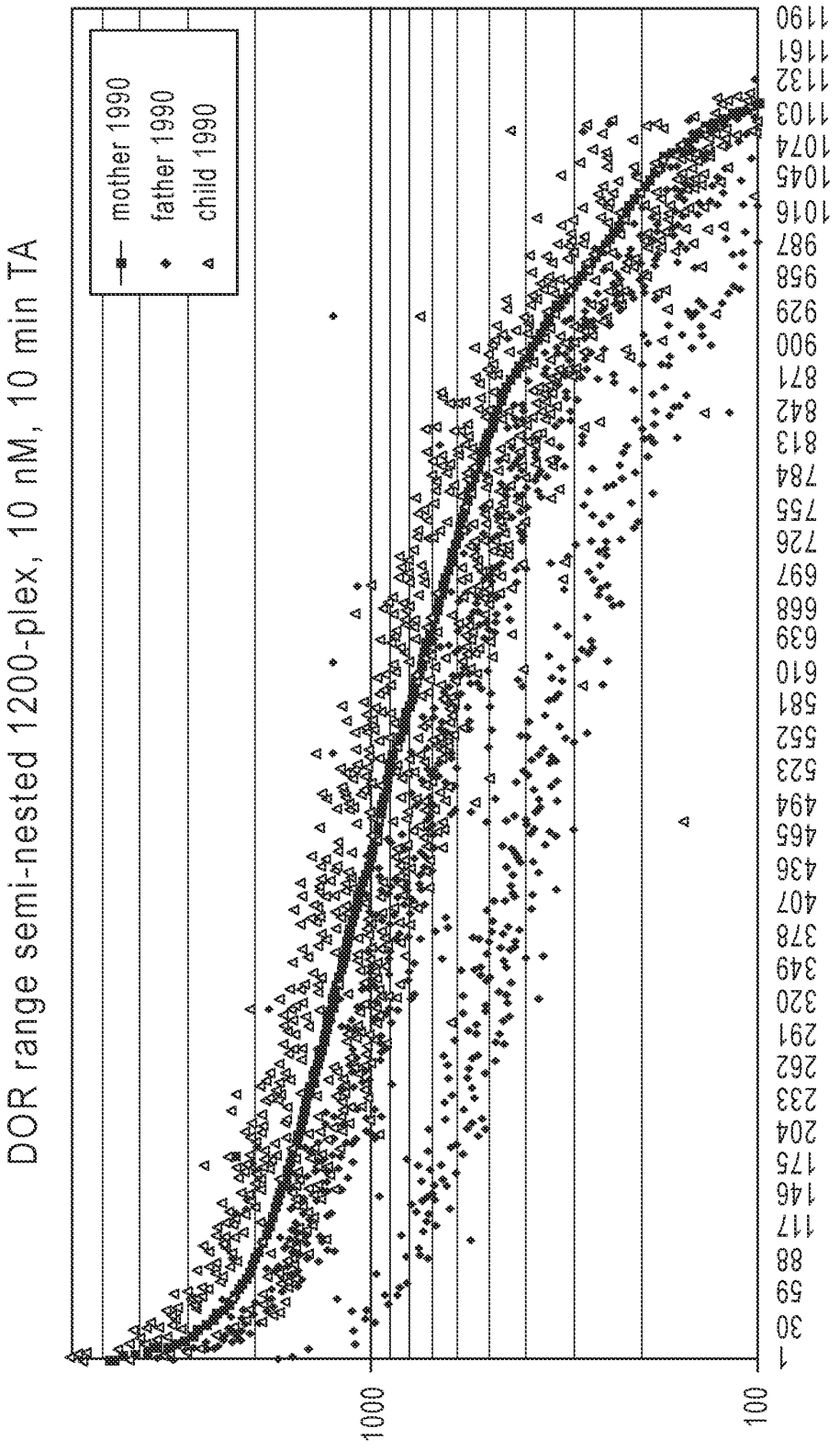

DOR range semi-nested 1200-plex, 10 nM, 10 min TA
mother 1990
father 1990
child 1990
1000
100
1190
1161
1132
1103
1074
1045
1016
987
958
929
900
871
842
813
784
755
726
697
668
639
610
581
552
523
494
465
436
407
378
349
320
291
262
233
204
175
146
117
88
59
30
1

FIG. 22

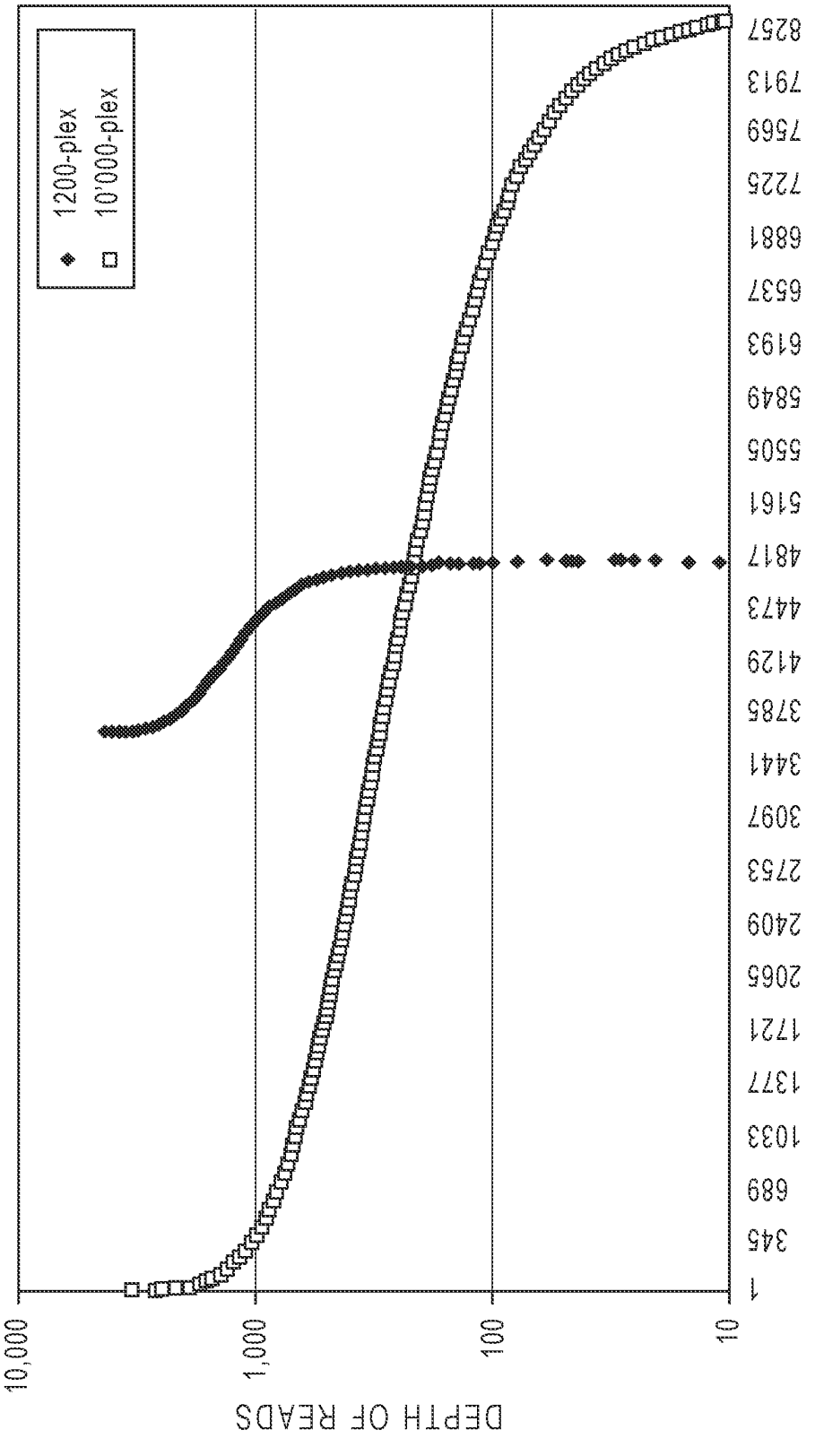

1200-plex
10'000-plex
10,000
1,000
100
10
DEPTH OF READS
1
345
689
1033
1377
1721
2065
2409
2753
3097
3441
3785
4129
4473
4817
5161
5505
5849
6193
6537
6881
7225
7569
7913
8257
RANKED ASSAY

FIG. 23

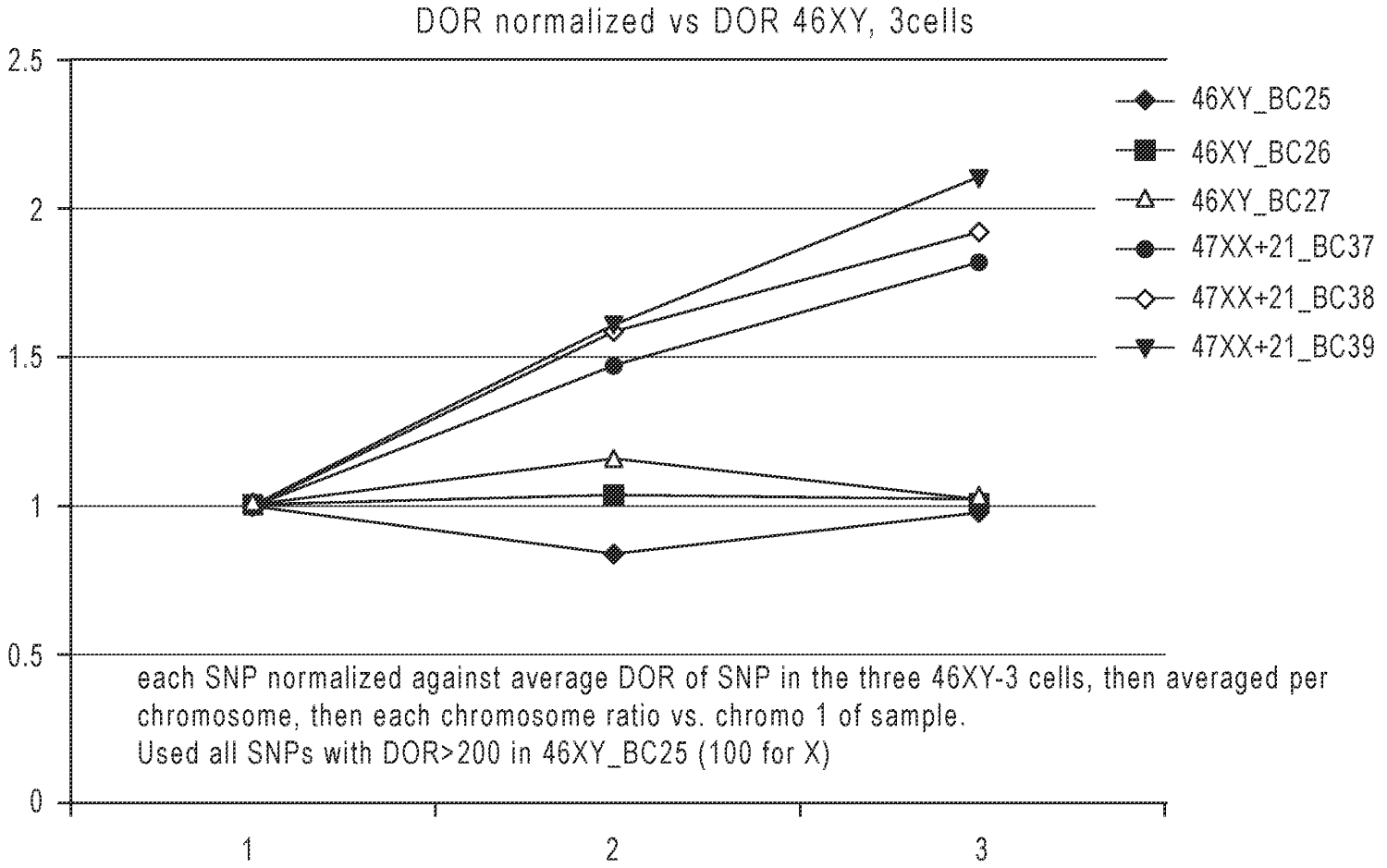


FIG. 24

NeoGenomics
Exhibit 1003 Page 807

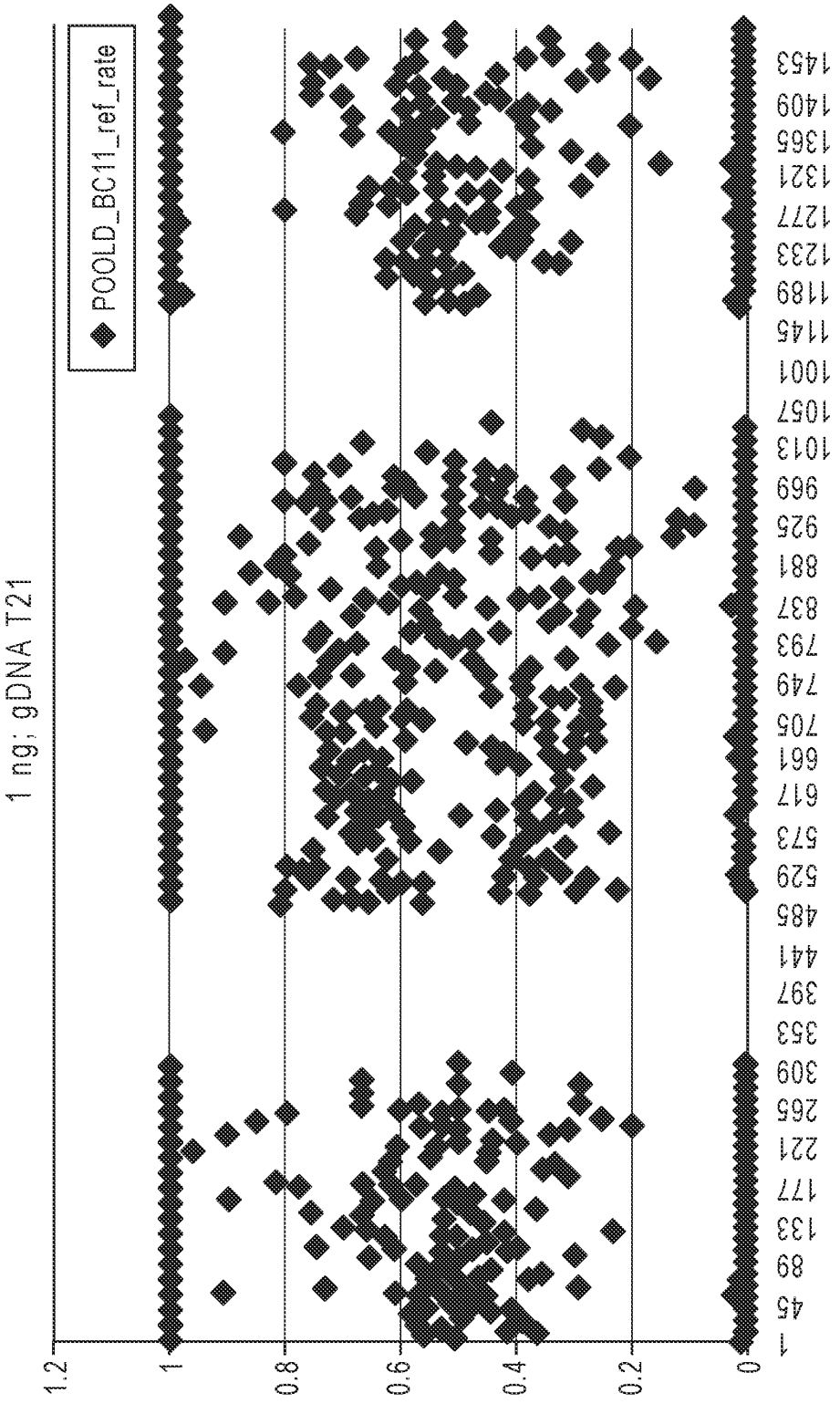

1 ng; gDNA T21
POOLD_BC11_ref_rate
1.2
1
0.8
0.6
0.4
0.2
0
1
45
89
133
177
221
265
309
353
397
441
485
529
573
617
661
705
749
793
837
881
925
969
1013
1057
1001
1145
1189
1233
1277
1321
1365
1409
1453

FIG. 25A

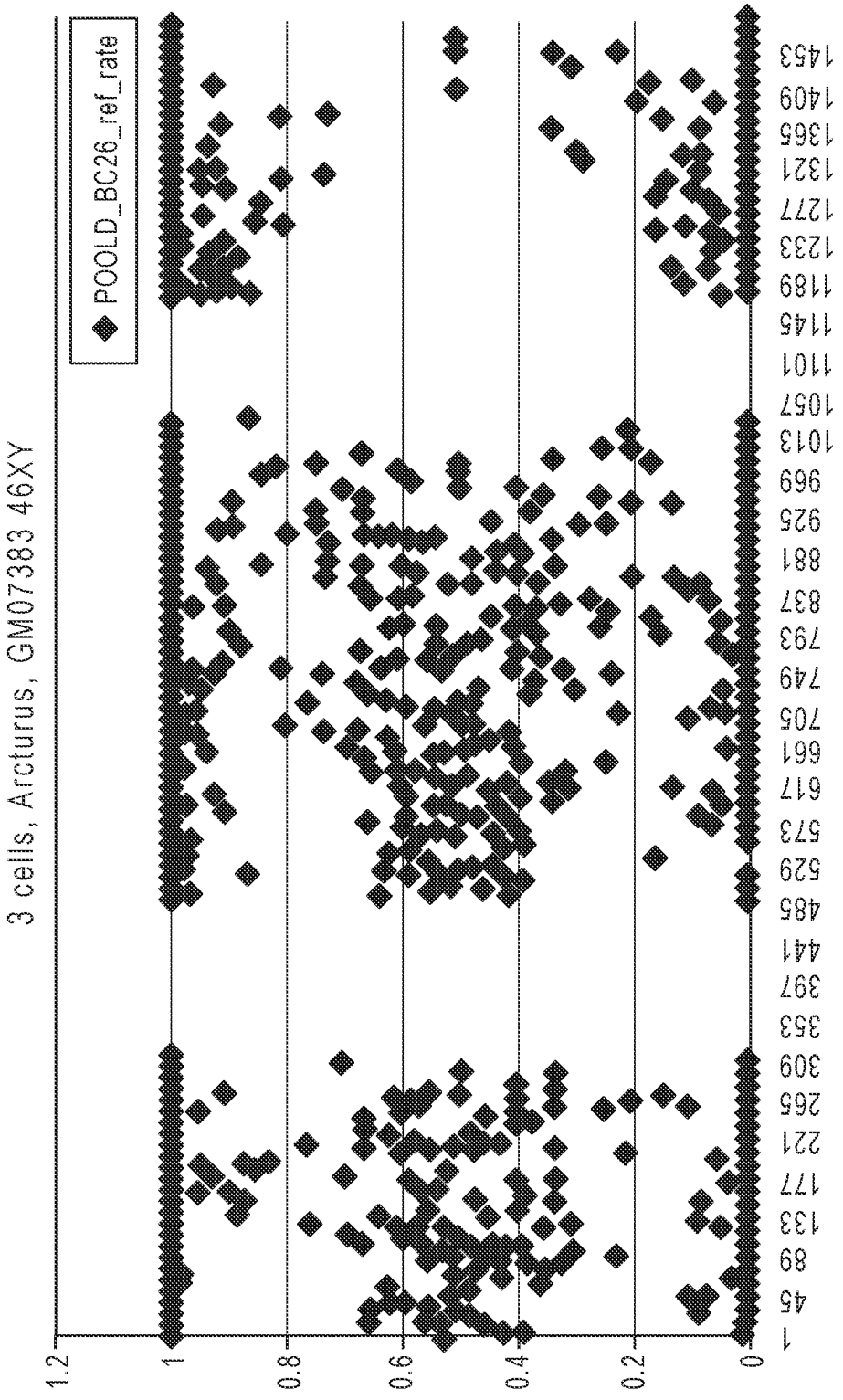

3 cells, Arcturus, GM07383 46XY
POOLD_BC26_ref_rate
1.2
1
0.8
0.6
0.4
0.2
0
1
45
89
133
177
221
265
309
353
397
441
485
529
573
617
661
705
749
793
837
881
925
969
1013
1057
1101
1145
1189
1233
1277
1321
1365
1409
1453

FIG. 25B

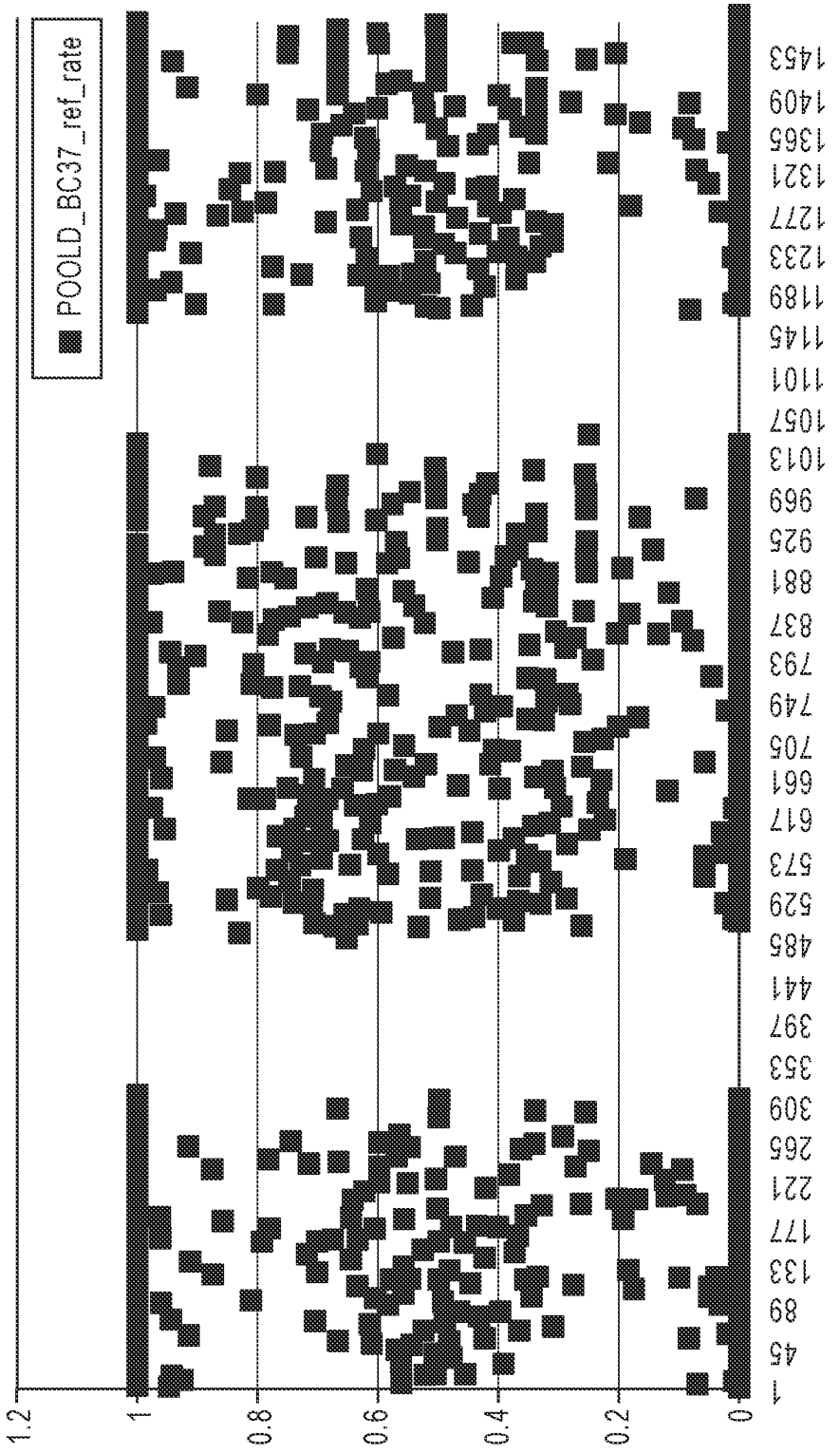

3 cells, ArcturusAG16777, 47 XX+21
POOLD_BC37_ref_rate
1.2
1
0.8
0.6
0.4
0.2
0
1
45
89
133
177
221
265
309
353
397
441
485
529
573
617
661
705
749
793
837
881
925
969
1013
1057
1101
1145
1189
1233
1277
1321
1365
1409
1453

FIG. 25C

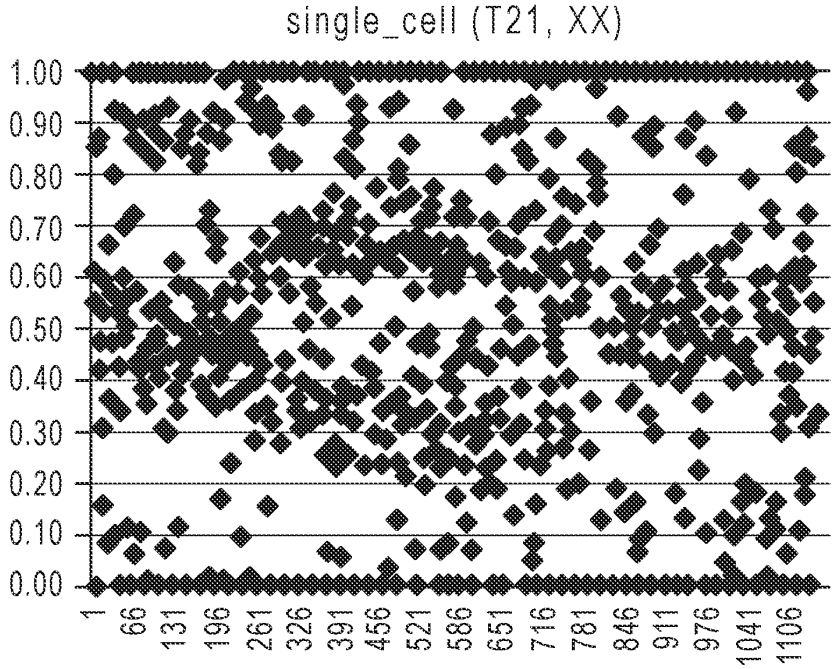


FIG. 26A

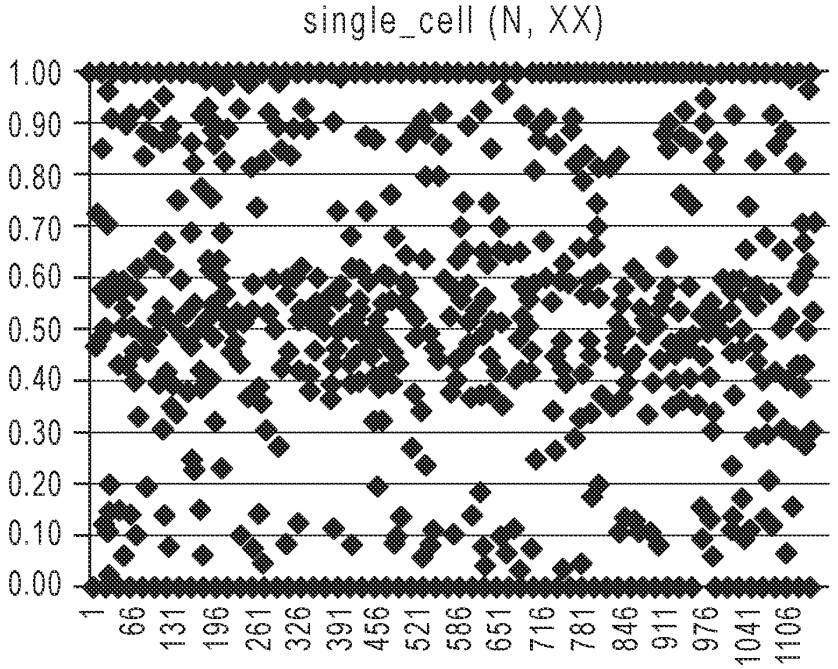


FIG. 26B

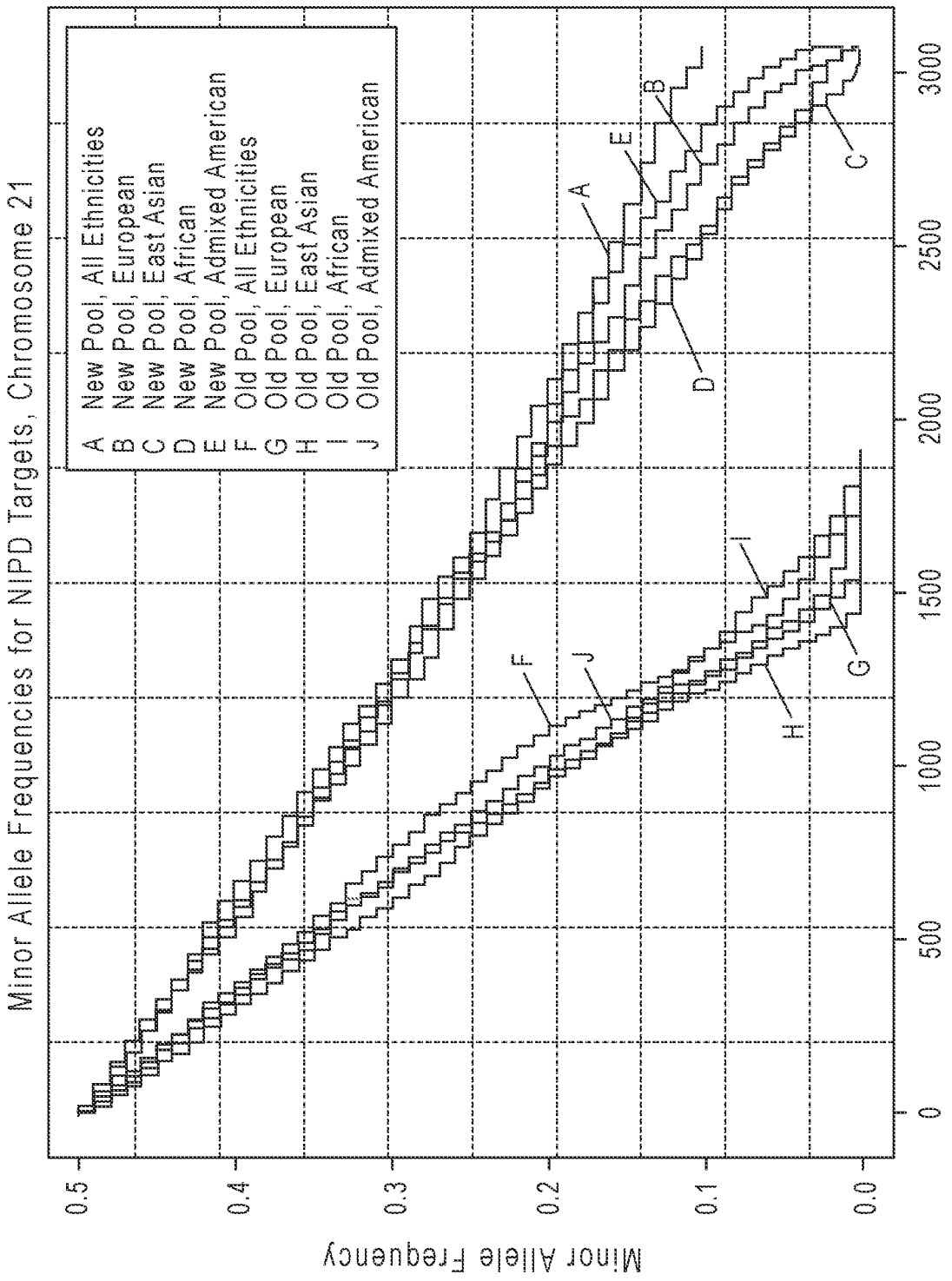

Minor Allele Frequencies for NIPD Targets, Chromosome 21
A New Pool, All Ethnicities
B New Pool, European
C New Pool, East Asian
D New Pool, African
E New Pool, Admixed American
F Old Pool, All Ethnicities
G Old Pool, European
H Old Pool, East Asian
I Old Pool, African
J Old Pool, Admixed American
Minor Allele Frequency
0.0
0.1
0.2
0.3
0.4
0.5
0
500
1000
1500
2000
2500
3000
Target Number

FIG. 27

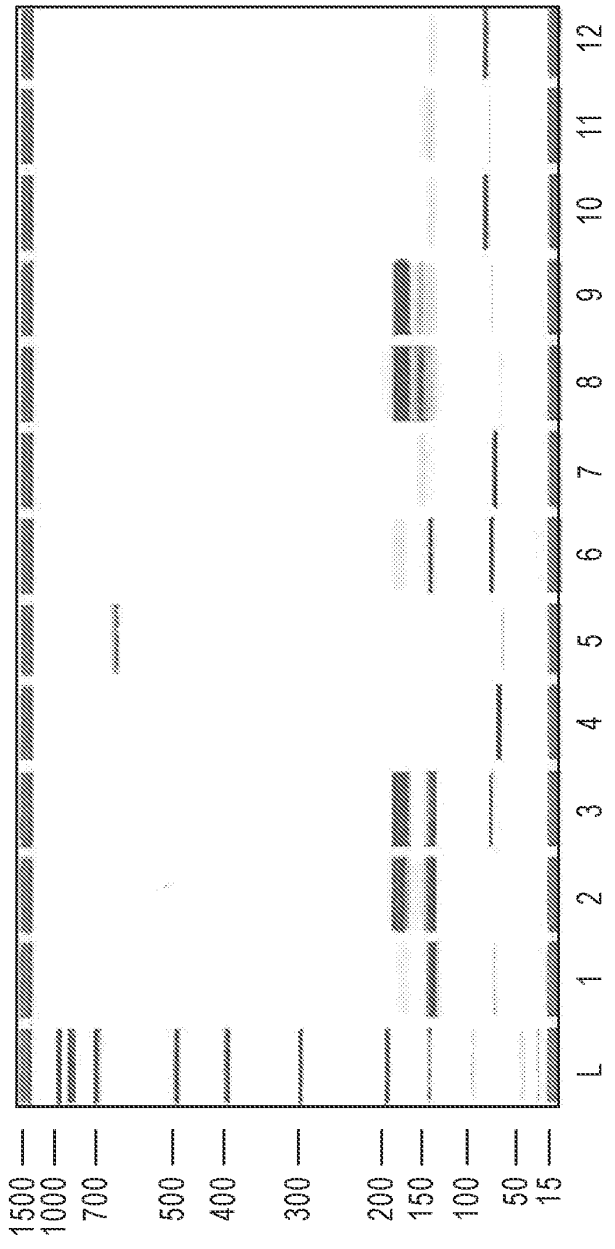


FIG. 28A

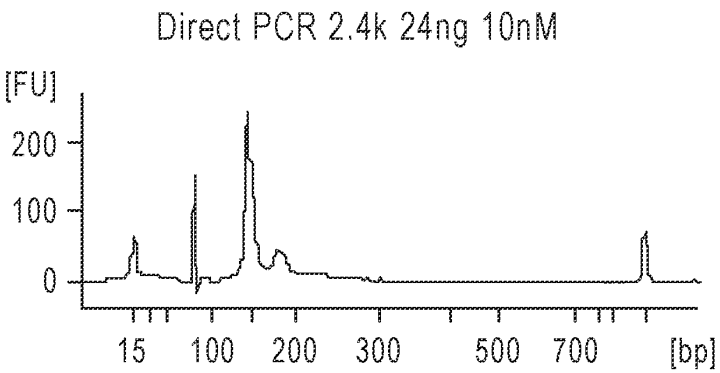


FIG. 28B

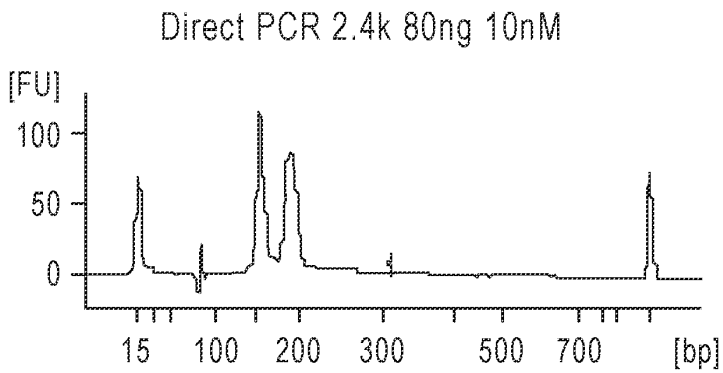


FIG. 28C

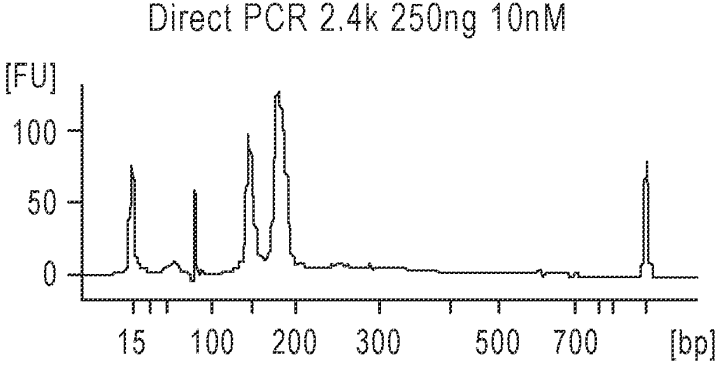


FIG. 28D

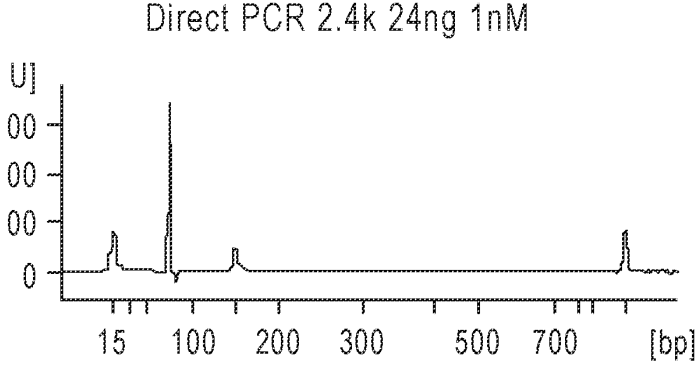


FIG. 28E

NeoGenomics
Exhibit 1003 Page 814

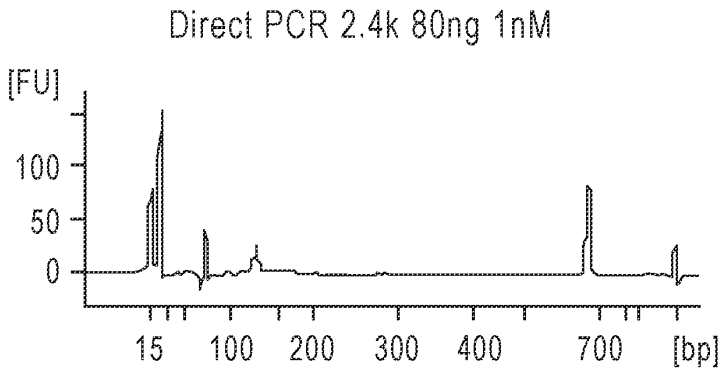


FIG. 28F

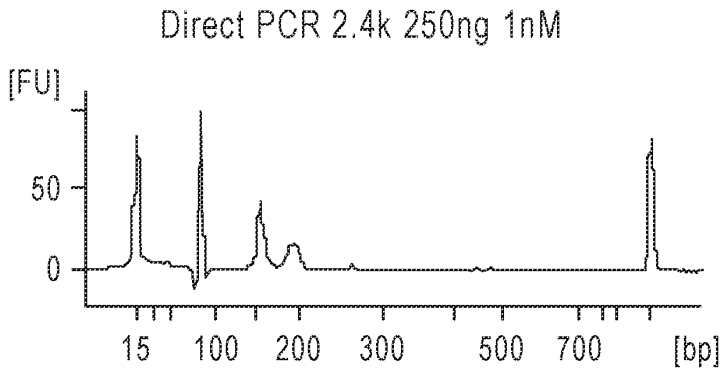


FIG. 28G

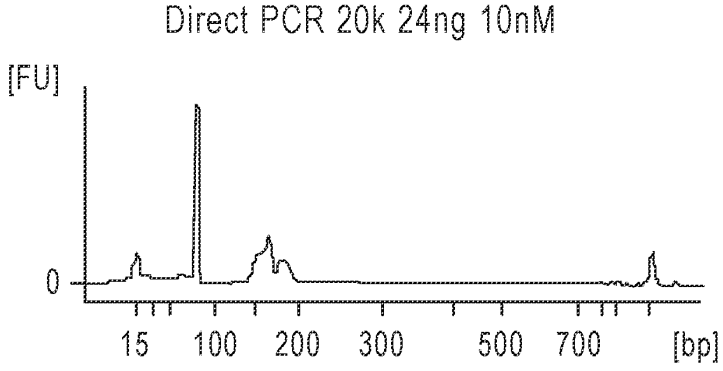


FIG. 28H

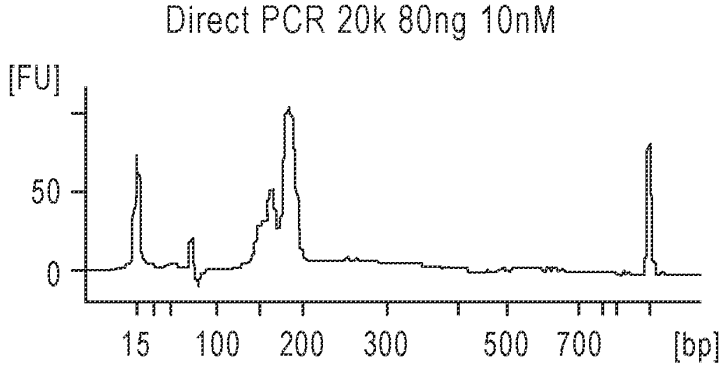


FIG. 28I

NeoGenomics
Exhibit 1003 Page 815

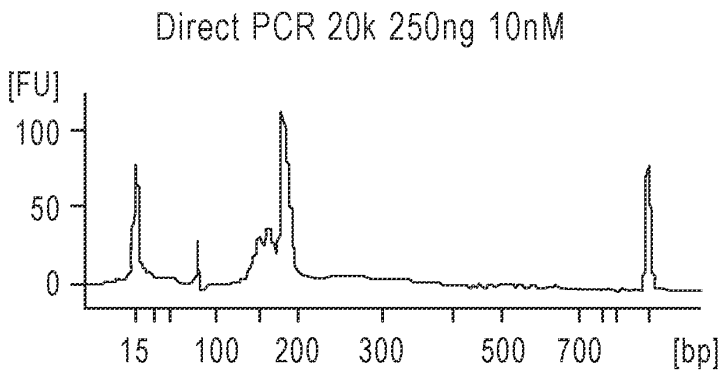


FIG. 28J

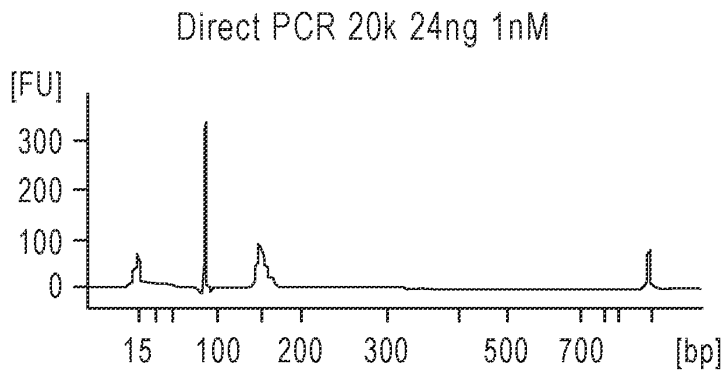


FIG. 28K

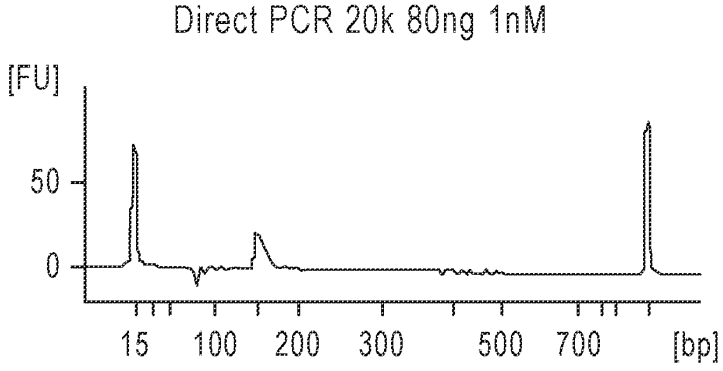


FIG. 28L

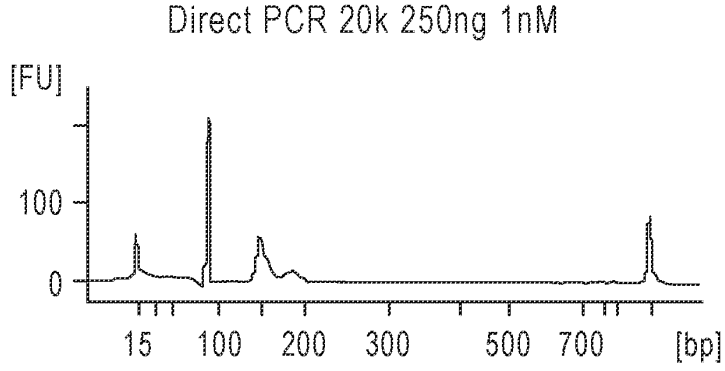


FIG. 28M

NeoGenomics
Exhibit 1003 Page 816

A
Maternal +/- Paternal Genotypic Data
Fetal + Fraction
B
Multiple Hypothesis for Each Chromosome
Crossover Frequency Data
C
Compare Predictions to Maternal Plasma Sequencing Data
D
Sum of Likelihood of Each Fetal Ploidy State
E
Correct Ploidy Call

FIG. 29

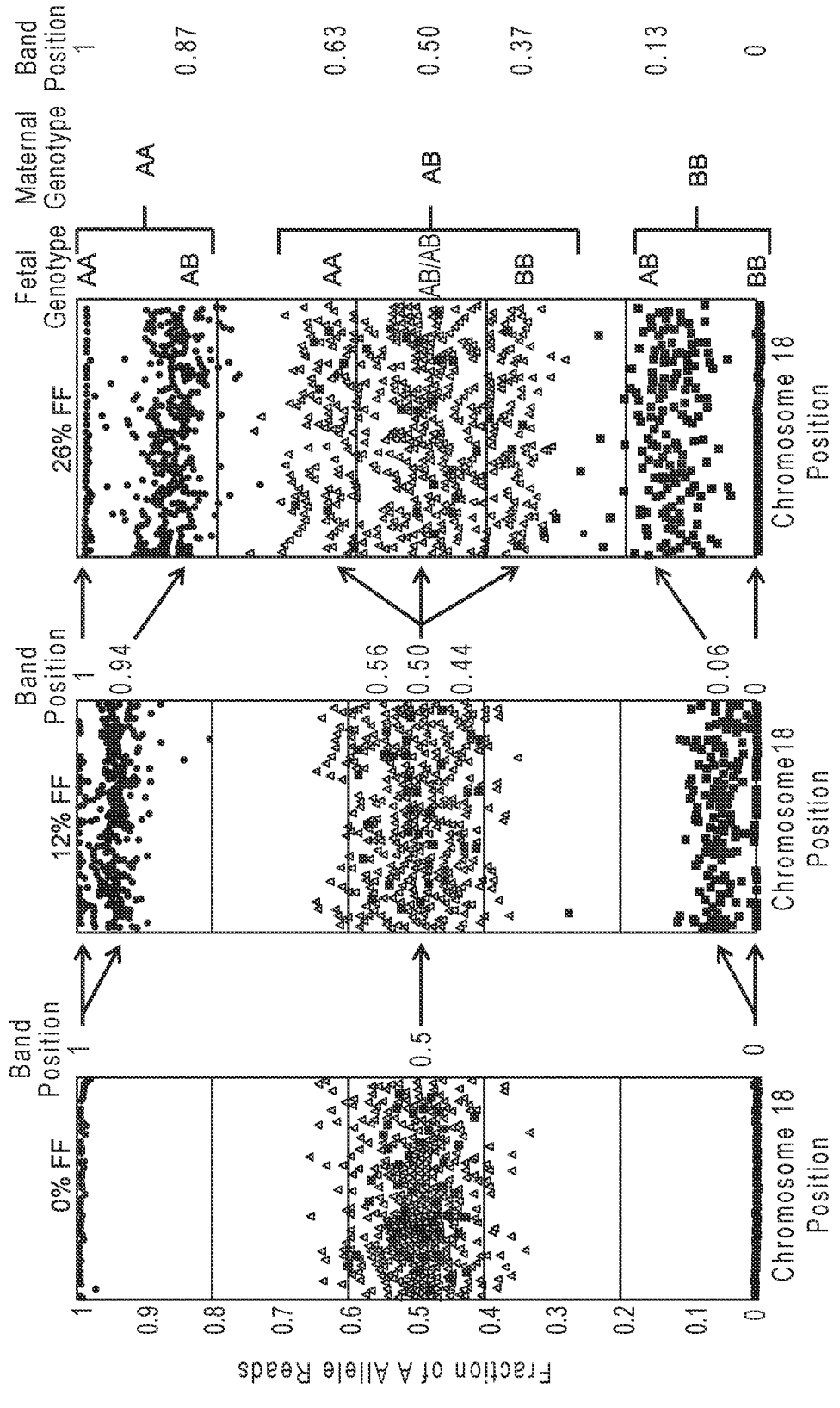

Fraction of A Allele Reads
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0% FF
12% FF
26% FF
Chromosome 18 Position
Band Position
1
0.5
0
0.94
0.56
0.50
0.44
0.06
Fetal Genotype
AA
AB
AB/AB
BB
Maternal Genotype
AA
AB
BB
0.87
0.63
0.50
0.37
0.13

FIG. 30

FIG. 30E

FIG. 30D

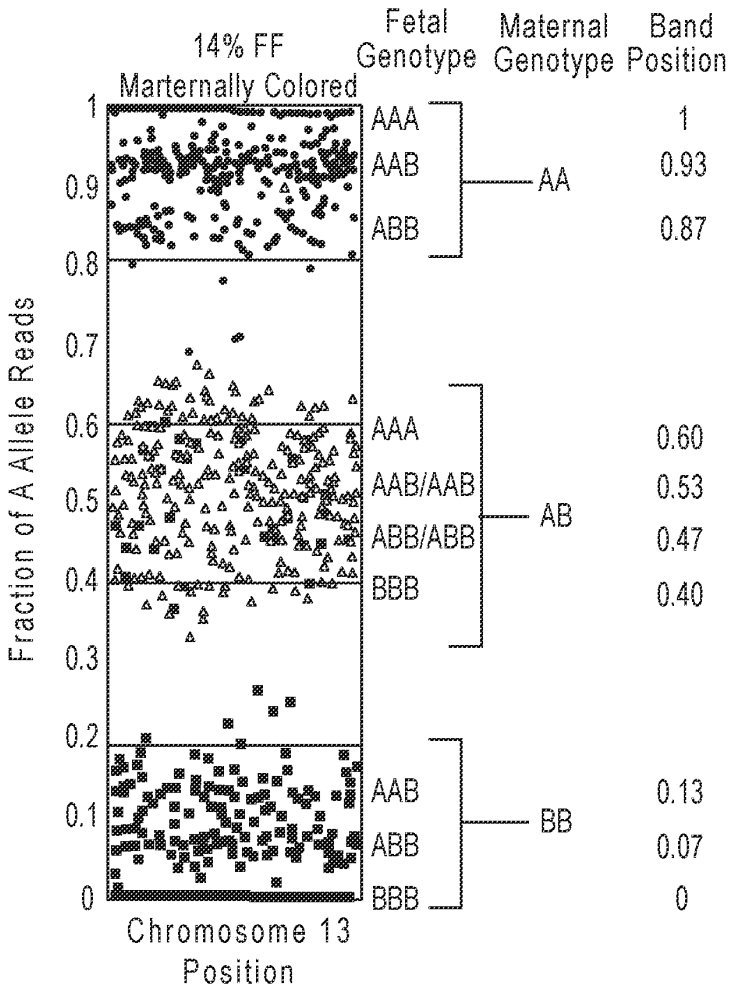


FIG. 30F

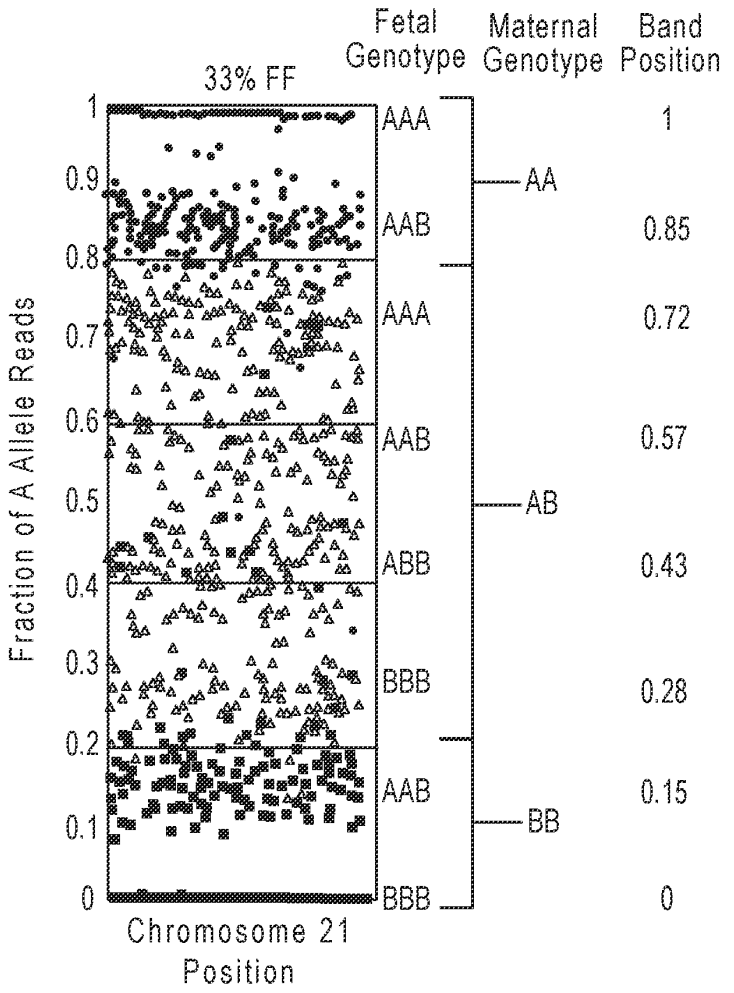


FIG. 30G

NeoGenomics
Exhibit 1003 Page 820

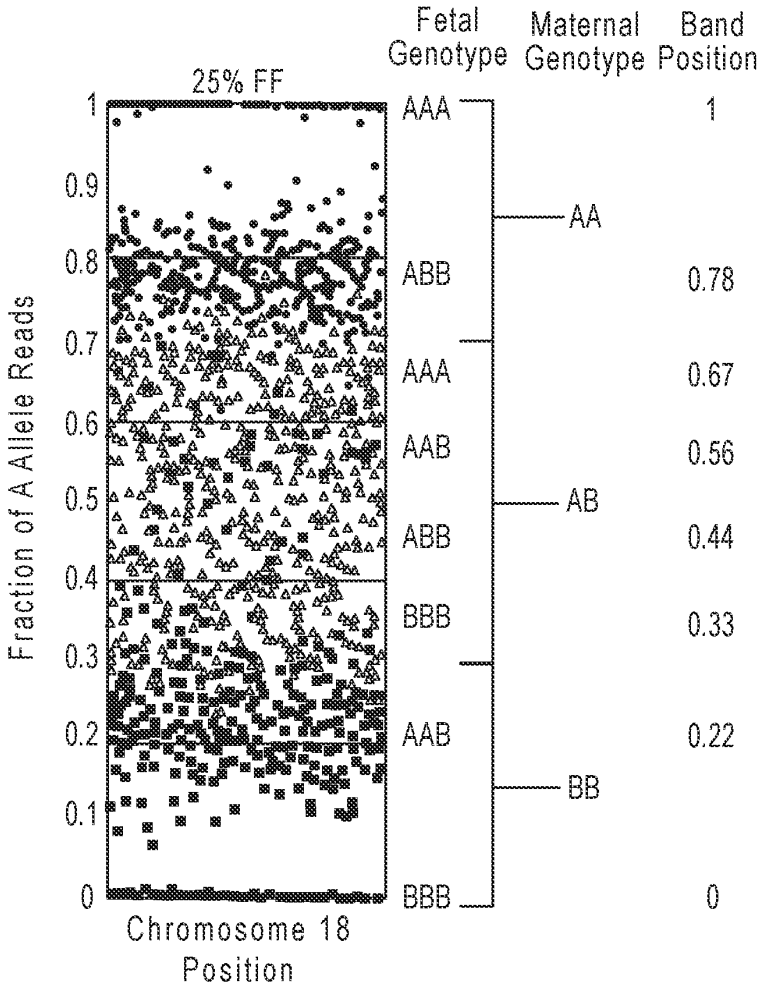

Fetal Genotype
Maternal Genotype
Band Position
25% FF
Fraction of A Allele Reads
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
AAA
ABB
AAA
AAB
ABB
BBB
AAB
BBB
AA
AB
BB
1
0.78
0.67
0.56
0.44
0.33
0.22
0
Chromosome 18 Position

FIG. 30H

FIG. 31A

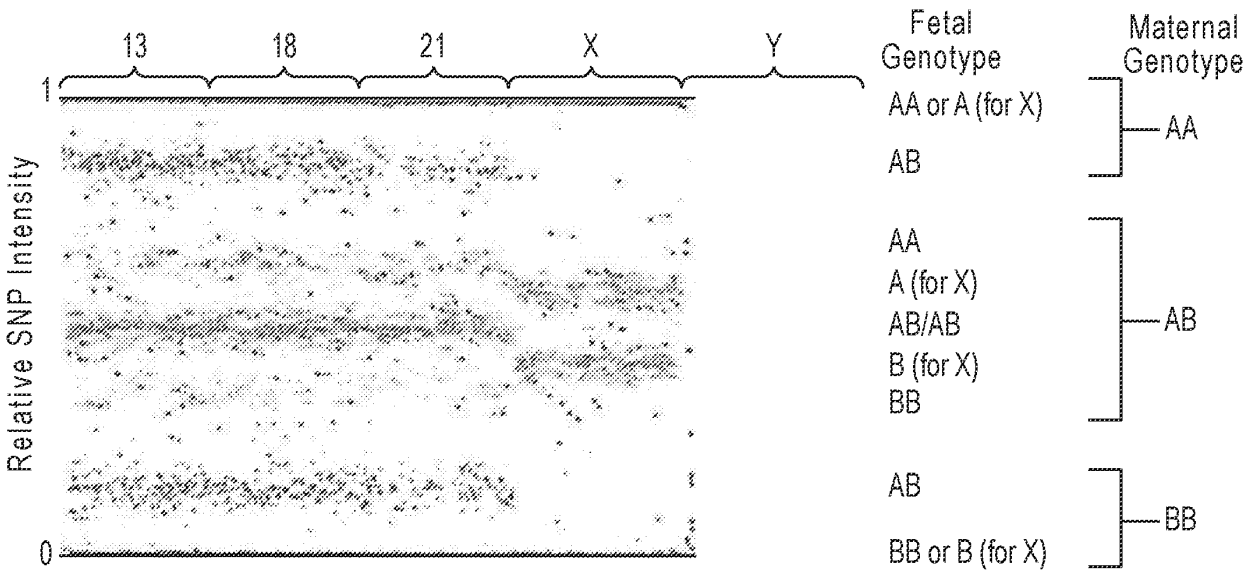
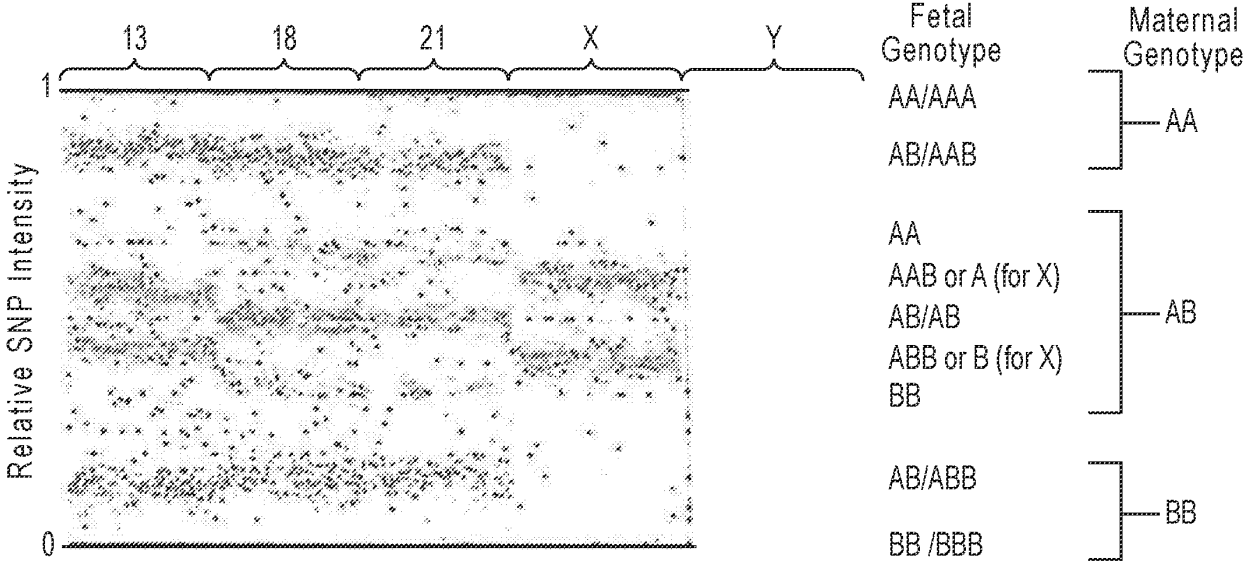


FIG. 31B



NeoGenomics
Exhibit 1003 Page 822

T13
13% FF
XY

FIG. 31C

T21
20% FF
XX

FIG. 31D

FIG. 31E

FIG. 31F

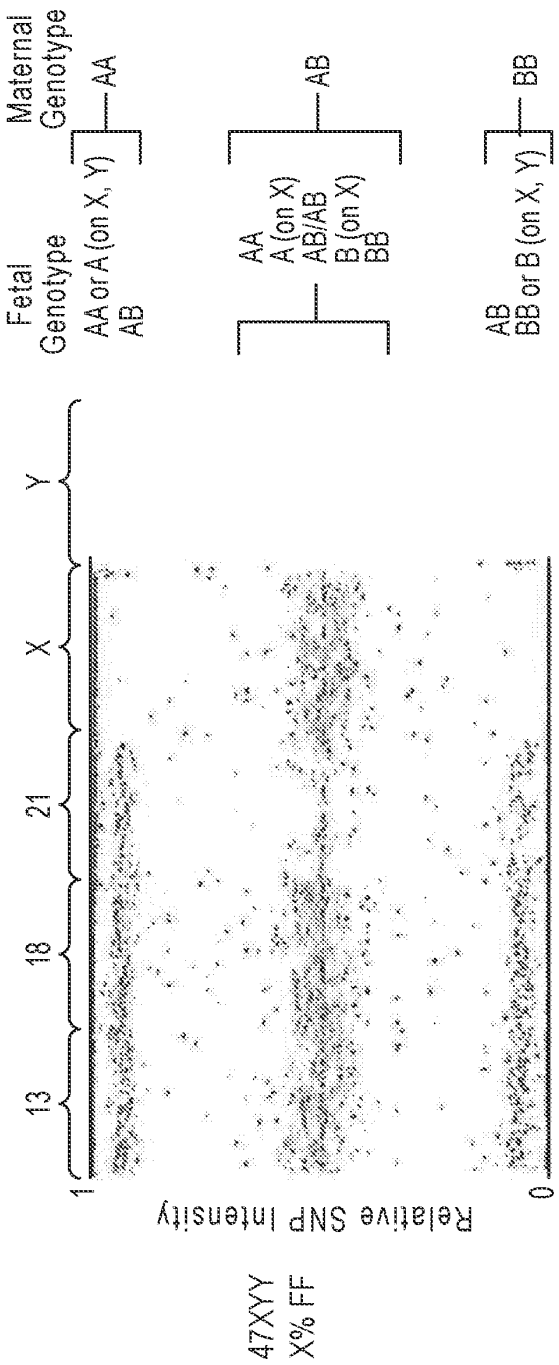

47XYY
X% FF
Relative SNP Intensity
1
0
13
18
21
X
Y
Fetal Genotype
AA or A (on X, Y)
AB
AA
A (on X)
AB/AB
B (on X)
BB
AB
BB or B (on X, Y)
Maternal Genotype
AA
AB
BB

FIG. 31G

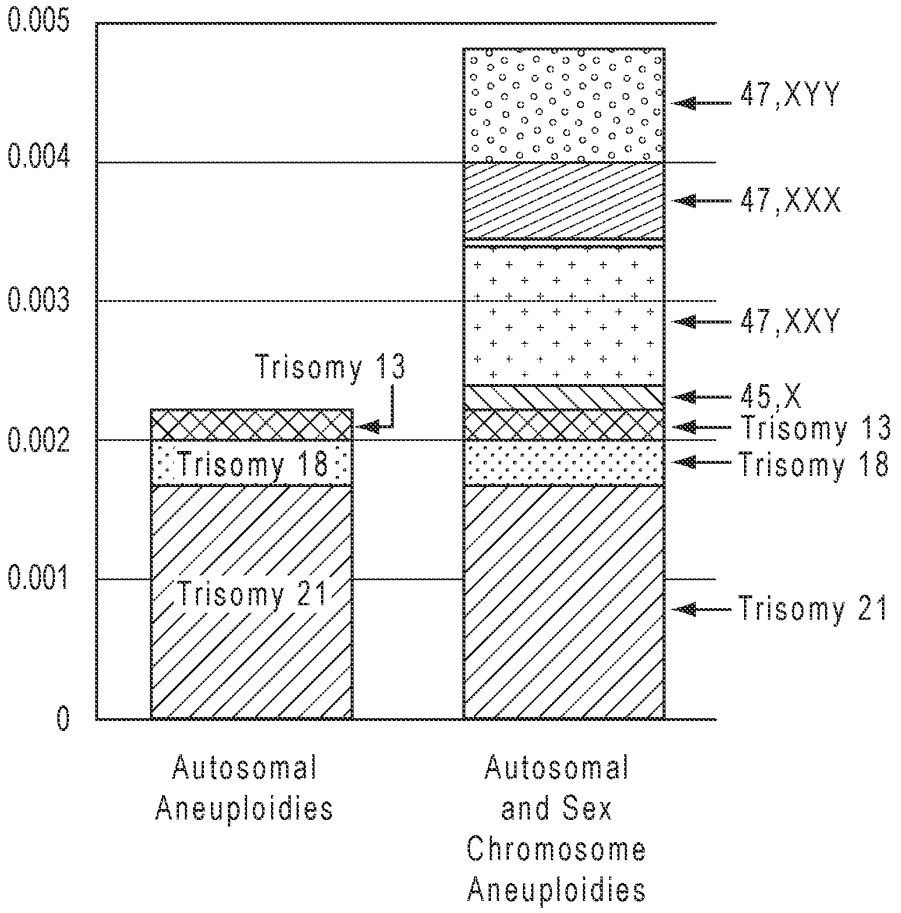

0.005
0.004
0.003
0.002
0.001
0
Trisomy 13
Trisomy 18
Trisomy 21
47,XYY
47,XXX
47,XXY
45,X
Trisomy 13
Trisomy 18
Trisomy 21
Autosomal Aneuploidies
Autosomal and Sex Chromosome Aneuploidies

FIG. 32

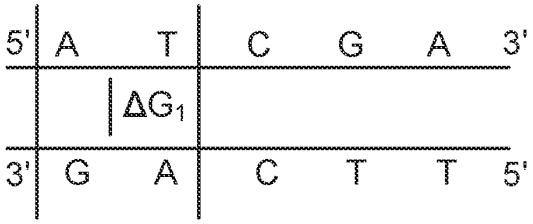
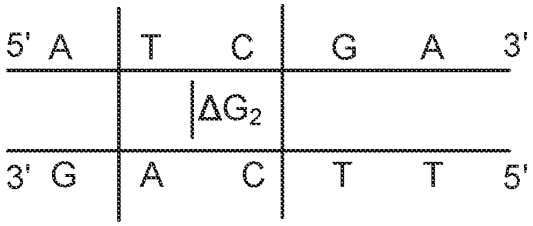


FIG. 33A



$$\Delta G = \Delta G_1 + \Delta G_2 + \ldots + \Delta G_x$$

FIG. 33B

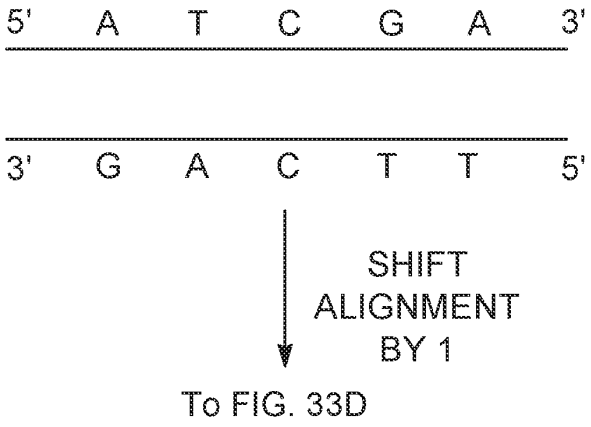


FIG. 33C

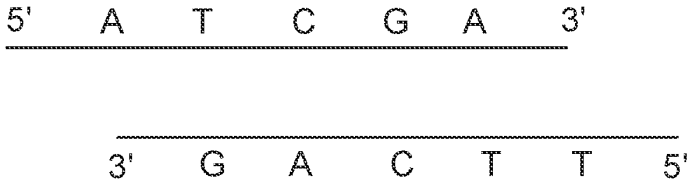


FIG. 33D

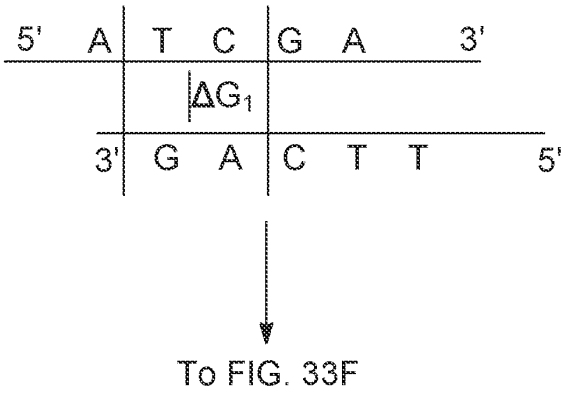


FIG. 33E

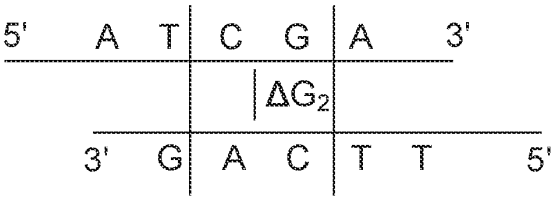


FIG. 33F

Description	MAPPED_READS	TOTAL_READS	%Mapped Reads
gMother	3,633,900	3,647,446	100%
gMother	3,567,685	3,578,549	100%
gMother	3,733,706	3,747,692	100%
gChild	3,725,554	3,737,742	100%
gChild	3,816,989	3,829,450	100%
gChild	3,524,956	3,536,569	100%
1 mother	3,467,493	7,564,869	46%
1 mother	3,868,210	7,107,028	54%
1 mother	4,918,140	7,613,240	65%
1 child	361,390	6,507,434	6%
1 child	1,885,864	6,496,348	29%
1 child	2,789,647	6,259,288	45%

FIG. 34

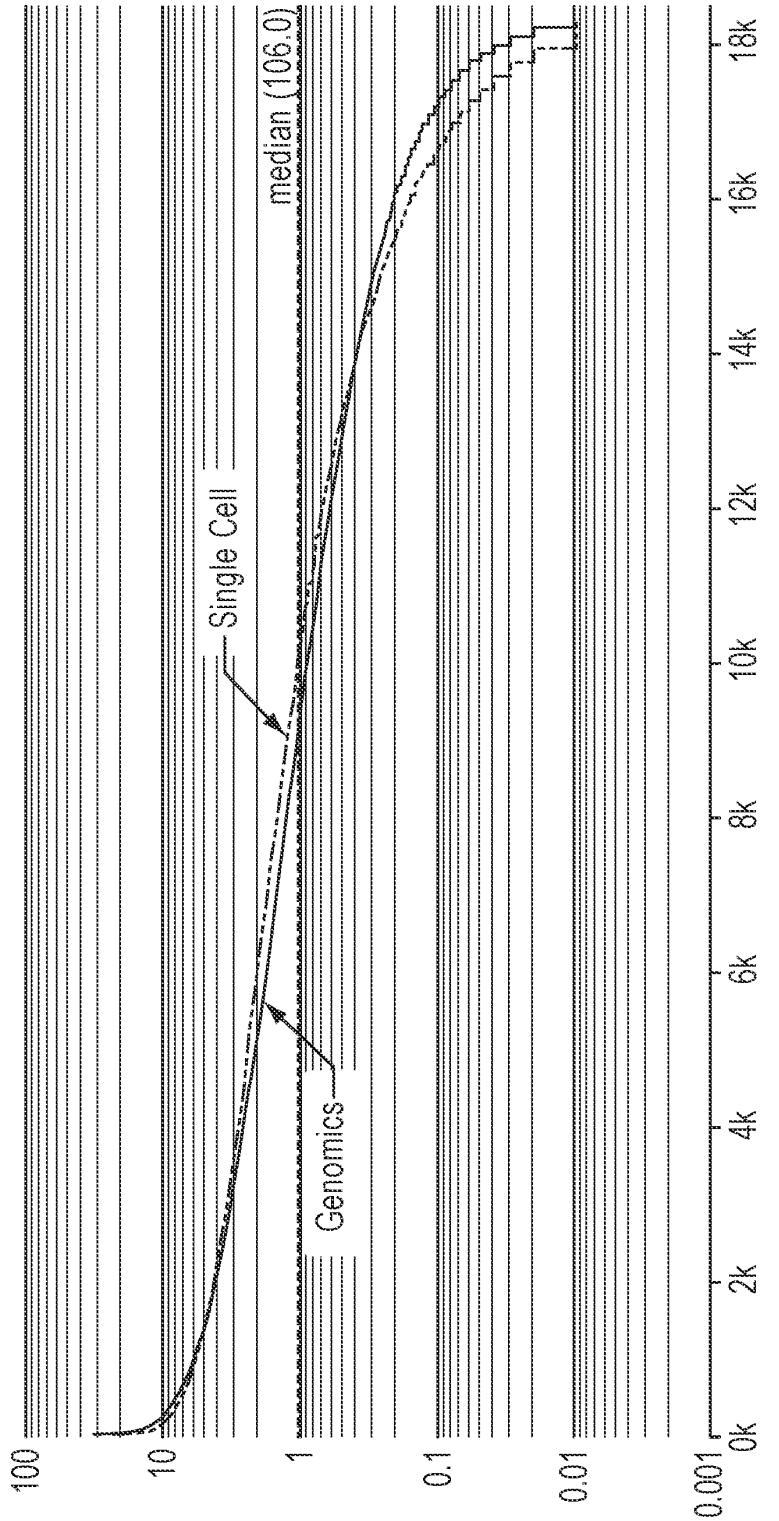

100
10
1
0.1
0.01
0.001
0k
2k
4k
6k
8k
10k
12k
14k
16k
18k
SNP INDEX
median (106.0)
Single Cell
Genomics

FIG. 35

Description	MAPPED_READS	TOTAL_READS	%Mapped Reads	
case 1 blastoceol	68,123	8,470,872	1%	
case 1 cell 1	4,340,613	8,248,598		53%
case 1 cell 2	5,480,580	8,230,870		67%
case 1 cell 3	4,664,577	7,846,040		59%
case 2 blastoceol	45,794	6,302,957	1%	
case 2 cell 1	6,988,854	8,622,495		81%
case 2 cell 2	7,083,600	8,843,495		80%
case 2 cell 3	5,811,364	8,256,310		70%

FIG. 36

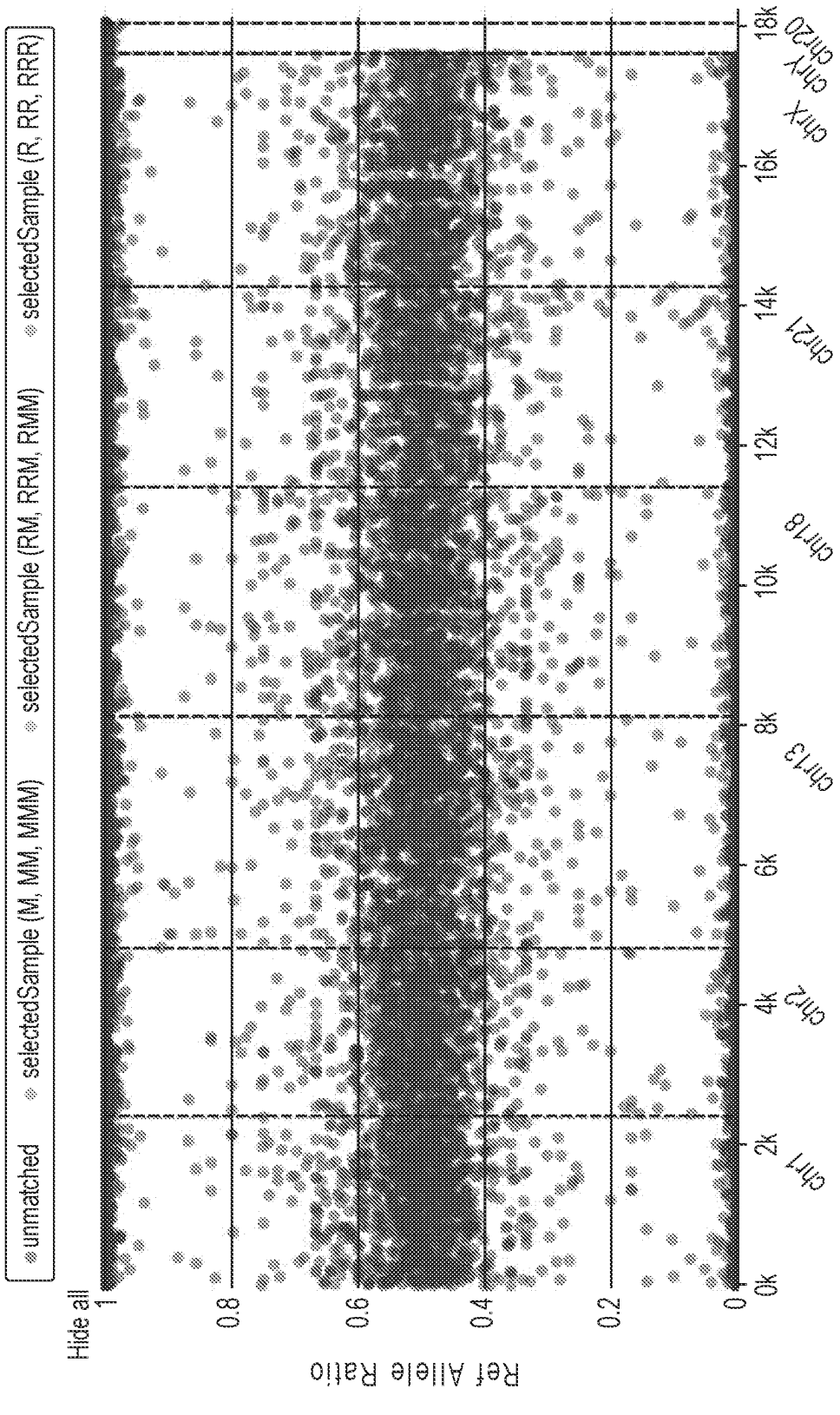

unmatched
selectedSample (M, MM, MMM)
selectedSample (RM, RRM, RMM)
selectedSample (R, RR, RRR)
Hide all
Ref Allele Ratio
1
0.8
0.6
0.4
0.2
0
0k
2k
4k
6k
8k
10k
12k
14k
16k
18k
chr1
chr2
chr13
chr18
chr21
chrX
chrY
chr20
Snp Index

FIG. 37

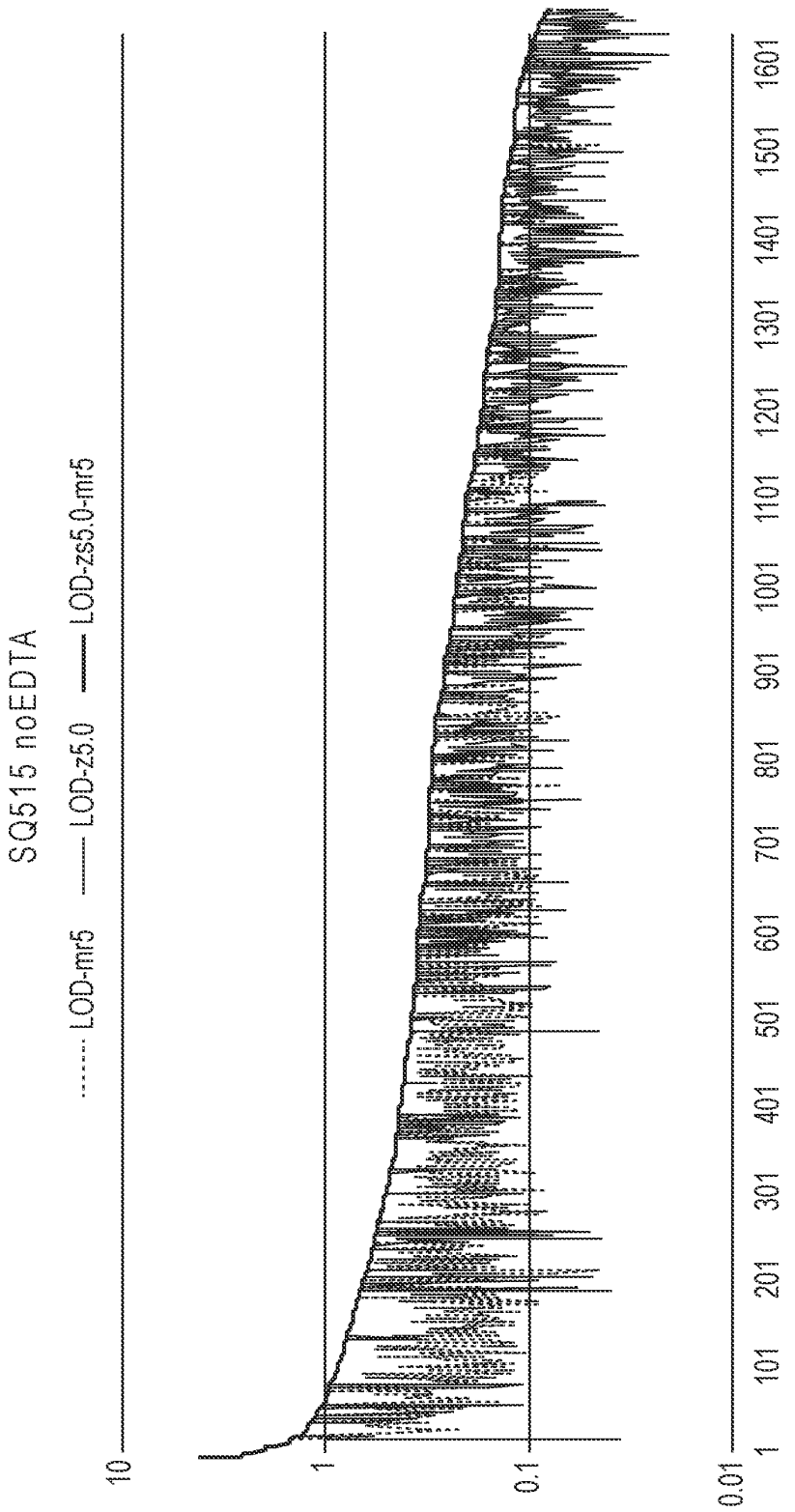

SQ515 noEDTA
LOD-mr5
LOD-z5.0
LOD-zs5.0-mr5
10
1
0.1
0.01
1
101
201
301
401
501
601
701
801
901
1001
1101
1201
1301
1401
1501
1601

FIG. 38

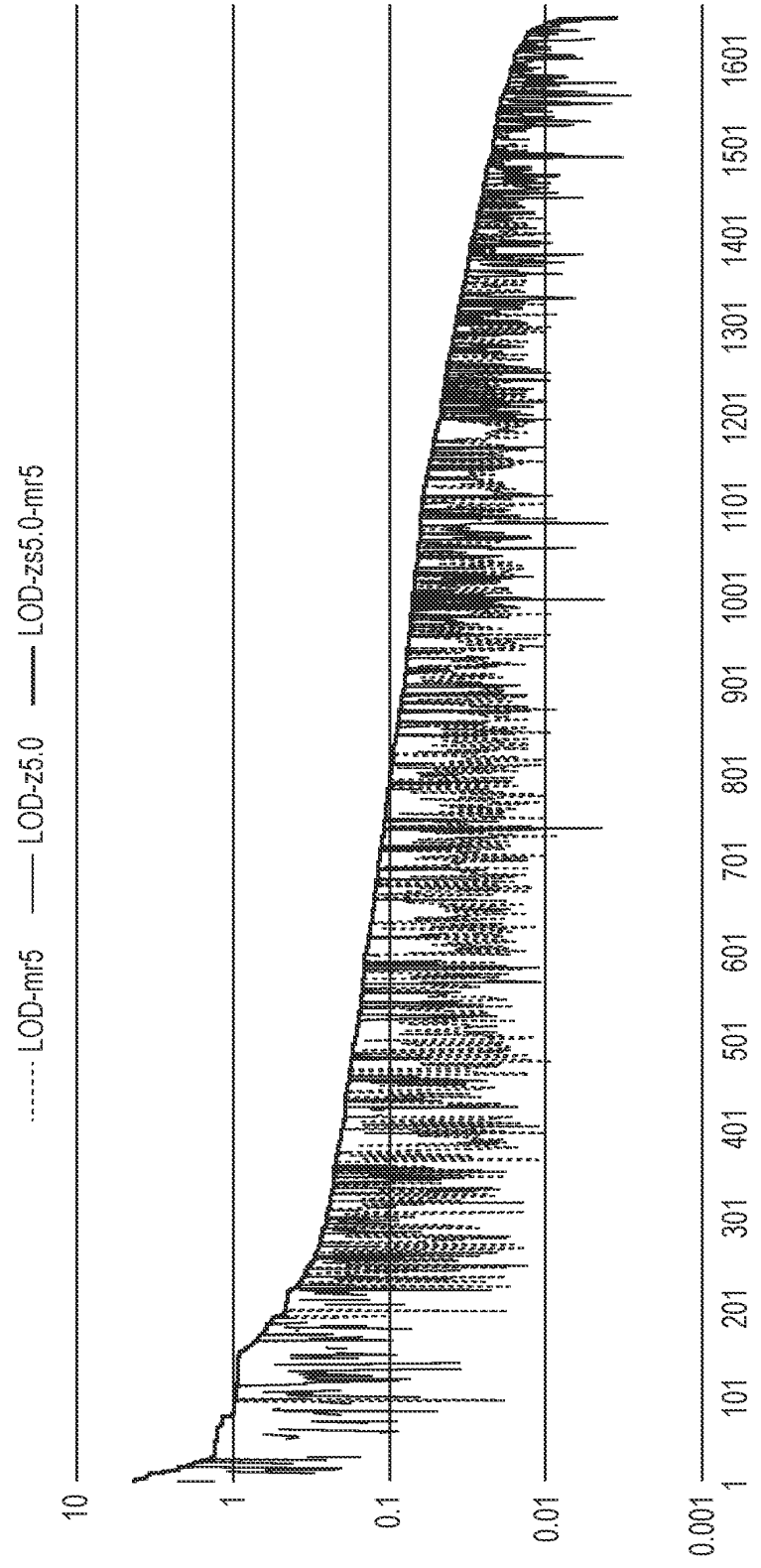

SQ589 noEDTA
LOD-mr5
LOD-z5.0
LOD-zs5.0-mr5
10
1
0.1
0.01
0.001
1
101
201
301
401
501
601
701
801
901
1001
1101
1201
1301
1401
1501
1601

FIG. 39

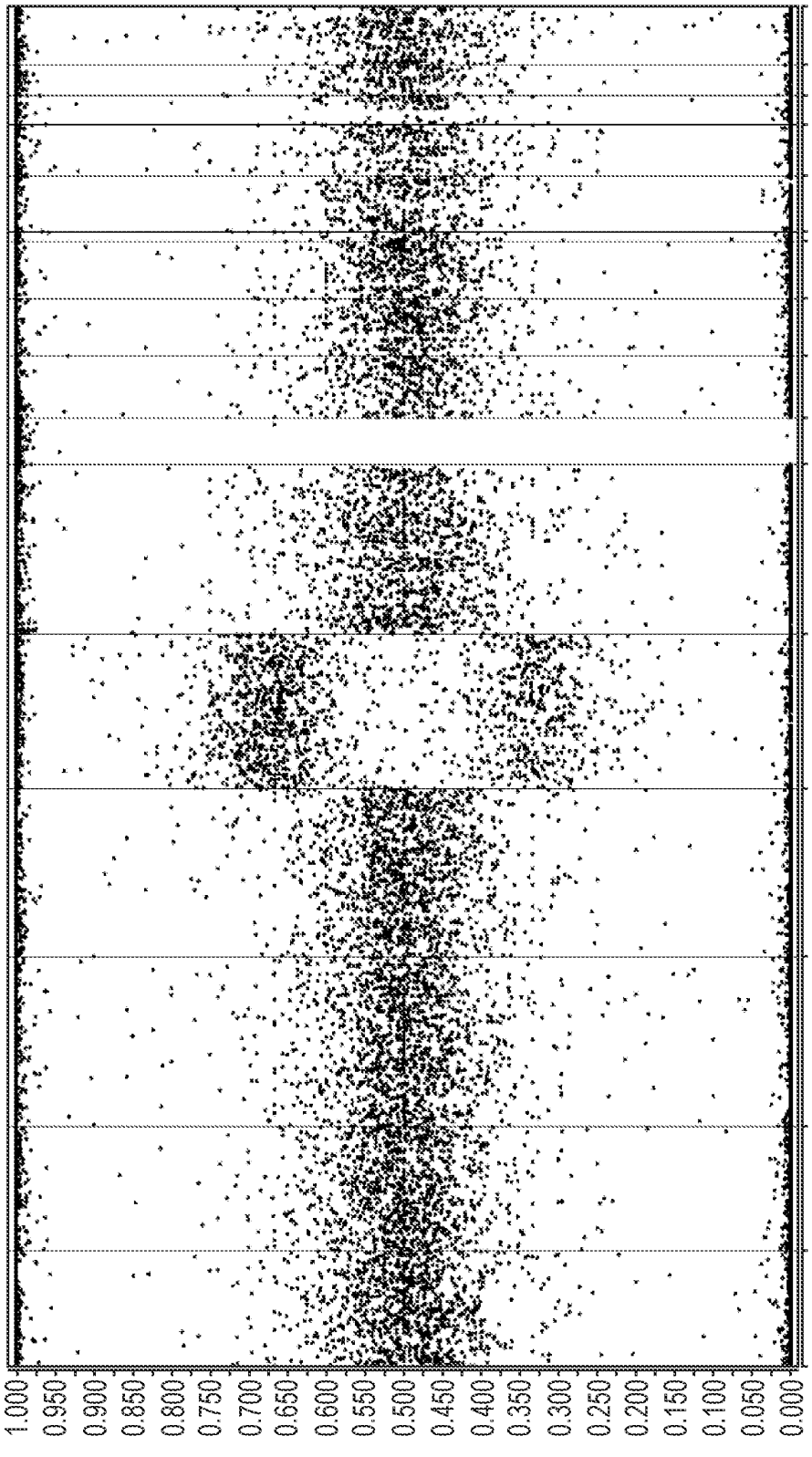

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
chr13
chr18
chr21
chrX
chr26
Genomics

FIG. 40A

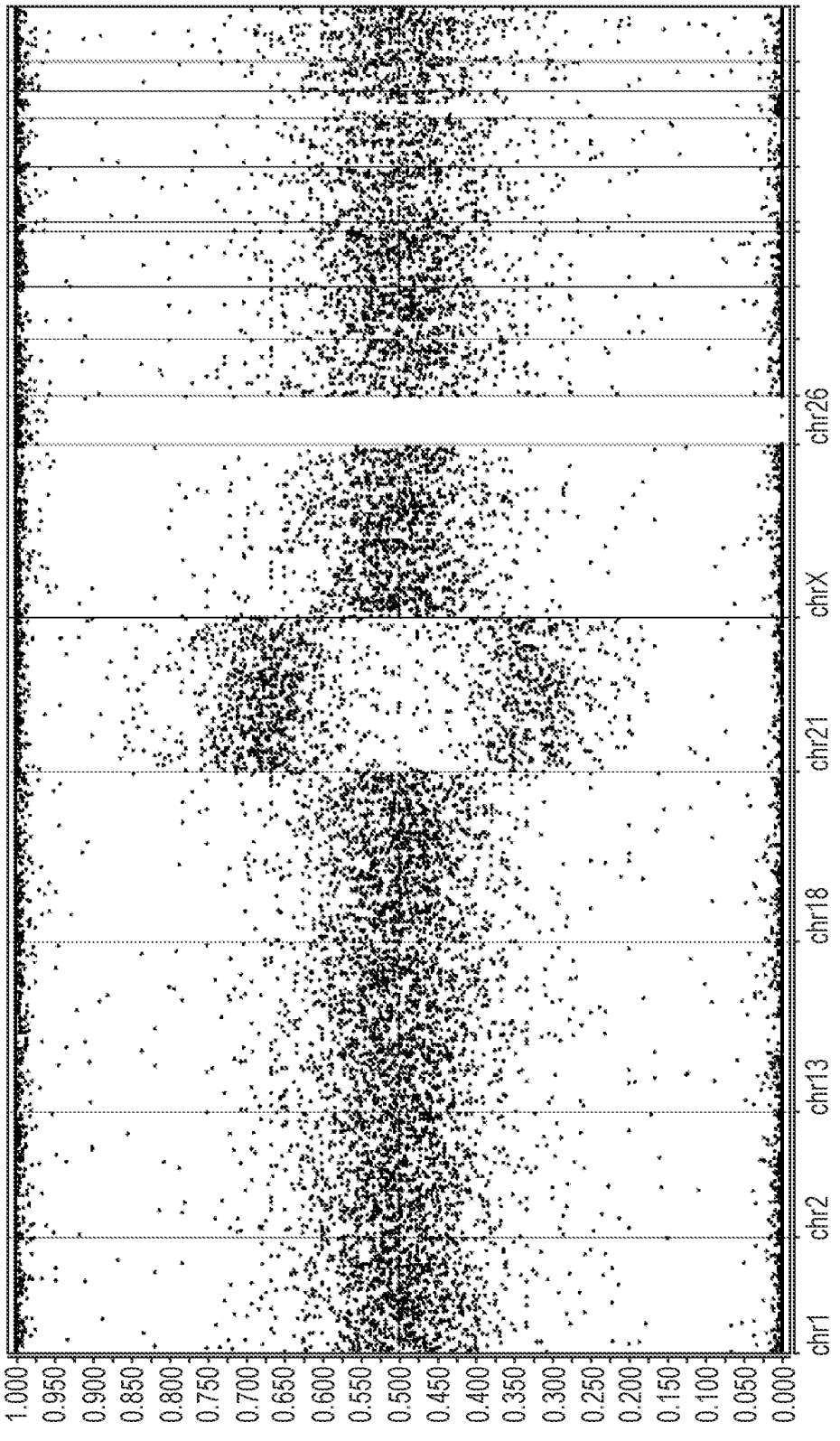

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
chr13
chr18
chr21
chrX
chr26
Single Cell

FIG. 40B

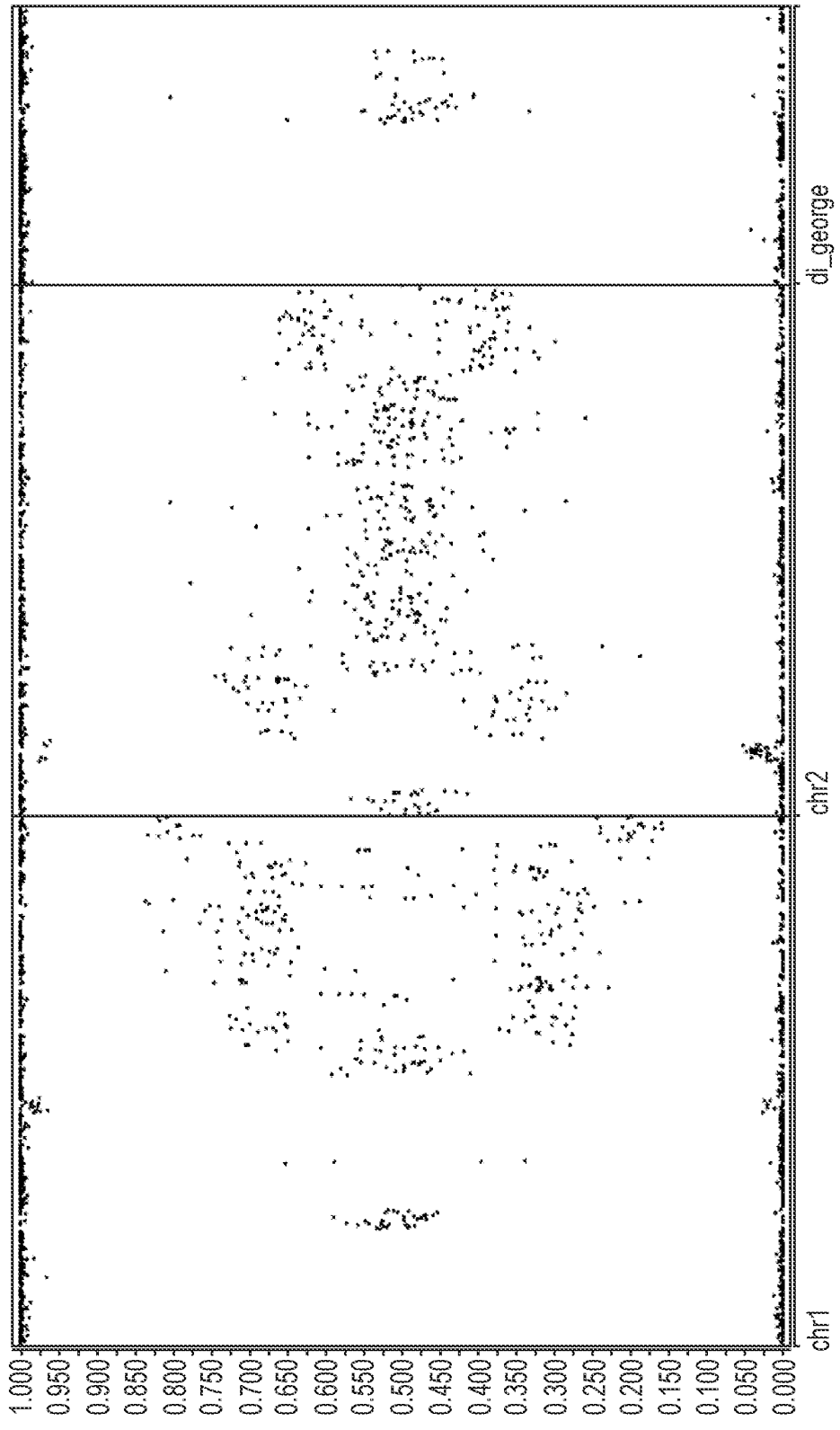
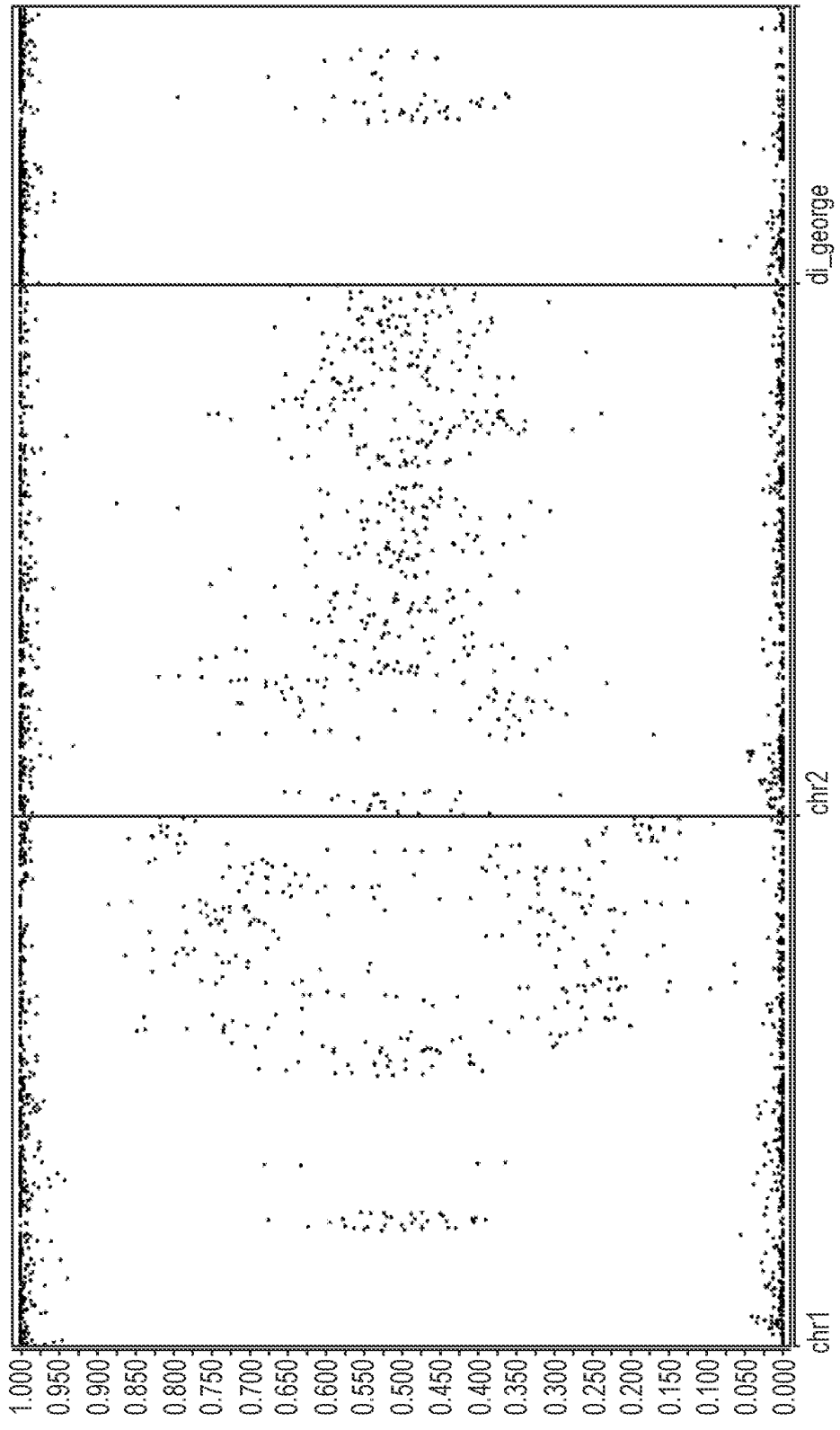

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
di_george
Genomics

FIG. 41A



Single Cell

FIG. 41B

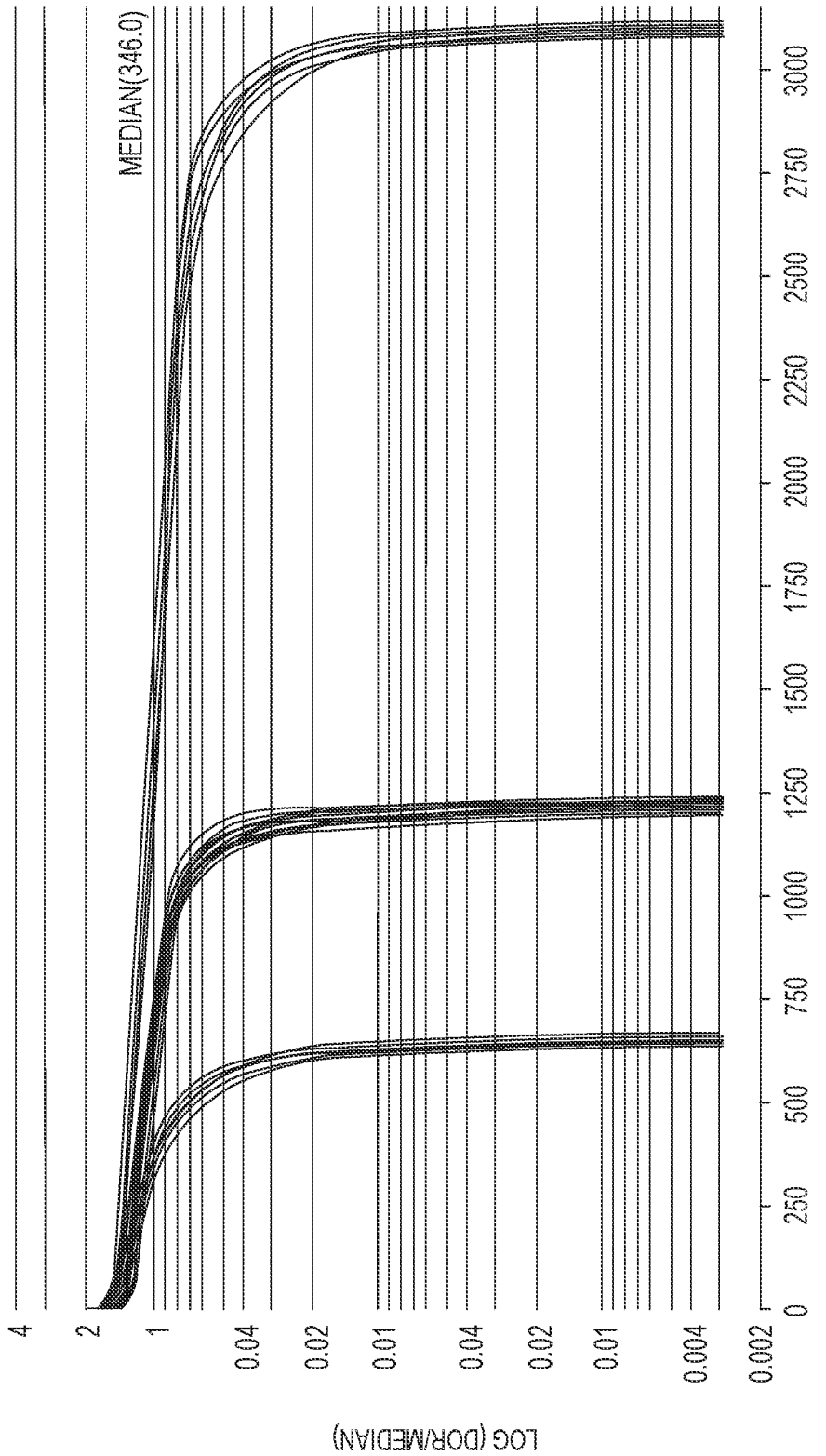

MEDIAN(346.0)
4
2
1
0.04
0.02
0.01
0.04
0.02
0.01
0.004
0.002
LOG (DOR/MEDIAN)
0
250
500
750
1000
1250
1500
1750
2000
2250
2500
2750
3000
SNP INDEX

FIG. 42

	gDNA	Single Cell
Count	75	510
Mean	0.15 %	0.51 %
Median	0.09 %	0.33 %
Max	1.03 %	10 %
Standard Deviation	0.16%	0.79 %
95th percentile	0.43 %	1.22 %
90th percentile	0.37 %	0.92 %

FIG. 43

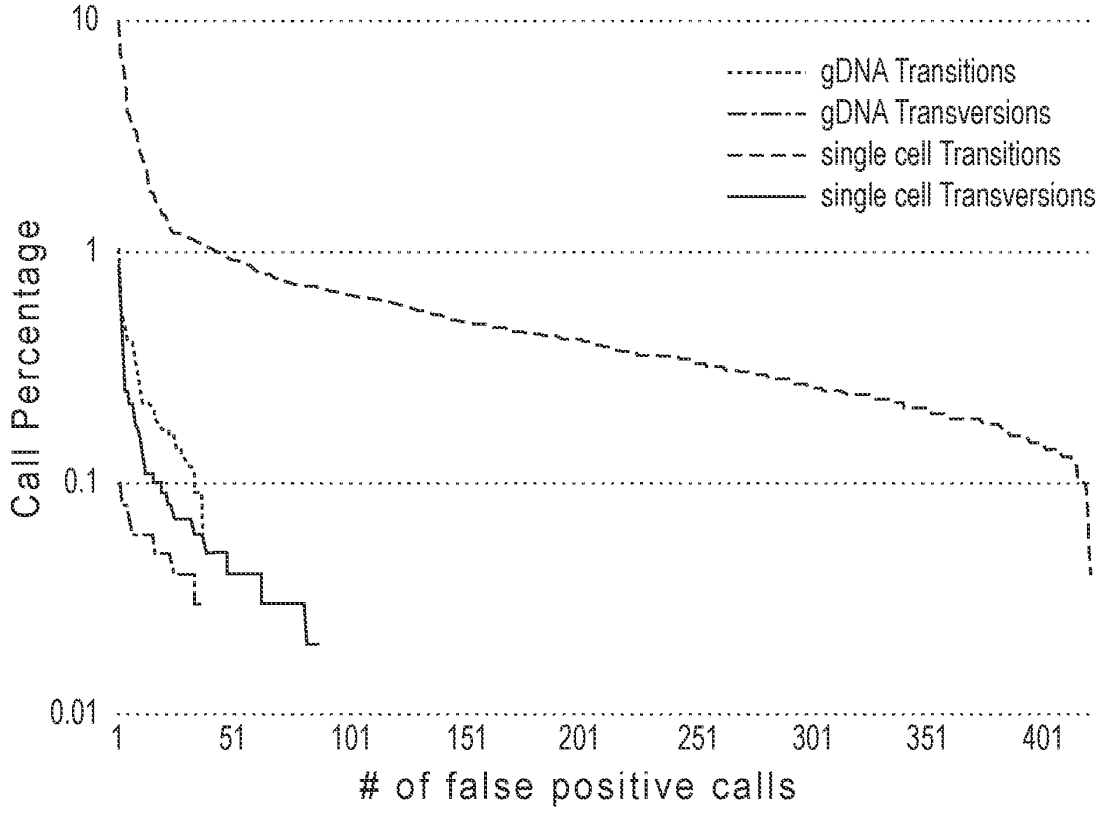


FIG. 44

DOE1	Mapped READS	TOTAL READS	% Mapped	Dropout Count	Median DOR All	NOR	Error Rate (%)
1xMM	1,112,007	1,262,558	80.0%	436	26.25	1,043,539	0.107%
2xMM	3,412,593	3,615,347	94.4%	105	147.75	3,206,478	0.141%
F-A	449,074	635,571	70.6%	1379	9.625	421,228	0.077%
F-B	3,293,944	3,519,378	93.7%	105	142.5	3,106,520	0.072%
F-D	4,028,128	4,109,448	98.0%	122	142.5	3,796,213	0.064%
F-J	3,676,617	3,922,330	93.7%	102	159.25	3,461,304	0.079%
F-A is : 25 mM Tris pH 7.8, 3 mM $MgCl_2$, **0 mM KCl, 10 mM $(NH_4)_2SO_4$, 50 U/mL Taq Gold** aka F-A Gold							
F-B is : 75 mM Tris pH 7.8, 6 mM $MgCl_2$, 0 mM KCl, 40 mM $(NH_4)_2SO_4$, 150 U/mL Taq Gold aka F-B Gold							
F-D is : 25 mM Tris **pH 8.2**, 3 mM $MgCl_2$, 30 mM KCl, 40 mM $(NH_4)_2SO_4$, 150 U/mL Taq Gold							
F-J is : 75 mM Tris pH 7.8, 6 mM $MgCl_2$, 0 mM KCl, 40 mM $(NH_4)_2SO_4$, 150 U/mL **Qiagen HS Taq** aka F-B Qiagen							

FIG. 45

NeoGenomics
Exhibit 1003 Page 842

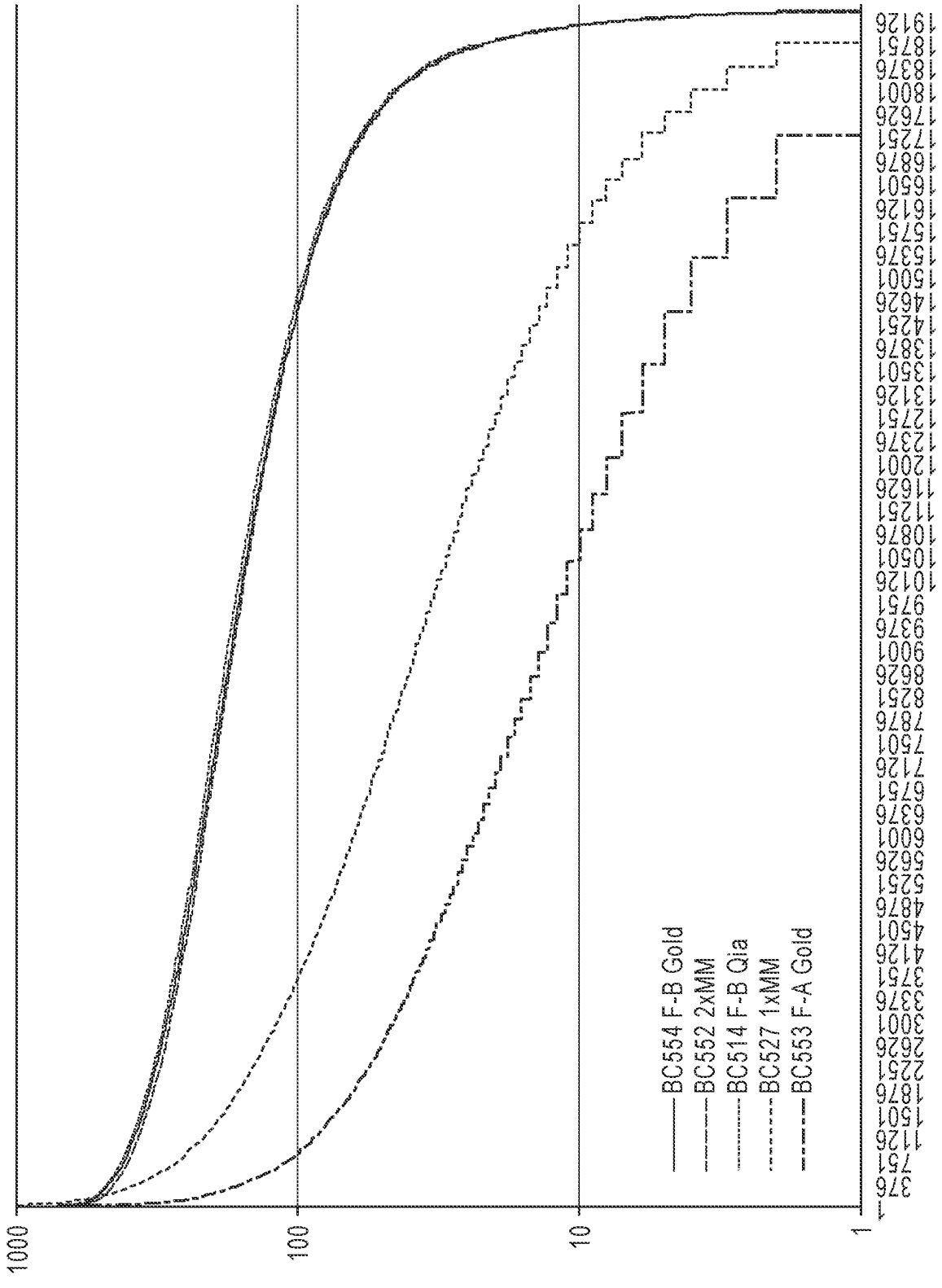

1000
100
10
1
BC554 F-B Gold
BC552 2xMM
BC514 F-B Qia
BC527 1xMM
BC553 F-A Gold

FIG. 46

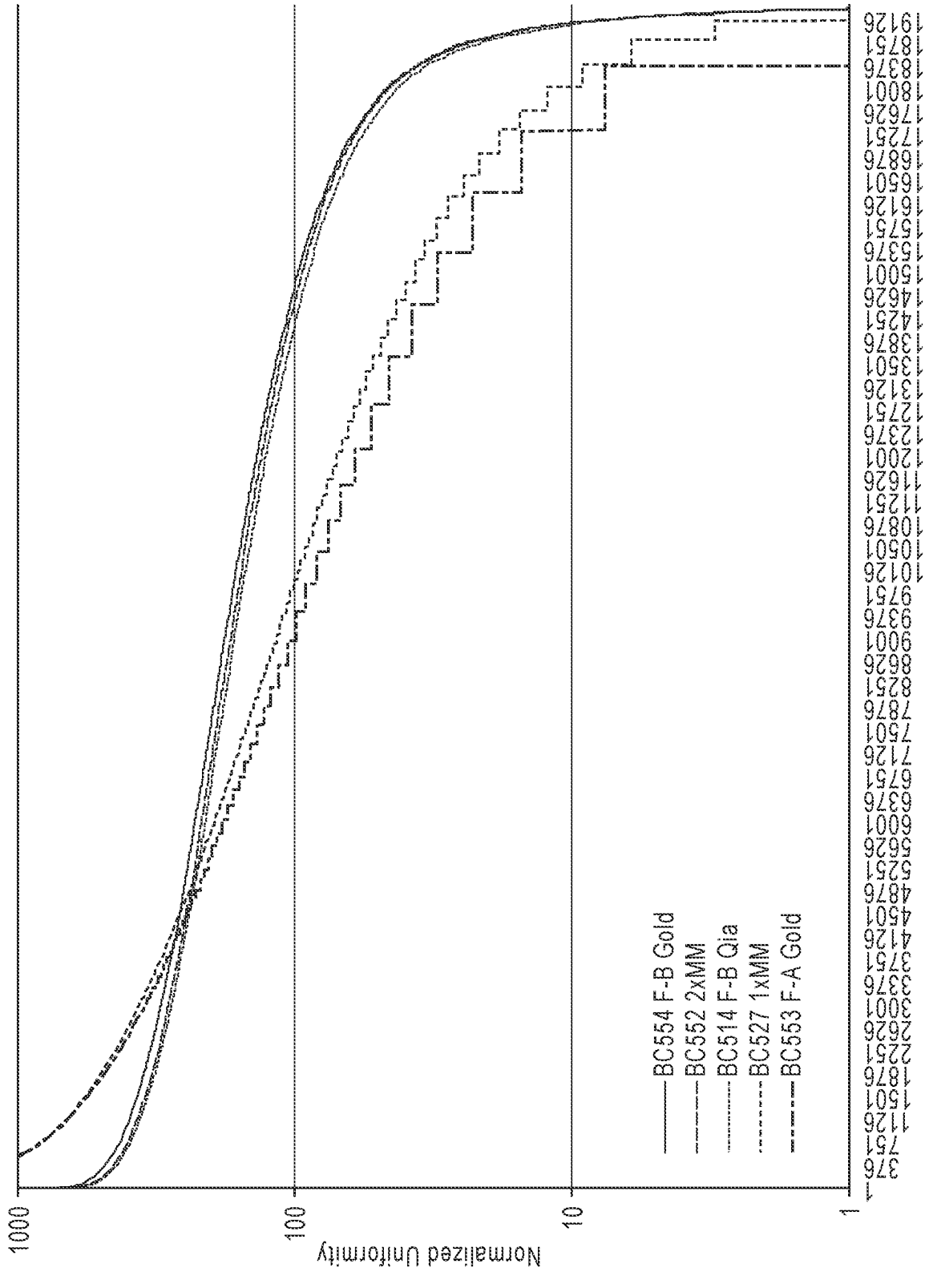

Normalized Uniformity
1000
100
10
1
BC554 F-B Gold
BC552 2xMM
BC514 F-B Qia
BC527 1xMM
BC553 F-A Gold

FIG. 47

Electronic Patent Application Fee Transmittal

Application Number:	16934407
Filing Date:	21-Jul-2020
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Filer:	Anton John Bokal/Angela McGowan
Attorney Docket Number:	N.012.US.32

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
		Total in USD ($)		**260**

Electronic Acknowledgement Receipt

EFS ID:	41278483
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	02-DEC-2020
Filing Date:	21-JUL-2020
Time Stamp:	18:04:39
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$260
RAM confirmation Number	E2020B2I05100452
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		01_N012US32_Response_to_Non_Final_Office_Action_dated_16SEPT2020_SIGNED.pdf	58611 2da1909f490757af32f8be057305bdfa6be7f2ea	yes	10

Multipart Description/PDF files in .zip description

Document Description	Start	End
Applicant Arguments/Remarks Made in an Amendment	6	10
Drawings-only black and white line drawings	5	5
Claims	2	4
Amendment/Req. Reconsideration-After Non-Final Reject	1	1

Warnings:

Information:

2	Information Disclosure Statement (IDS) Form (SB08)	03_N012US32_SB08_SIGNED.pdf	94278 9dba89562da9cb9a5750621a337b3c2352f67e0d	no	6

Warnings:

Information:

This is not an USPTO supplied IDS fillable form

3	Foreign Reference	WO2007073171A2.pdf	1096739 49a095580df21c1d2cd8c5e41d0dc6fa3358a20a	no	61

Warnings:

Information:

4	Foreign Reference	WO2010127186A1.pdf	1077269 f013230545d13ee9caca6979edebec9ec2fdf68d	no	65

Warnings:

Information:

5	Foreign Reference	WO2011051283A1.PDF	1750555 70a440764689ac90bff3f7e534a32aa590e6422f	no	46
Warnings:					
Information:					
6	Foreign Reference	WO2018136562A2.pdf	1806241 a791bb58bbb29a7852c68861f4d149b0b9d65653	no	159
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Information:					
7	Foreign Reference	WO2019046817A1.pdf	1120849 446c8b11442e2d324acd890b4cdb9d15a24292f9	no	107
Warnings:					
Information:					
8	Foreign Reference	WO2020214547A1.pdf	3752719 24c95182cc6b8e1459626b6f464ea5e46c31d79c	no	78
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Information:					
9	Non Patent Literature	BASHASHATI_2013_p21_NPL.pdf	1914753 352d83c46e86a43bd493485b02397bc605aab400	no	14
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10	Non Patent Literature	BINLADEN_2007_9pgs_NPL.PDF	832428 ee1a1528689c5fa002c641c48d97acdaf624c529	no	9
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11	Non Patent Literature	DE_JONG_2009_p225_NPL.pdf	3303804 dbe954e19ea5c28a1cd6db42758ba9a78b7a08fb	no	18
Warnings:					
Information:					

12	Non Patent Literature	FAHAM_2012_p5173_NPL.pdf	648814 6199ccf946a7826b17dc50521c7bf5eee0be4c1c	no	8
Warnings:					
Information:					
13	Non Patent Literature	GAO_2013_8pgs_NPL.PDF	1576699 9ff0039b034068b365b201868d511f73e64ff6e6	no	8
Warnings:					
Information:					
14	Non Patent Literature	GNIRKE_2009_p182_NPL.PDF	776585 2ed780445427bde28a494c41940819d2b259b3b8	no	8
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Information:					
15	Non Patent Literature	HODGKINSON_2014_p897_NPL.pdf	1533604 1d9fe5e9175288c17868ddeb772853578f1f90b9	no	9
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16	Non Patent Literature	HOU_2016_p651_NPL.pdf	6363093 8f823944e8439d230e95d40480f2953237faebdb	no	17
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18	Non Patent Literature	KELLER_2009_p1823_NPL.pdf	563382 de932bc242ab246b81a16d76491717db700d0cee	no	4
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19	Non Patent Literature	KUKITA_2015_p269_NPL.pdf	802136 98eed6bebc4703f5dc13dd569c410aad329c2eb2	no	9
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20	Non Patent Literature	SCARPA_2013_6pgs_NPL.pdf	861299 a3eb1cddd623042ab50048ea6fffe38a125a3017	no	6
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21	Non Patent Literature	SHORT_2020_p1670_NPL.pdf	831082 7684eef428eb8e8db15cd11565bd0b1b1c30473b	no	8
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22	Non Patent Literature	SIEBERT_1995_p1087_NPL.pdf	468473 bc3719cb197f3ae15925a808f9c3802b461f181d	no	2
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Warnings:					
Information:					
24	Non Patent Literature	ZHOU_2002_p219_NPL.PDF	821351 5a954530bcd2e70297a40bb79a971ed7065d4b90	no	7
Warnings:					
Information:					
25	Drawings-other than black and white line drawings	02_N012US32_Replacement_Drawings.pdf	1968283 5da4d97f84236802255cbcce7ccda2f3138b109f	no	58
Warnings:					
Information:					

26	Fee Worksheet (SB06)	fee-info.pdf	30600 dce732ae5e73e9969b943c0c646774806a685637	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	35525224	

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New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

Amendments to the Claims:

This listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

1. (**Currently Amended**) A method for amplifying and sequencing DNA, comprising:

tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject;

amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplification steps comprises targeted amplification of a plurality of single nucleotide polymorphism (SNP) loci, wherein one of the amplifying steps introduces a barcode and one or more sequencing tags; and

sequencing [[a]]the plurality of SNP loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of SNP loci comprises 25-2,000 loci.

2. (**Currently Amended**) The method of claim 1, wherein ~~the~~ tagging the cell free DNA comprises ligating the one or more universal tail adaptors to the cell free DNA.

3. (Original) The method of claim 2, wherein the one or more universal tail adaptors each comprise a first strand and a second strand, wherein a first end of each of the universal tail adaptors comprises a double-stranded section comprising the 5' portion of the first strand and the 3' portion of the second strand, wherein the first end is ligated to the cell free DNA.

4. (**Currently Amended**) The method of claim 3, wherein ~~the~~ amplifying the tagged products comprises a first amplifying step and a second amplifying step, wherein the first amplifying step comprises using a first target-specific primer that specifically anneals to a target

sequence and a first adaptor primer having a nucleotide sequence identical to a first portion of the first strand to generate a first amplification product.

5. (**Currently Amended**) The method of claim 4, wherein the second amplifying step comprises using a second target-specific primer that specifically anneals to the first amplification product and a second adaptor primer having a nucleotide sequence identical to a second portion of the first strand to generate the final amplification product.

6. (Original) The method of claim 5, wherein the second adaptor primer is nested relative to the first adaptor primer.

7. (Original) The method of claim 6, wherein the second target-specific primer comprises an index tag.

8. (**Currently Amended**) The method of claim 7, wherein the second amplifying step further comprises using an index primer comprising a sequence complementary to the index tag.

9. (Original) The method of claim 8, wherein the index primer comprises the barcode and a first sequencing tag.

10. (Original) The method of claim 1, wherein the one or more universal tail adaptors comprise a second barcode.

11. (Original) The method of claim 1, wherein the one or more universal tail adaptors comprise a second sequencing tag.

12. (Original) The method of claim 1, wherein the one or more universal tail adaptors comprise a first universal tail adaptor and a second universal tail adaptor.

13. (**Currently Amended**) The method of claim 12, wherein ~~the~~ tagging the cell free DNA comprises amplifying the cell free DNA with a first primer comprising the first universal tail adaptor and a second primer comprising the second universal tail adaptor.

14. (**Currently Amended**) The method of claim 12, wherein ~~the~~ amplifying the tagged products comprises a single amplifying step.

15. (**Currently Amended**) The method of claim 14, wherein ~~the~~ amplifying the tagged products comprises using a third primer and a fourth primer, wherein the third primer comprises a first sequencing tag and wherein the fourth primer comprises a second sequencing tag.

Amendments to the Drawings:

The drawing sheet attached in connection with the above-identified application containing Figure 12 is being presented to be substituted for the previously submitted drawing sheet or sheets. The drawing Figure 12 has been amended. Appended to this amendment is an annotated copy of the previous drawing sheet which has been marked to show changes presented in the replacement sheet of the drawing.

The specific changes which have been made to Figure 12 are addition of the required sequence identifiers.

NeoGenomics
Exhibit 1003 Page 856

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

Status of Claims

Claims 1-15 were pending in the subject case. With this submission, claims 1, 2, 4, 5, 8, and 13-15 are amended to more clearly and particularly describe the claimed invention. Support for the amendments to claim 1 can be found in the as-filed specification at paragraphs 0349 and 0364. No new matter has been introduced. Upon entry of the foregoing amendments, claims 1-15 will remain pending in this application.

Claim Rejection under 35 U.S.C. 112

Claims 4, 5, 8, and 13-15 are rejected under 35 U.S.C. 112, second paragraph, for alleged indefiniteness. For the sole purpose of expediting prosecution and without acquiescing to the rejection, Applicant has amended claims 4, 5, 8, and 13-15 pursuant to the Examiner's suggestion on page 2 of the Office Action, thereby resolving the issue. Accordingly, Applicant respectfully requests withdrawal of the subject rejection.

Sequence Compliance

The Office Action states "Figure 12 includes nucleic acid sequences that are 10 or more nucleotide residues in length and require corresponding sequence identifiers (SEQ ID Nos)." A replacement sheet of Figure 12 is submitted herewith to resolve the issue. Accordingly, Applicant respectfully requests withdrawal of the subject rejection.

Double Patenting

Claims 1 and 2 are rejected on the ground of nonstatutory double patenting as allegedly being unpatentable over claims 1, 3, 5 and 22 of U.S. Pat. No. 10,731,220. Claims 1 and 2 are rejected on the ground of nonstatutory double patenting as allegedly being unpatentable over

claims 1, 3-4 and 22 of U.S. Pat. No. 10,538,814. Claims 1-2 and 6 are rejected on the ground of nonstatutory double patenting as allegedly being unpatentable over claims 1, 3-4 and 22 of U.S. Pat. No. 10,557,172.

For the sole purpose of expediting prosecution, Applicant submits herewith a terminal disclaimer over U.S. Pat. Nos. 10,731,220, 10,538,814, and 10,557,172 to overcome the subject rejection. Accordingly, Applicant respectfully requests withdrawal of the subject rejection.

Claim Rejection under 35 U.S.C. 102

Claims 1-5 and 10-15 are rejected under 35 U.S.C. 102 for allegedly being anticipated by US 2010/0112575 ("Fan"). Applicant respectfully traverses this rejection.

For the sole purpose of expediting prosecution and without acquiescing to the rejections, Applicant has amended claim 1 to recite:

> 1. A method for amplifying and sequencing DNA, comprising:
>
> tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject;
>
> amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplification steps comprises targeted amplification of a plurality of single nucleotide polymorphism (SNP) loci, wherein one of the amplifying steps introduces a barcode and one or more sequencing tags; and
>
> sequencing [[a]]the plurality of SNP loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of SNP loci comprises 25-2,000 loci.

Fan fails to teach or suggest targeted amplification of 25-2,000 SNP loci followed by massively parallel sequencing of the amplified SNP loci. The Office Action cites paragraph 0076 of Fan. That paragraph, however, refers to use of digital PCR for purpose of quantifying the amount of male DNA in a female plasma sample, whereas Fan separately discloses "direct shotgun sequencing" as an alternative to rather than in combination with digital PCR. See Fan

abstract ("Disclosed is a method to achieve digital quantification of DNA…using direct shotgun sequencing followed by mapping to the chromosome of origin and enumeration of fragments per chromosome.") and paragraph 0012 ("An alternative method to achieve digital quantification of DNA is direct shotgun sequencing followed by mapping to the chromosome of origin and enumeration of fragments per chromosome."). There is no teaching or suggestion about targeted amplification of 25-2,000 SNP using Fan's digital PCR, or about massively parallel sequencing of the amplicons produced by Fan's digital PCR.

Accordingly, so far as Fan fails to disclose each and every limitation of the claimed invention, the anticipation rejection cannot be sustained. Applicant therefore respectfully requests reconsideration and withdrawal of the subject rejection.

Claim Rejection under 35 U.S.C. 103

Claim 6 is rejected under 35 U.S.C. 103 for allegedly being unpatentable over Fan in view of Wright et al. 2009 ("Wright"). Claims 7-9 are rejected under 35 U.S.C. 103 for allegedly being unpatentable over Fan in view of Cronn et al. 2008 ("Cronn"). Applicant respectfully traverses these rejections.

As discussed in the foregoing section, Fan fails to teach or suggest targeted amplification of 25-2,000 SNP loci followed by massively parallel sequencing of the amplified SNP loci. To the opposite, Fan's entire methodology is "polymorphism-independent", which teaches away from targeted amplification and massively parallel sequencing of polymorphic loci. See Fan, paragraph 0021 ("Exemplified below is the successful use of shotgun sequencing and mapping of DNA to detect fetal trisomy 21 (Down syndrome), trisomy 18 (Edward syndrome), and trisomy 13 (Patau syndrome), carried out non-invasively using cell-free fetal DNA in maternal plasma. This forms the basis of a universal, **polymorphism-independent** non-invasive diagnostic test for fetal aneuploidy."); paragraph 0052 ("We showed in this study the successful development of a truly universal, **polymorphism-independent** non-invasive test for fetal aneuploidy. By directly sequencing maternal plasma DNA, we could detect fetal trisomy 21 as early as 14th week of gestation."); paragraph 0083 ("The sequencing approach is

polymorphism-independent and therefore universally applicable for the non-invasive detection of fetal aneuploidy.").

Accordingly, Fan would have motivated one of ordinary skill in the art to rely on Fan's polymorphism-independent methodology for analyzing cell-free DNA, and would have taught one of ordinary skill in the art away from the presently claimed invention which requires targeted amplification of 25-2,000 SNP loci followed by massively parallel sequencing of the amplified SNP loci. In addition, changing such fundamental design of Fan's workflow would have altered the principle of operation of Fan, in contravention of M.P.E.P. § 2143.01(VI) ("*[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious*").

Neither Wright nor Cronn could cure the aforementioned deficiencies of Fan. For at least these reasons, one of ordinary skill in the art would have found the presently claimed invention inventive and unobvious over the cited references. Applicant respectfully requests reconsideration and withdrawal of the subject rejection.

Concluding Remarks

Applicant believes that the application is in condition for allowance. Favorable consideration is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-6075. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account No. 50-6075.

Respectfully submitted,

Date 12-2-2020

By /Tianran Yan/

Tianran Yan
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Customer No. 110711
202-295-4781
IP@natera.com
Attorney for Applicant

NeoGenomics
Exhibit 1003 Page 861

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Joshua BABIARZ
Title:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
Application No.:	16/934,407
Filing Date:	7/21/2020
Examiner:	MUMMERT, STEPHANIE KANE
Art Unit:	1637
Conf. No.:	2396

AMENDMENT AND REPLY UNDER 37 CFR 1.111

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

Commissioner:

This communication is responsive to the non-final Office Action mailed September 16, 2020, concerning the above-referenced patent application:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this document.

Amendments to the Drawings begin on page 5 of this document and include an attached replacement drawing sheet.

Remarks begin on page 6 of this document.

NeoGenomics
Exhibit 1003 Page 862

DocCode – SCORE

SCORE Placeholder Sheet for IFW Content

Application Number: 16934407 Document Date: 12/02/2020

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

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

- Drawing

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- USPTO employees may access SCORE content via DAV or via the SCORE web page.
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Form Revision Date: March 1, 2019

Doc Code: DIST.E.FILE **Document Description: Electronic Terminal Disclaimer - Filed**	PTO/SB/26 U.S. Patent and Trademark Office Department of Commerce

Electronic Petition Request	**TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT**
Application Number	16934407
Filing Date	21-Jul-2020
First Named Inventor	Joshua BABIARZ
Attorney Docket Number	N.012.US.32
Title of Invention	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

☒ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action

☒ This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent Interest
Natera, Inc.	100%

The owner(s) with percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

10557172

10538814

10731220

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:
- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

◉ Terminal disclaimer fee under 37 CFR 1.20(d) is included with Electronic Terminal Disclaimer request. ○ I certify, in accordance with 37 CFR 1.4(d)(4), that the terminal disclaimer fee under 37 CFR 1.20(d) required for this terminal disclaimer has already been paid in the above-identified application.	
Applicant claims the following fee status: ○ Small Entity ○ Micro Entity ◉ Regular Undiscounted I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.	
THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES I certify, in accordance with 37 CFR 1.4(d)(4) that I am: ◉ An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application Registration Number 51243 ○ A sole inventor ○ A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors as evidenced by the power of attorney in the application ○ A joint inventor; all of whom are signing this request	
Signature	/Anton Bokal/
Name	Anton Bokal

*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner).
Form PTO/SB/96 may be used for making this certification. See MPEP § 324.

Electronic Patent Application Fee Transmittal

Application Number:	16934407
Filing Date:	21-Jul-2020
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Filer:	Anton John Bokal/Angela McGowan
Attorney Docket Number:	N.012.US.32

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
STATUTORY OR TERMINAL DISCLAIMER	1814	1	170	170
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**170**

Doc Code: DISQ.E.FILE
Document Description: Electronic Terminal Disclaimer – Approved

Application No.: 16934407

Filing Date: 21-Jul-2020

Applicant/Patent under Reexamination: BABIARZ

Electronic Terminal Disclaimer filed on December 2, 2020

☒ APPROVED

This patent is subject to a terminal disclaimer

☐ DISAPPROVED

Approved/Disapproved by: Electronic Terminal Disclaimer automatically approved by EFS-Web

U.S. Patent and Trademark Office

Electronic Acknowledgement Receipt

EFS ID:	41278259
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	02-DEC-2020
Filing Date:	21-JUL-2020
Time Stamp:	17:51:37
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$170
RAM confirmation Number	E2020B2H51340241
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Terminal Disclaimer-Filed (Electronic)	eTerminal-Disclaimer.pdf	33808 b1598426d1a87f1a1dc53a359190e459e54e96d2	no	2
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30507 d45edf9644c05f1123d2a380335be6f35e122d38	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	64315		

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<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 16/934,407	Filing Date 07/21/2020	☐ To be Mailed

ENTITY: ☑ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $100 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $460 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	12/02/2020	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 15	Minus	** 20	= 0		x $100 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $480 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

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

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

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

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

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/934,407	07/21/2020	1637	3720	N.012.US.32	15	1

CONFIRMATION NO. 2396

UPDATED FILING RECEIPT

110711
Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

OC000000121382560

Date Mailed: 11/17/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

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Applicant(s)

Natera, Inc., San Carlos, CA;

Assignment For Published Patent Application

Natera, Inc., San Carlos, CA

Power of Attorney: The patent practitioners associated with Customer Number 110711

Domestic Priority data as claimed by applicant

This application is a CON of 16/743,724 01/15/2020 PAT 10731220
which is a CON of 16/399,268 04/30/2019 PAT 10538814
which is a CON of 16/140,298 09/24/2018
which is a CON of 14/918,544 10/20/2015 PAT 10316362
which is a CIP of 14/877,925 10/07/2015 ABN

and is a CIP of 14/692,703 04/21/2015 PAT 10179937
and is a CIP of 14/538,982 11/24/2014 PAT 9677118
and claims benefit of 62/148,173 04/15/2015
and claims benefit of 62/147,377 04/14/2015
and claims benefit of 62/146,188 04/10/2015
and claims benefit of 62/066,514 10/21/2014
and said 14/877,925 10/07/2015
is a CIP of 14/225,356 03/25/2014 ABN
and is a CIP of 13/780,022 02/28/2013 ABN
and is a CON of 13/683,604 11/21/2012 ABN
and said 14/692,703 04/21/2015
claims benefit of 62/148,173 04/15/2015
and claims benefit of 62/147,377 04/14/2015
and claims benefit of 62/146,188 04/10/2015
and claims benefit of 62/066,514 10/21/2014
and claims benefit of 61/994,791 05/16/2014
and claims benefit of 61/987,407 05/01/2014
and claims benefit of 61/982,245 04/21/2014
and said 14/538,982 11/24/2014
claims benefit of 62/066,514 10/21/2014
and claims benefit of 61/994,791 05/16/2014
and claims benefit of 61/987,407 05/01/2014
and claims benefit of 61/982,245 04/21/2014
and said 14/225,356 03/25/2014
is a CON of PCT/US2012/058578 10/03/2012
and said 13/780,022 02/28/2013
is a CIP of 13/683,604 11/21/2012 ABN
and is a CIP of PCT/US2012/058578 10/03/2012
and is a CIP of 13/335,043 12/22/2011 PAT 10113196
which is a CIP of 13/300,235 11/18/2011 PAT 10017812
which is a CIP of 13/110,685 05/18/2011 PAT 8825412
and said 13/780,022 02/28/2013
claims benefit of 61/634,431 02/29/2012
and said 13/683,604 11/21/2012
is a CIP of 13/300,235 11/18/2011 PAT 10017812
and is a CIP of 13/110,685 05/18/2011 PAT 8825412
and claims benefit of 61/675,020 07/24/2012
and said PCT/US2012/058578 10/03/2012
is a CIP of 13/300,235 11/18/2011 PAT 10017812
and claims benefit of 61/683,331 08/15/2012
and claims benefit of 61/542,508 10/03/2011
and said 13/335,043 12/22/2011
is a CIP of 13/300,235 11/18/2011 PAT 10017812
and is a CIP of 13/110,685 05/18/2011 PAT 8825412
and claims benefit of 61/426,208 12/22/2010
and said 13/300,235 11/18/2011
is a CIP of 13/110,685 05/18/2011 PAT 8825412
and claims benefit of 61/542,508 10/03/2011
and claims benefit of 61/571,248 06/23/2011
and said 13/110,685 05/18/2011
claims benefit of 61/516,996 04/12/2011

and claims benefit of 61/448,547 03/02/2011
and claims benefit of 61/448,547 03/02/2011
and claims benefit of 61/462,972 02/09/2011
and claims benefit of 61/398,159 06/21/2010
and claims benefit of 61/395,850 05/18/2010

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

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

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

If Required, Foreign Filing License Granted: 07/27/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/934,407**

Projected Publication Date: Not Applicable

Non-Publication Request: No

Early Publication Request: No
Title

METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

Preliminary Class

435

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

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

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

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

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

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from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 16/934,407

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	320
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	700
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	800
TOTAL CLAIMS (37 CFR 1.16(i))	15 minus 20 =	*			OR	x 100 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*				x 480 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						2100
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	3920

APPLICATION AS AMENDED - PART II

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

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

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32

CONFIRMATION NO. 2396

110711
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San Carlos, CA 94070

PUBLICATION NOTICE

OC000000121158113

Title:METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

Publication No.US-2020-0347454-A1
Publication Date:11/05/2020

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently https://portal.uspto.gov/pair/PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

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Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

DocCode – SCORE

SCORE Placeholder Sheet for IFW Content

Application Number: 16934407 Document Date: 09/21/2020

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- Drawing

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- External customers may access SCORE content via PAIR using the Supplemental Content tab.

Form Revision Date: March 1, 2019

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Joshua BABIARZ, et al.	Confirmation No.: 2396
Application No.: 16/934,407	Art Unit: 1637
Filed: July 21, 2020	Examiner: MUMMERT, STEPHANIE KANE
For: Natera, Inc.	Atty. Docket: N.012.US.32

RESPONSE TO NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES
Filing Date Granted

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This communication is filed in response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures dated September 18, 2020.

Applicant respectfully submits Replacement Drawings wherein the required sequence identifiers have been added in FIG. 12. No new matter has been added.

The Examiner is invited to telephone the undersigned at the number provided to facilitate prosecution of this application.

Respectfully submitted,

Date: 9-21-2020

/Tianran Yan/
Tianran Yan
Registration No. 67162
Customer No. 110711
202-295-4781
IP@natera.com
Attorney for Applicant

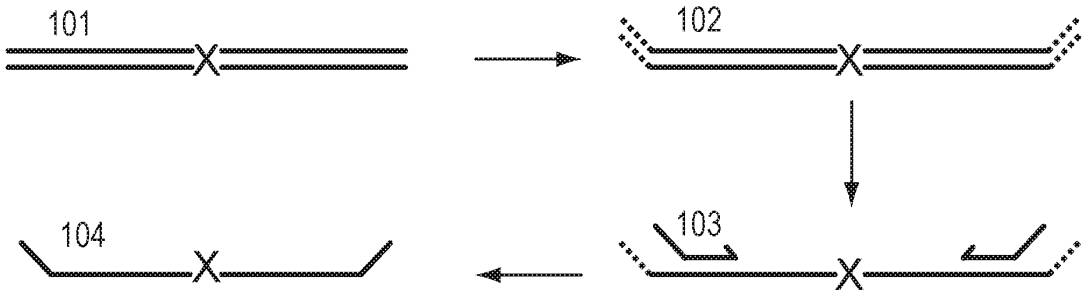


FIG. 1

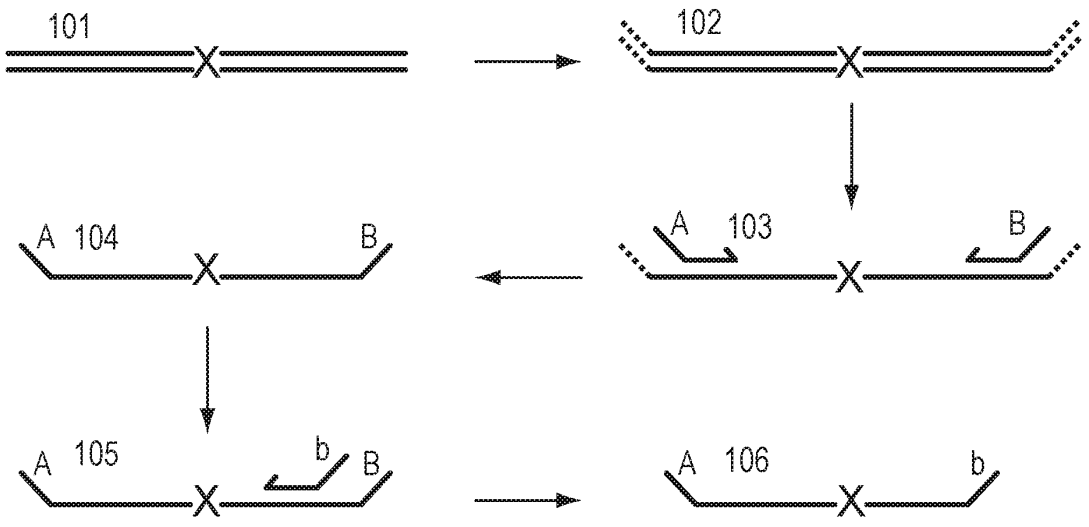


FIG. 2

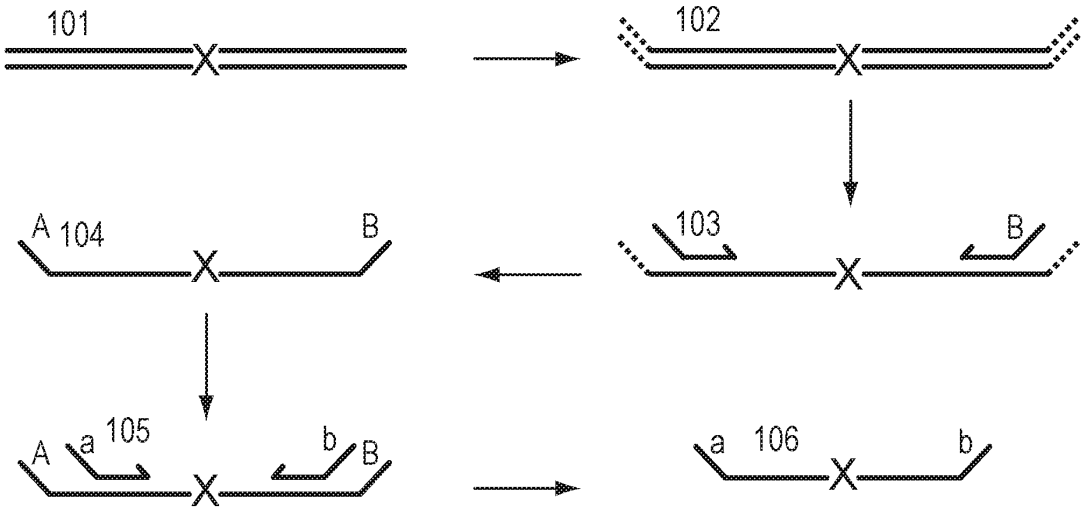

101
102
A 104
B
103
B
A
a 105
b
B
a 106
b

FIG. 3

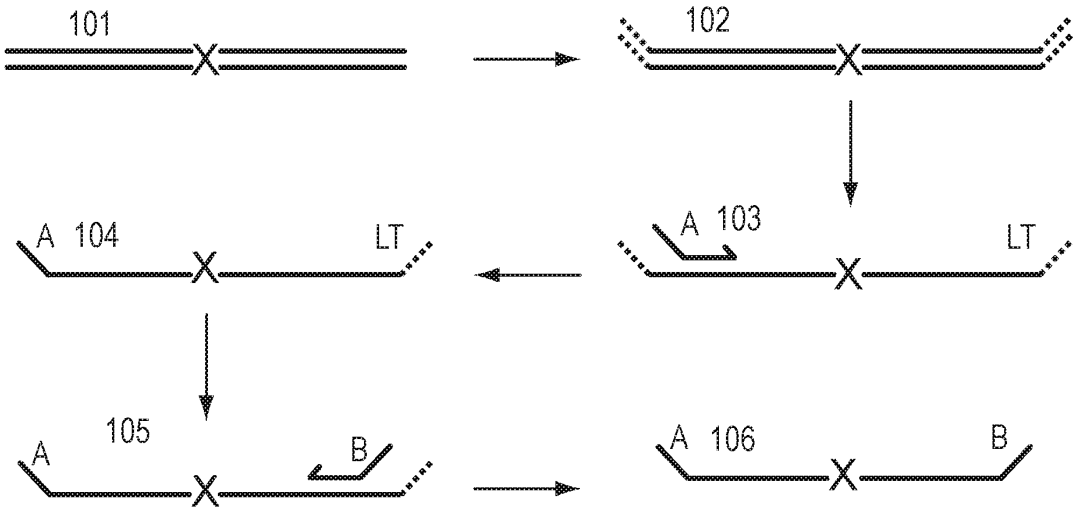

101
102
A 104
LT
A 103
LT
105
A
B
A 106
B

FIG. 4

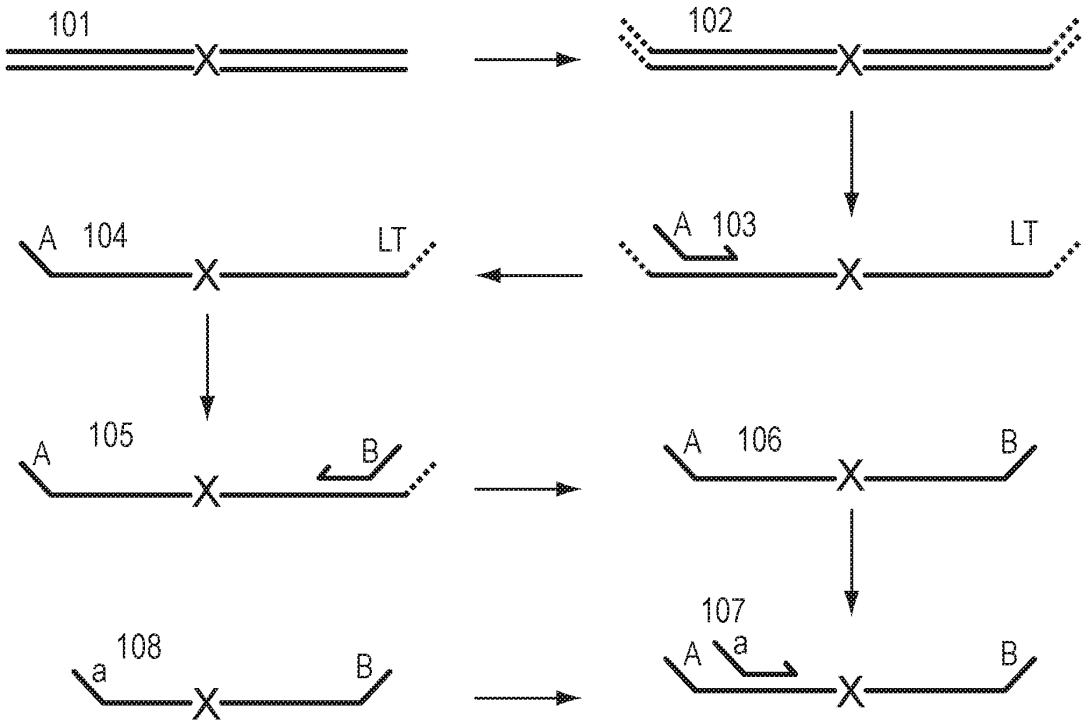

101
102
A 104
LT
A 103
LT
A 105
B
A 106
B
108
a
B
107
A
a
B

FIG. 5

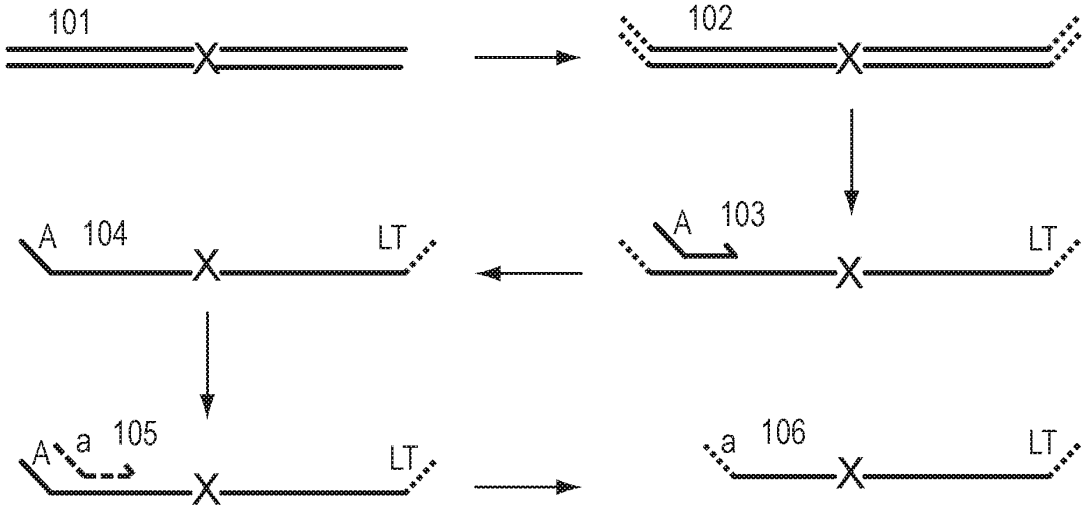

101
102
A 104
LT
A 103
LT
A
a 105
LT
a 106
LT

FIG. 6

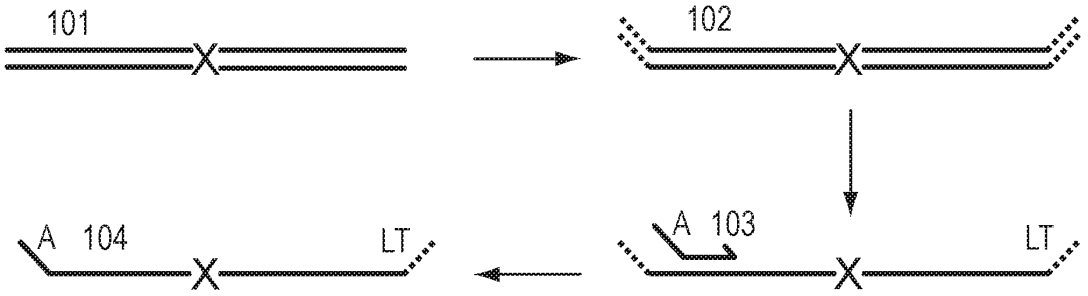


FIG. 7

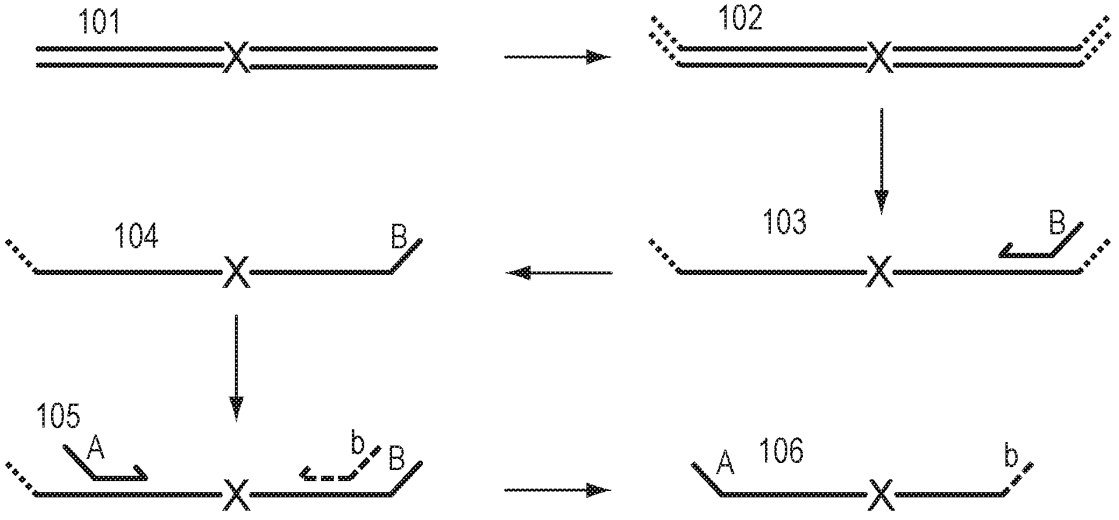


FIG. 8

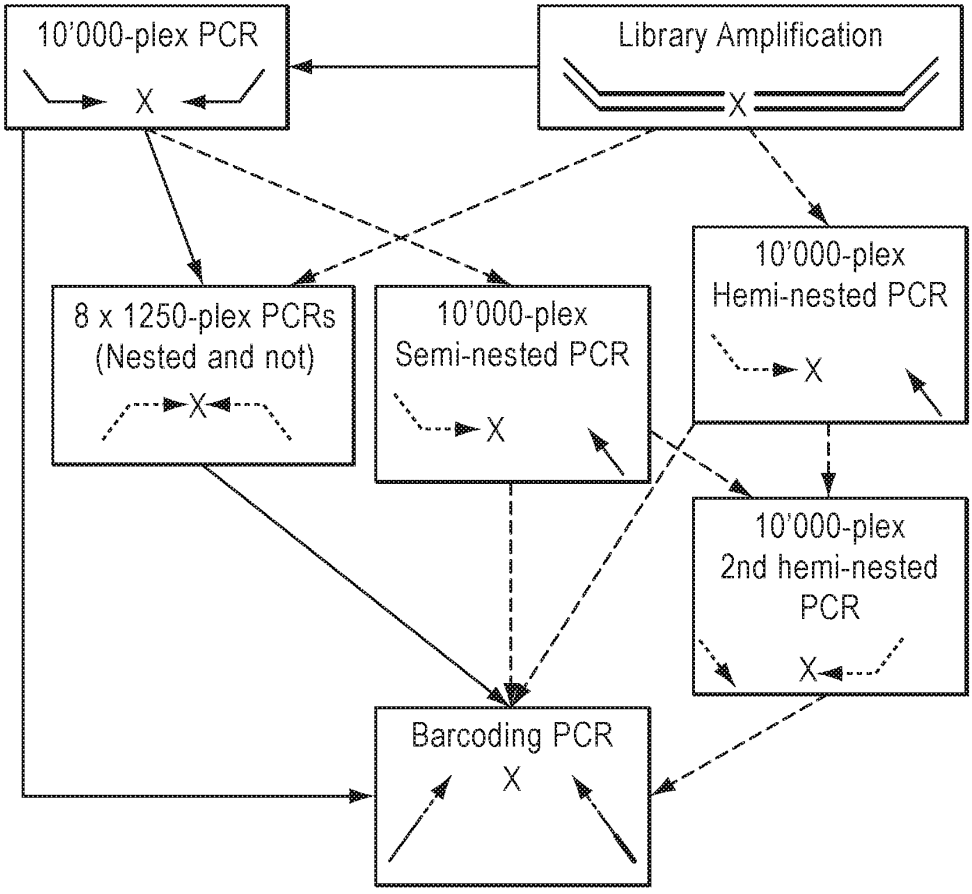

10'000-plex PCR
X
Library Amplification
X
8 x 1250-plex PCRs
(Nested and not)
X
10'000-plex
Semi-nested PCR
X
10'000-plex
Hemi-nested PCR
X
10'000-plex
2nd hemi-nested
PCR
X
Barcoding PCR
X

FIG. 9

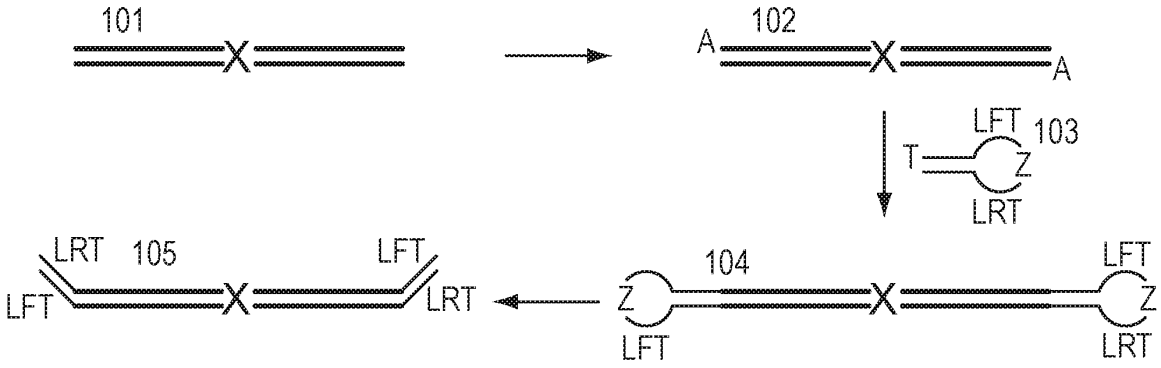

101
102
A
A
LFT
103
T
Z
LRT
LRT
105
LFT
LFT
LRT
104
Z
LFT
LFT
Z
LRT

FIG. 10

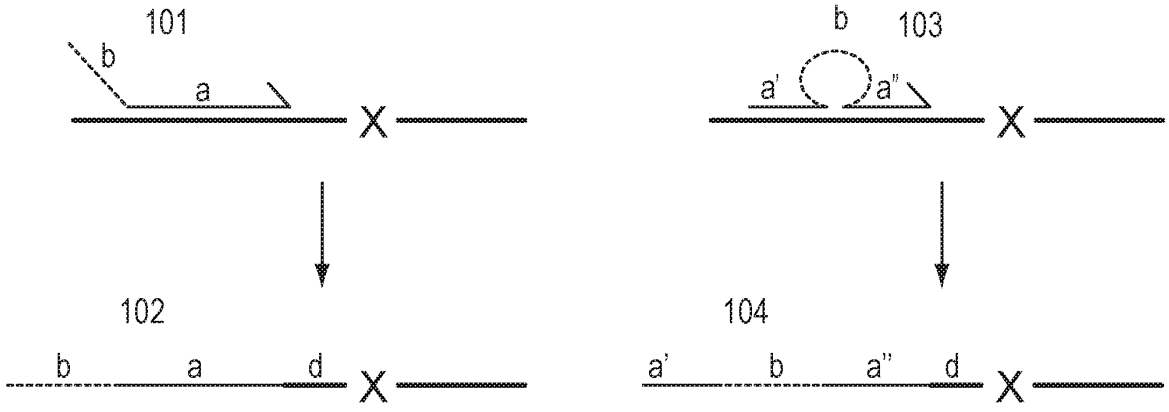


FIG. 11

			SEQ ID NO:
The sequencing-adaptor sequence is located inside the primer sequence and flanked by target specific sequence on both sides. 10 bases are target-specific at the 3'-end of each primer. Primers were tested successfully in real-time PCR. For sequencing this reduces the number of primer bases that need to be sequenced.			
rs8130564	int-tag 1.10	AACTCACATAGC*ACACGACGCTCTTCCGATCT*TGCAAGCACA	44611
rs2832093	int-tag 2.10	TCCTCTGTG*ACACGACGCTCTTCCGATCT*CCCTGCTCTT	44612
rs12011281	int-tag 3.10	tcctctctctACACGACGCTCTTCCGATCTcGGGCTGTCA	44613
rs6719561	int-tag 4.10	TACATCCTTGAGACACGACGCTCTTCCGATCTGCTGTGCAGT	44614
rs10187018	int-tag 5.10	tttgcttgagctACACGACGCTCTTCCGATCTcgggagtttc	44615
rs10460481	int-tag 6.10	gtcttatggtggACACGACGCTCTTCCGATCTcaaagccagt	44616
The sequencing-adaptor sequence is located inside the primer sequence and flanked by target specific sequence on both sides. The internal tag is formed into a hairpin structure by 10 complementary bases on either end. This brings the target-specific ends of the primer into close proximity and hinders unspecific binding to the "internal tag". 10 bases are target-specific at the 3'-end of each primer. Primers were tested successfully in real-time PCR.			
rs8130564	loop-int-tag 1.10	AACTCACATAGC*tgatcggtACACGACGCTCTTCCGATCT*TGCAAGCACA	44617
rs2832093	loop-int-tag 2.10	TCCTCTGTG*tgatcggtACACGACGCTCTTCCGATCT*CCCTGCTCTT	44618
rs12011281	loop-int-tag 3.10	tcctctcttgatcggtACACGACGCTCTTCCGATCTcGGGCTGTCA	44625
rs6719561	loop-int-tag 4.10	TACATCCTTGAGtgatcggtACACGACGCTCTTCCGATCTGCTGTGCAGT	44620
rs10187018	loop-int-tag 5.10	tttgcttgagcttgatcggtACACGACGCTCTTCCGATCTcgggagtttc	44621
rs10460481	loop-int-tag 6.10	gtcttatggtggtgatcggtACACGACGCTCTTCCGATCTcaaagccagt	44622

FIG. 12

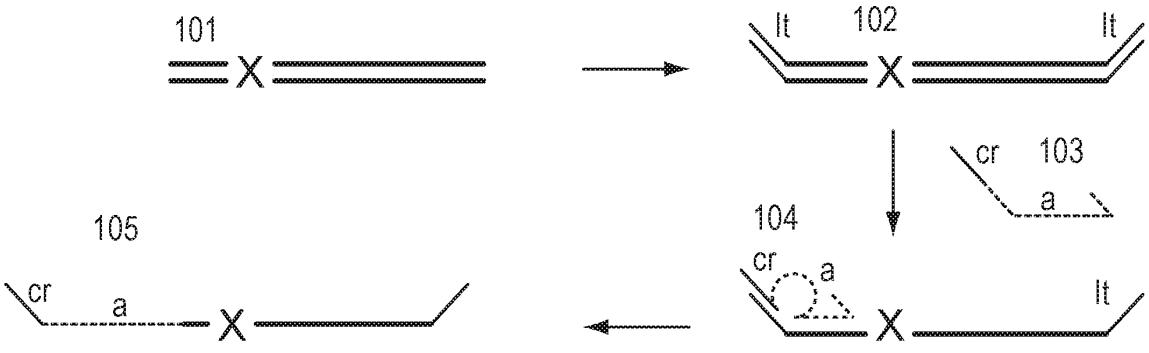

101
lt
102
lt
cr
103
a
104
cr
a
lt
105
cr
a

FIG. 13

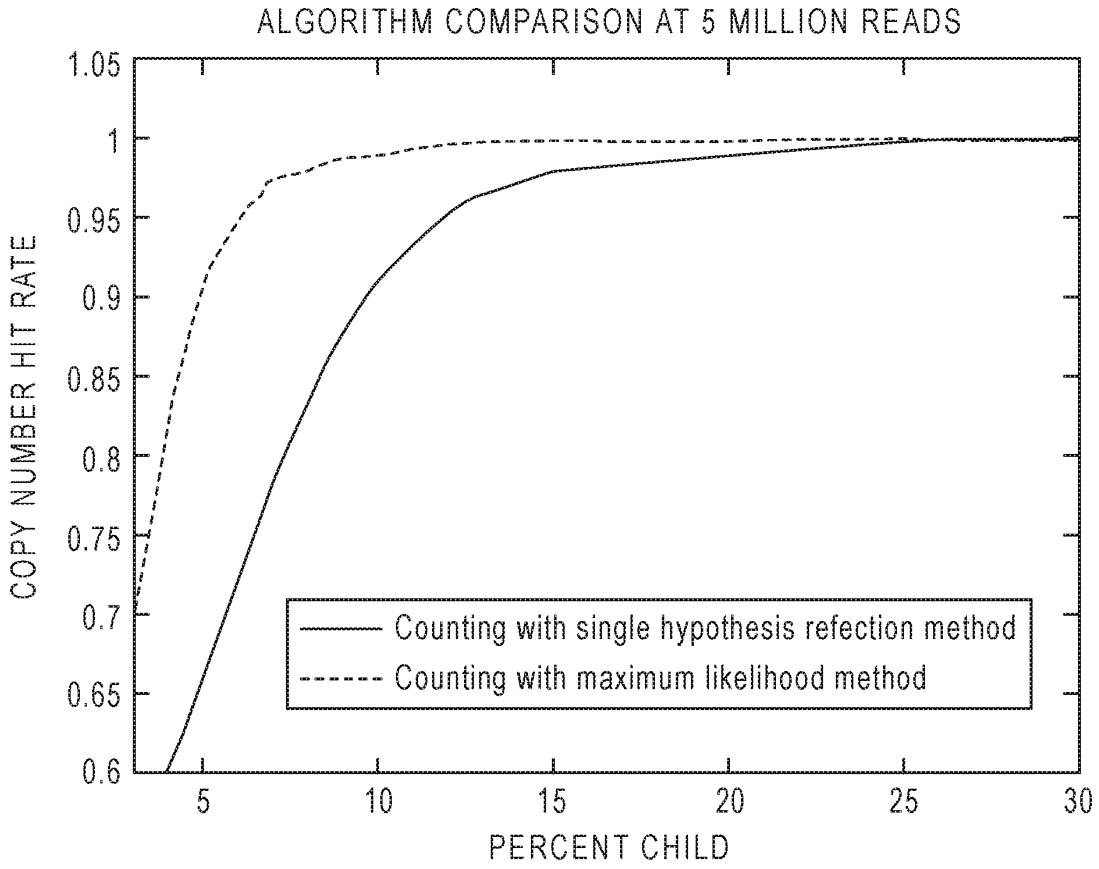

ALGORITHM COMPARISON AT 5 MILLION READS
COPY NUMBER HIT RATE
1.05
1
0.95
0.9
0.85
0.8
0.75
0.7
0.65
0.6
5
10
15
20
25
30
PERCENT CHILD
Counting with single hypothesis refection method
Counting with maximum likelihood method

FIG.14

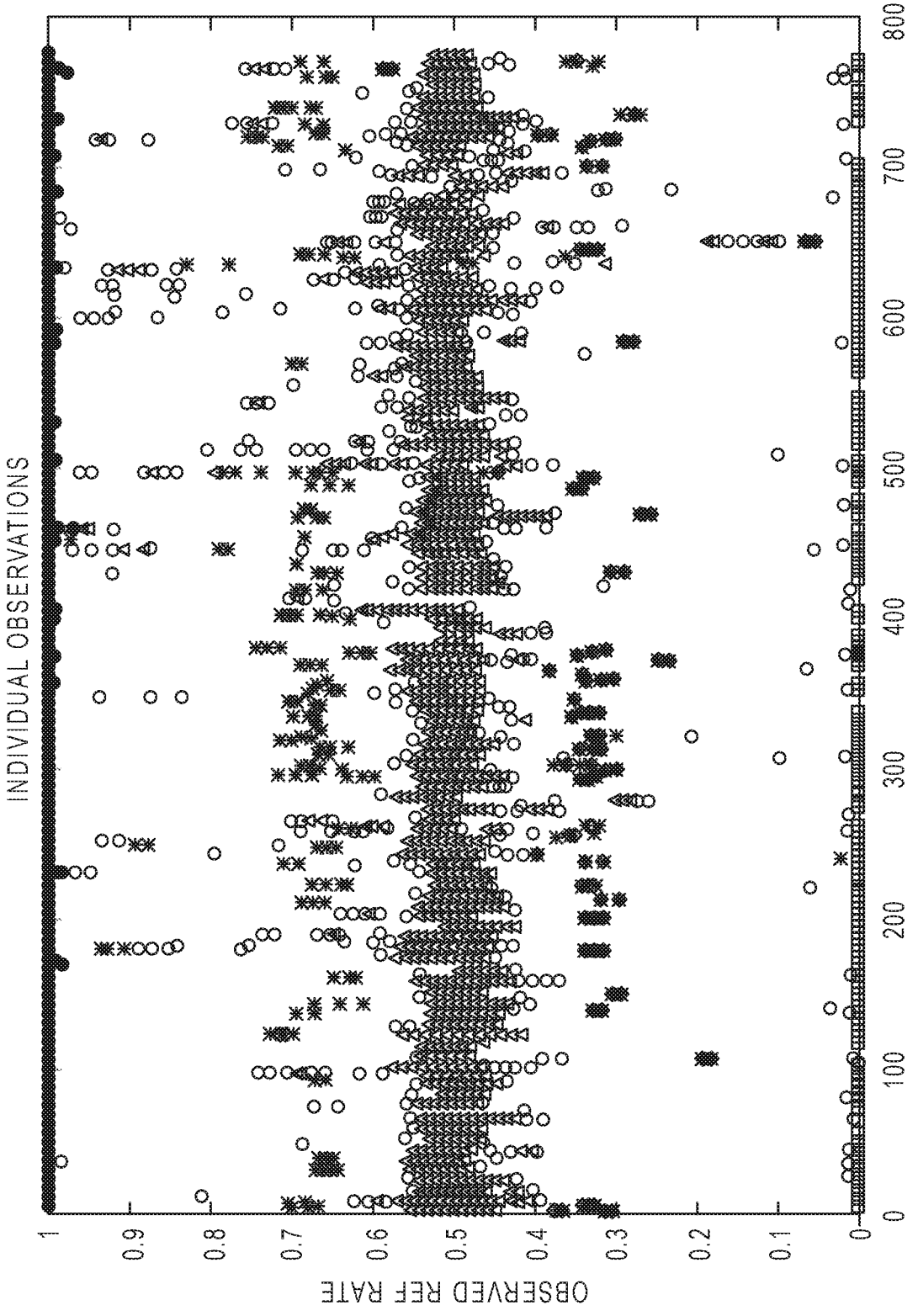

INDIVIDUAL OBSERVATIONS
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
OBSERVED REF RATE
0
100
200
300
400
500
600
700
800
SNP

FIG. 15

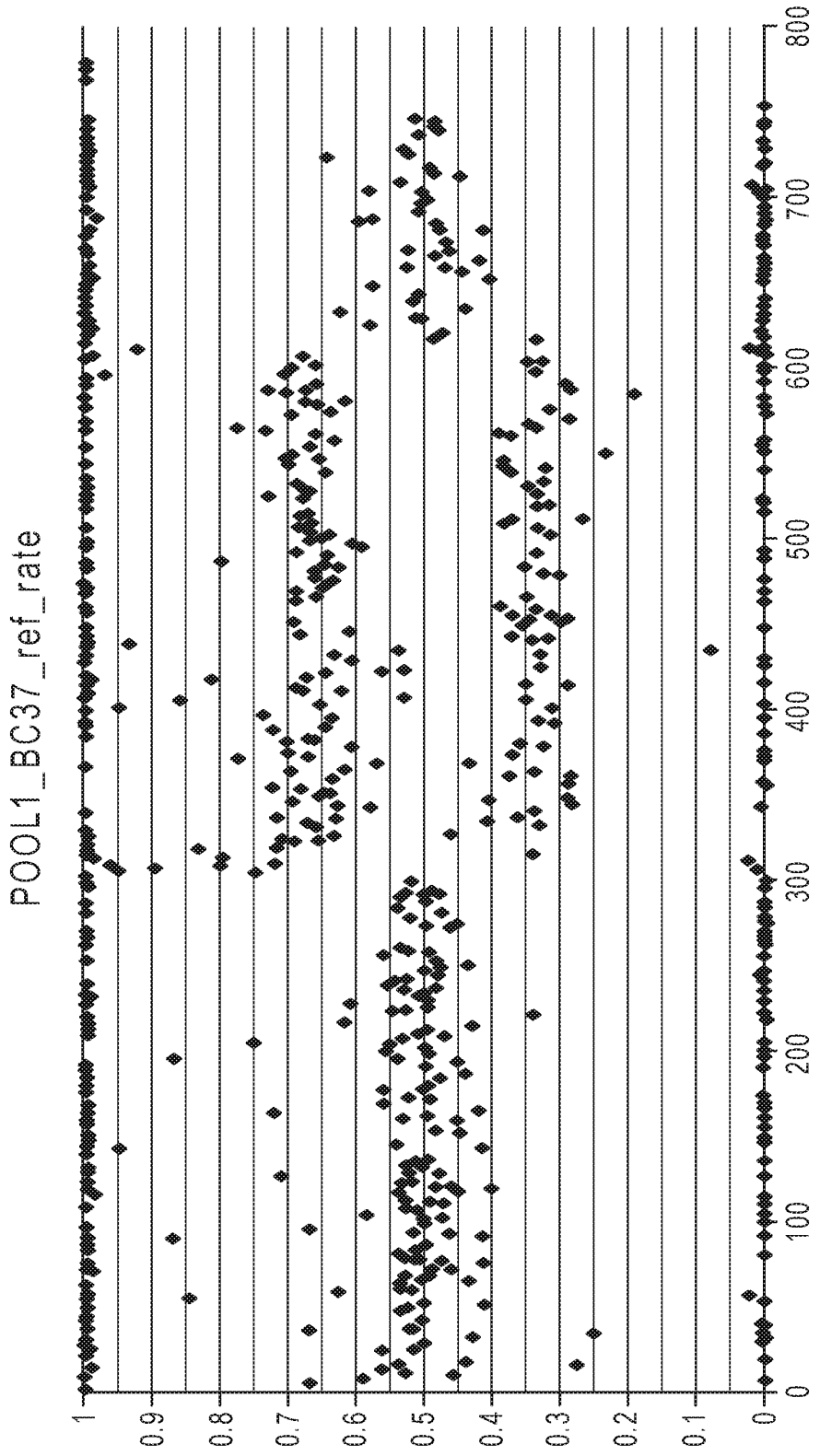

POOL1_BC37_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 16

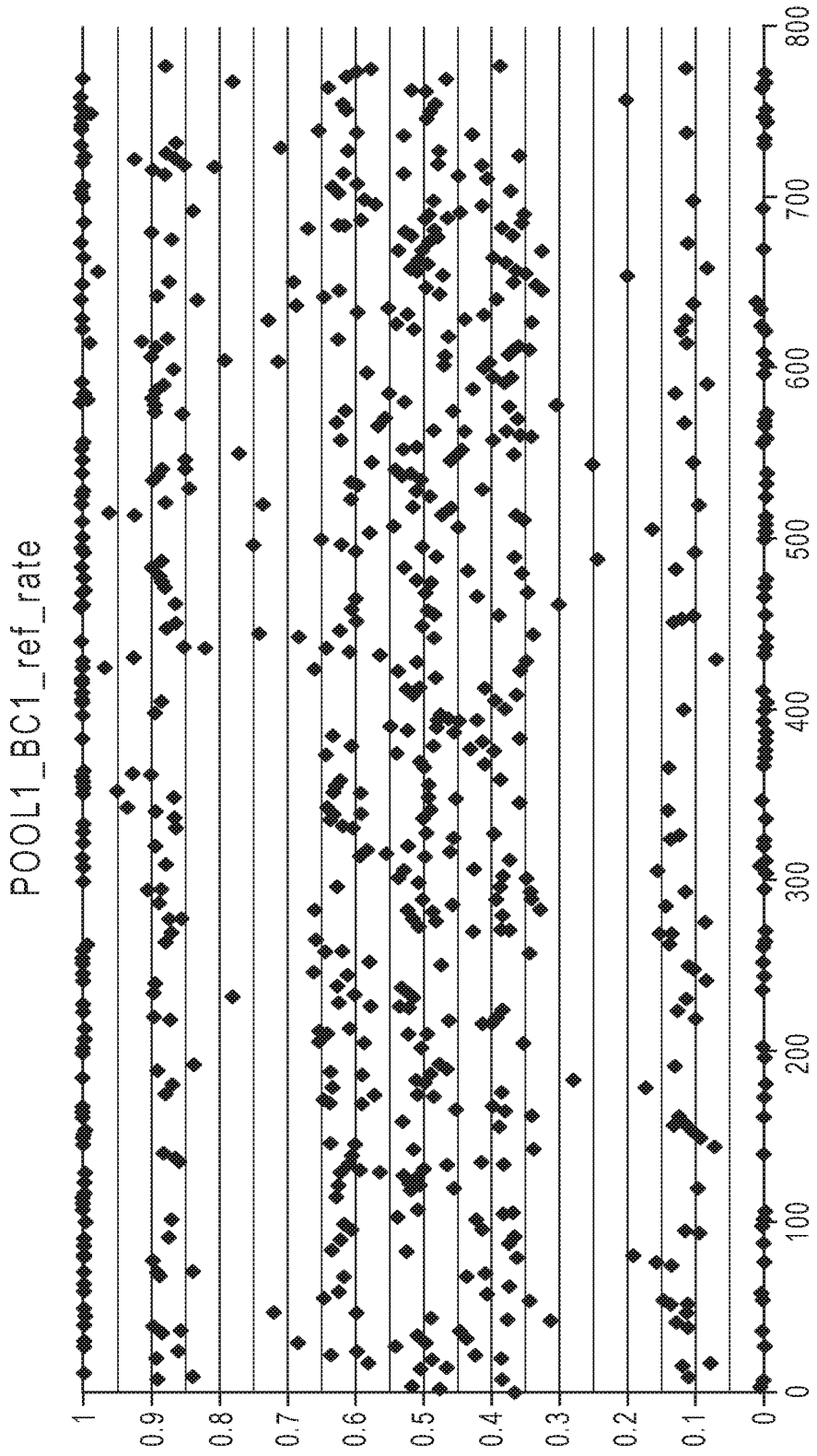

POOL1_BC1_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17A

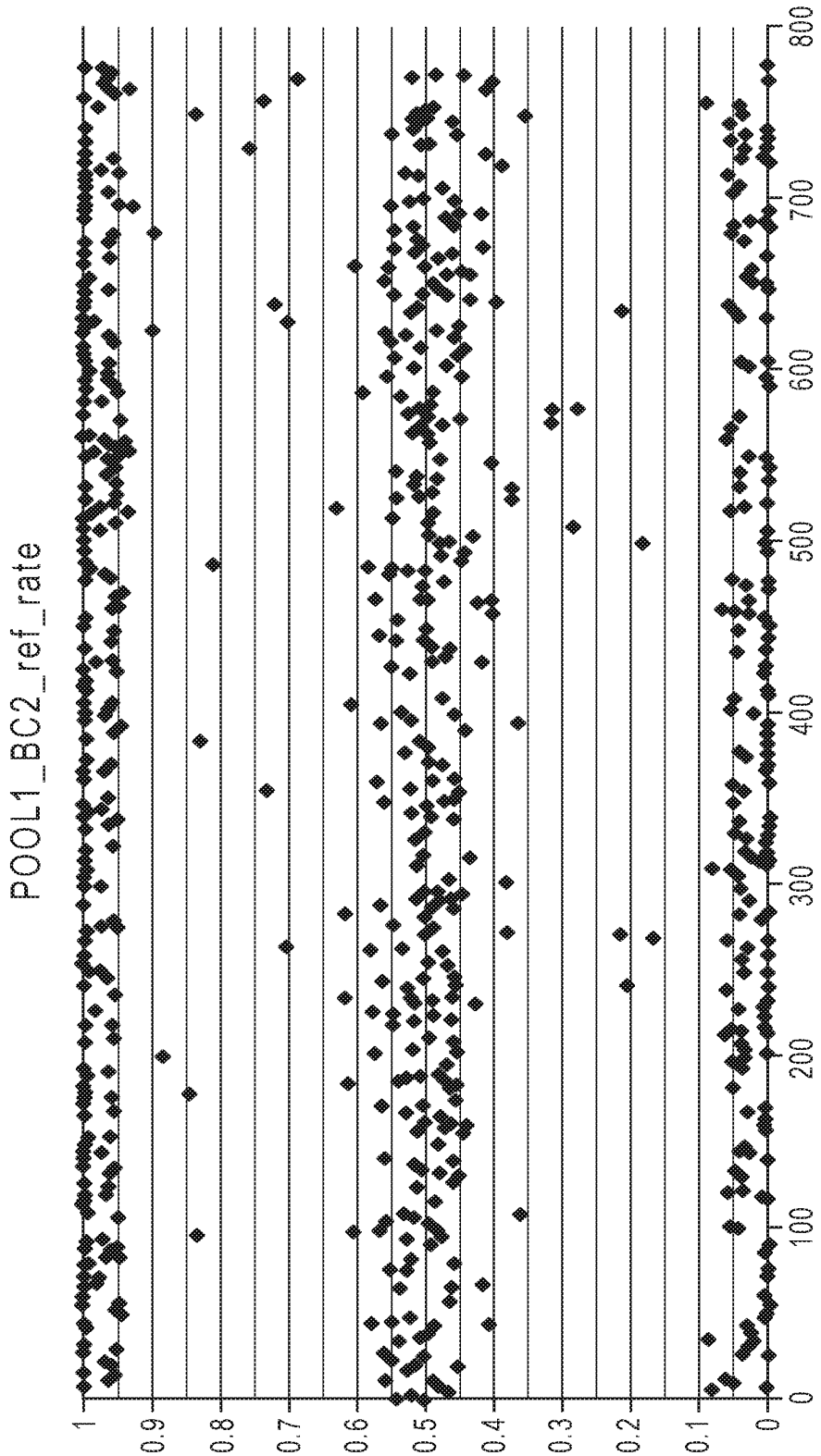

POOL1_BC2_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17B

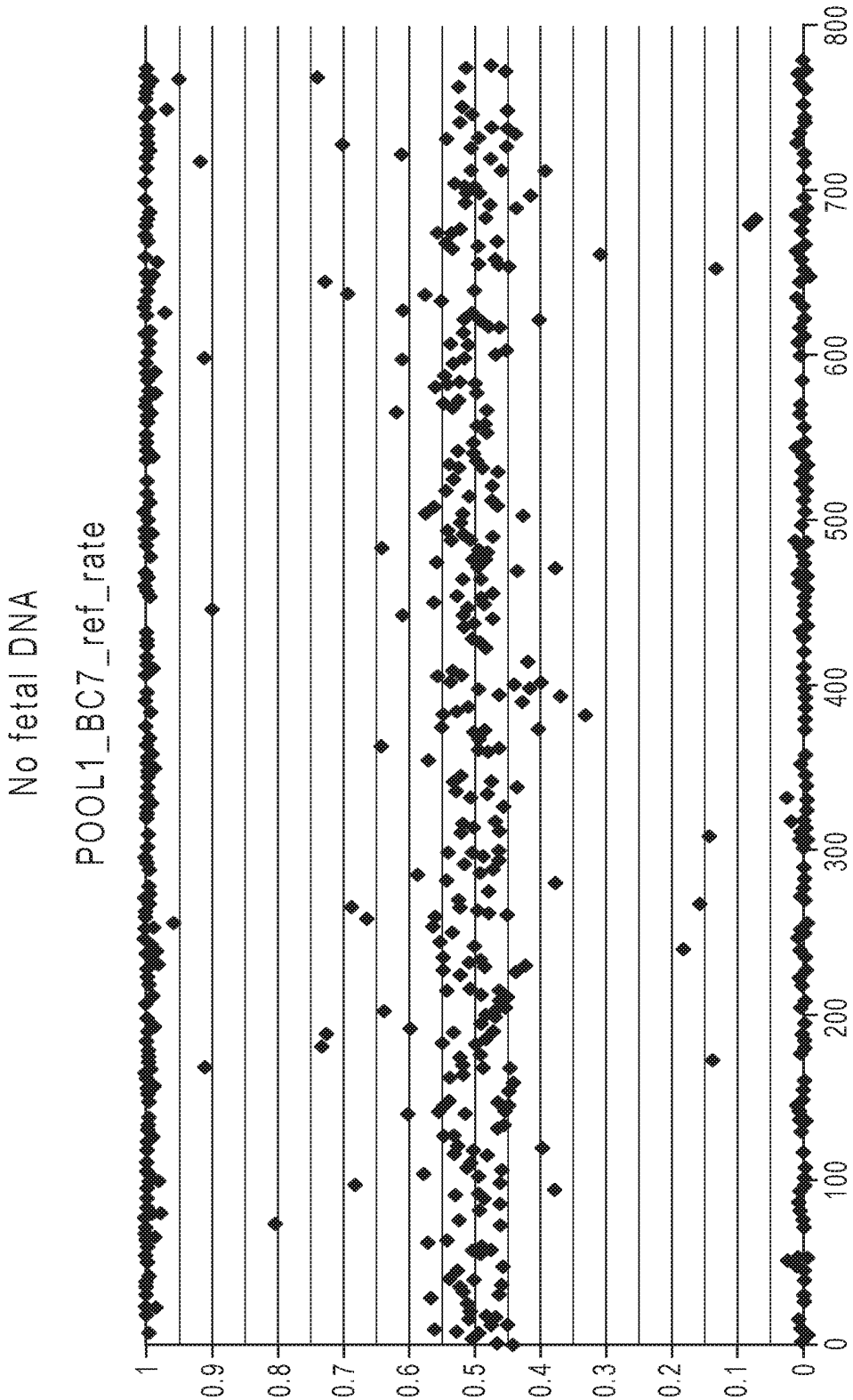

No fetal DNA
POOL1_BC7_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17C

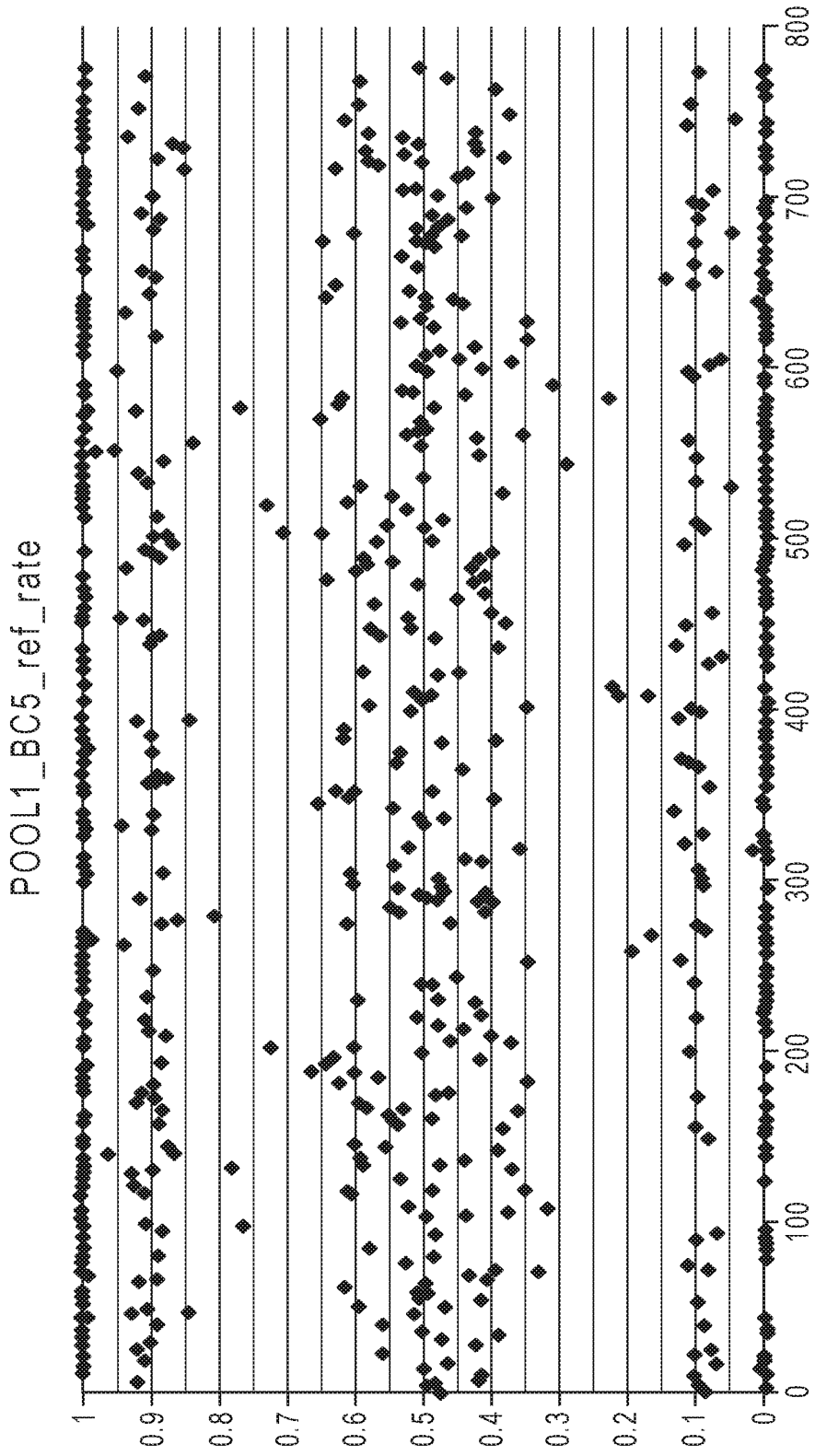

POOL1_BC5_ref_rate
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100
200
300
400
500
600
700
800

FIG. 17D

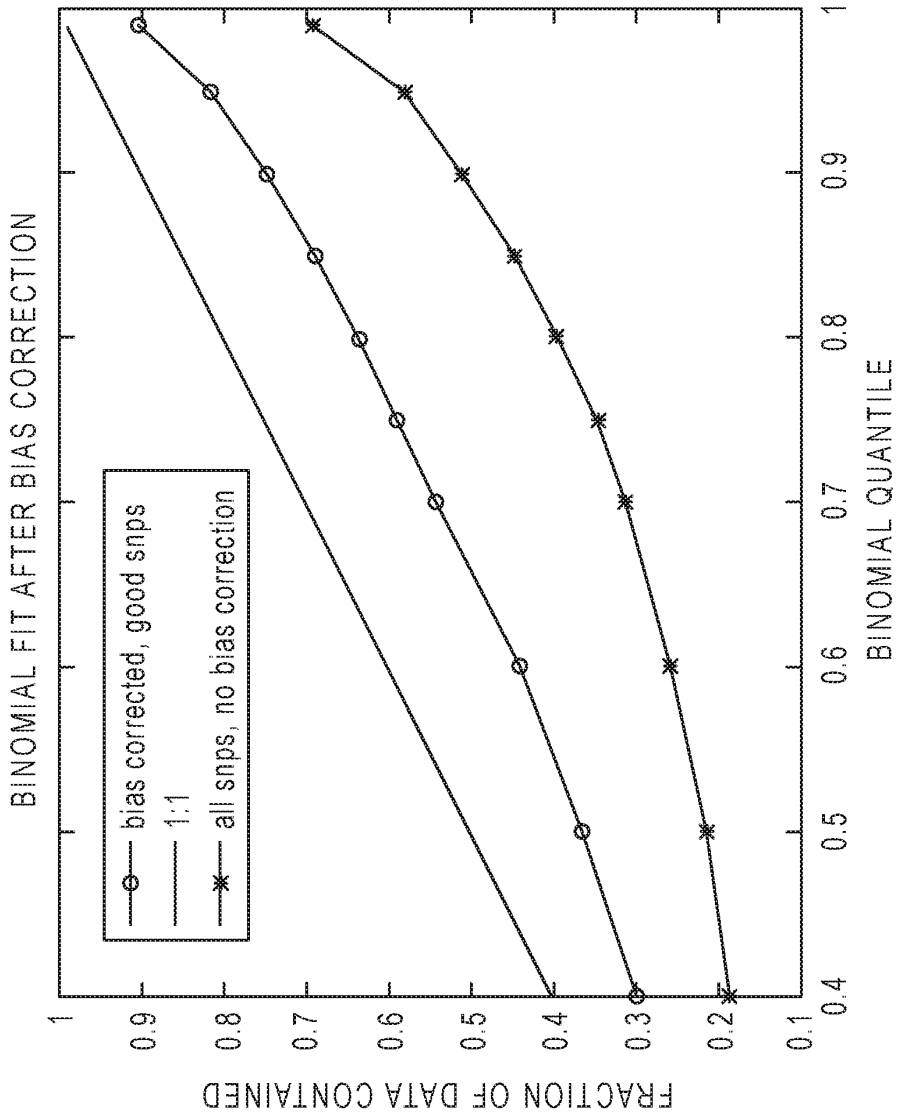

BINOMIAL FIT AFTER BIAS CORRECTION
FRACTION OF DATA CONTAINED
BINOMIAL QUANTILE
bias corrected, good snps
1:1
all snps, no bias correction
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0.4
0.5
0.6
0.7
0.8
0.9
1

FIG. 18

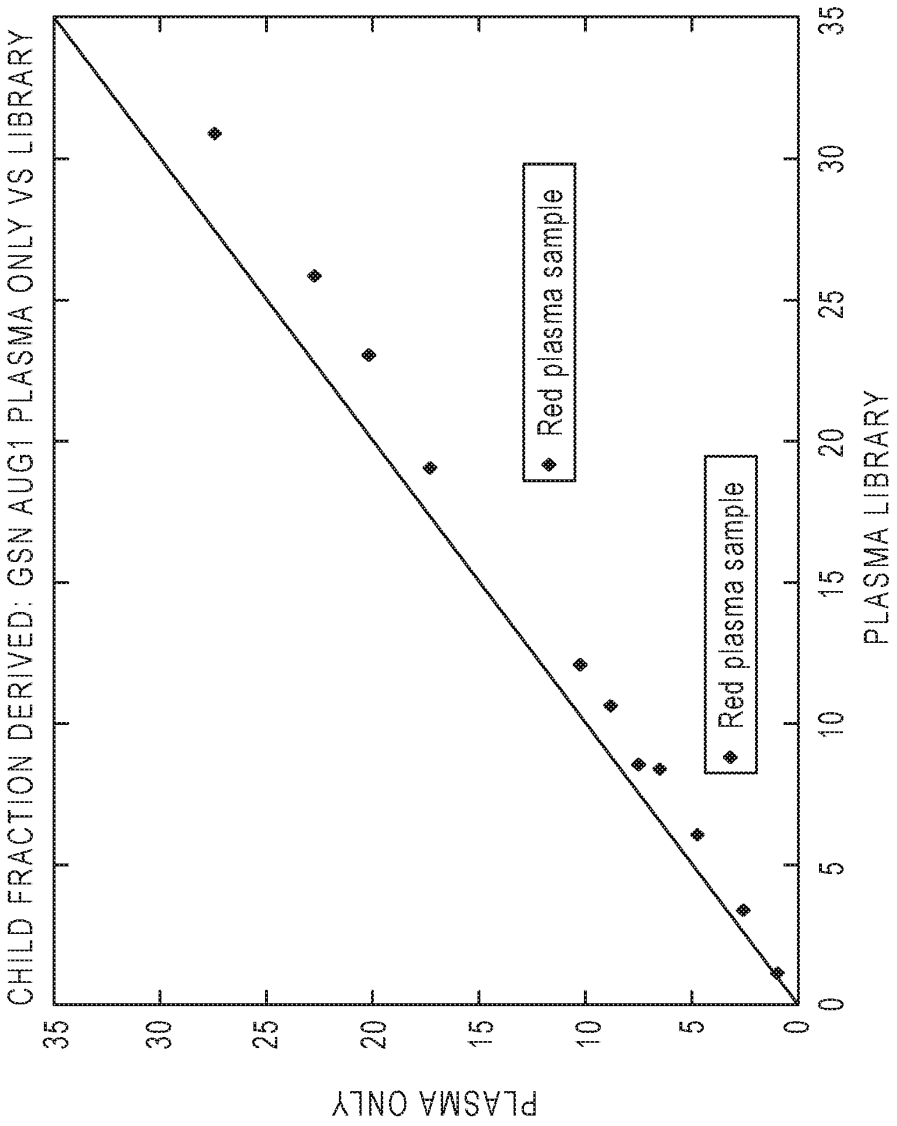

CHILD FRACTION DERIVED: GSN AUG1 PLASMA ONLY VS LIBRARY
PLASMA ONLY
PLASMA LIBRARY
0
5
10
15
20
25
30
35
Red plasma sample
Red plasma sample

FIG. 19

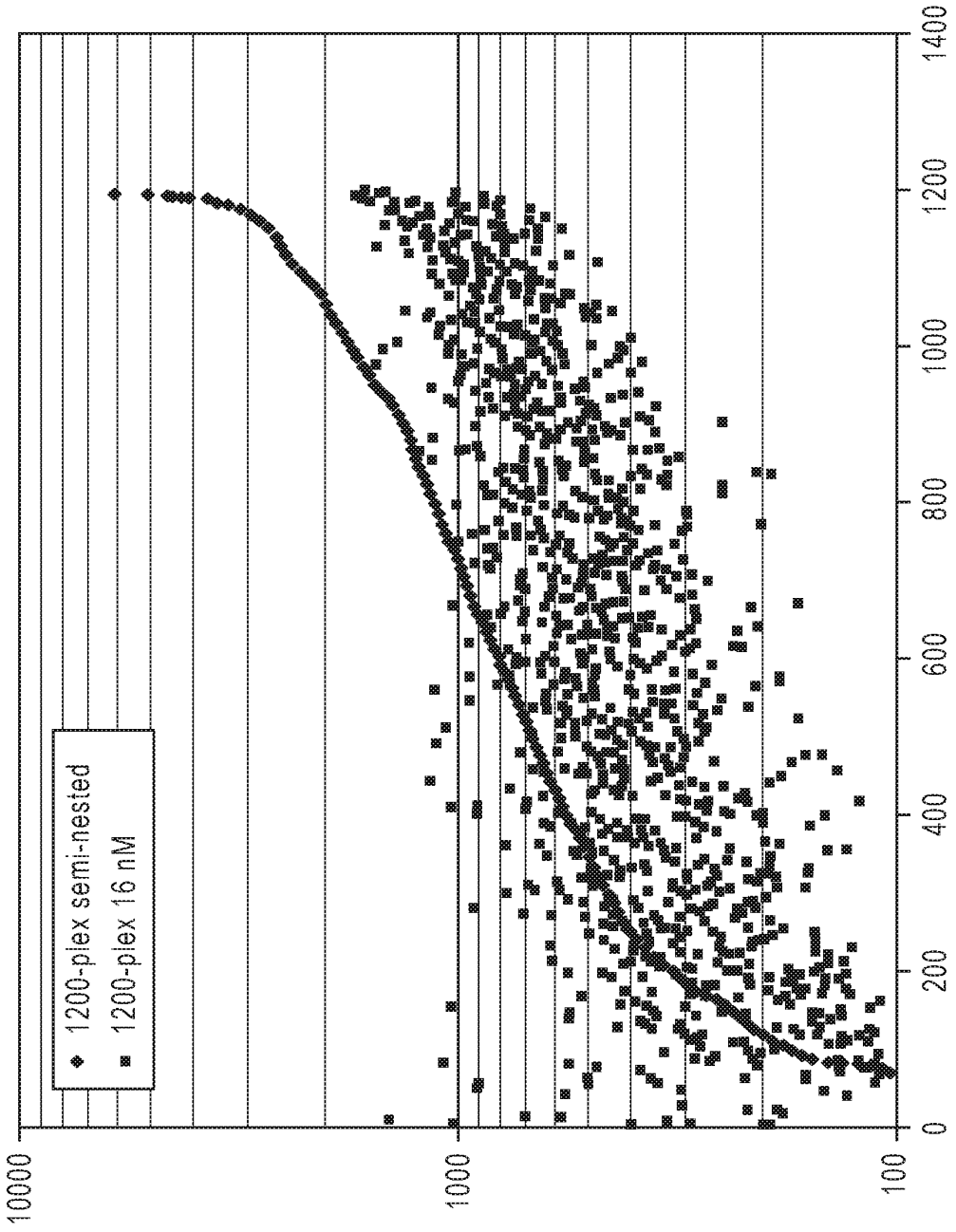

1200-plex semi-nested
1200-plex 16 nM
10000
1000
100
0
200
400
600
800
1000
1200
1400

FIG. 20

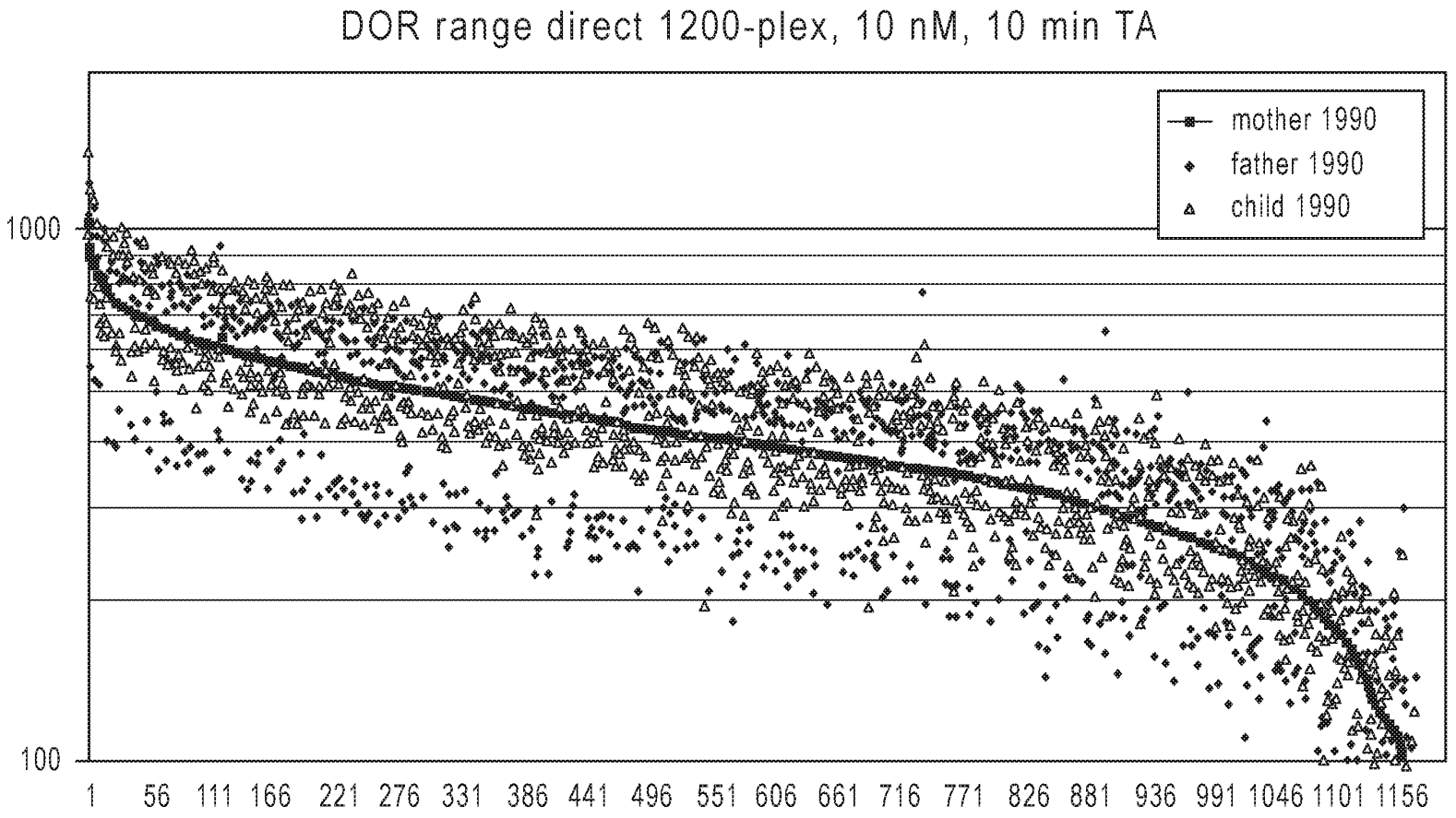


FIG. 21

NeoGenomics
Exhibit 1003 Page 898

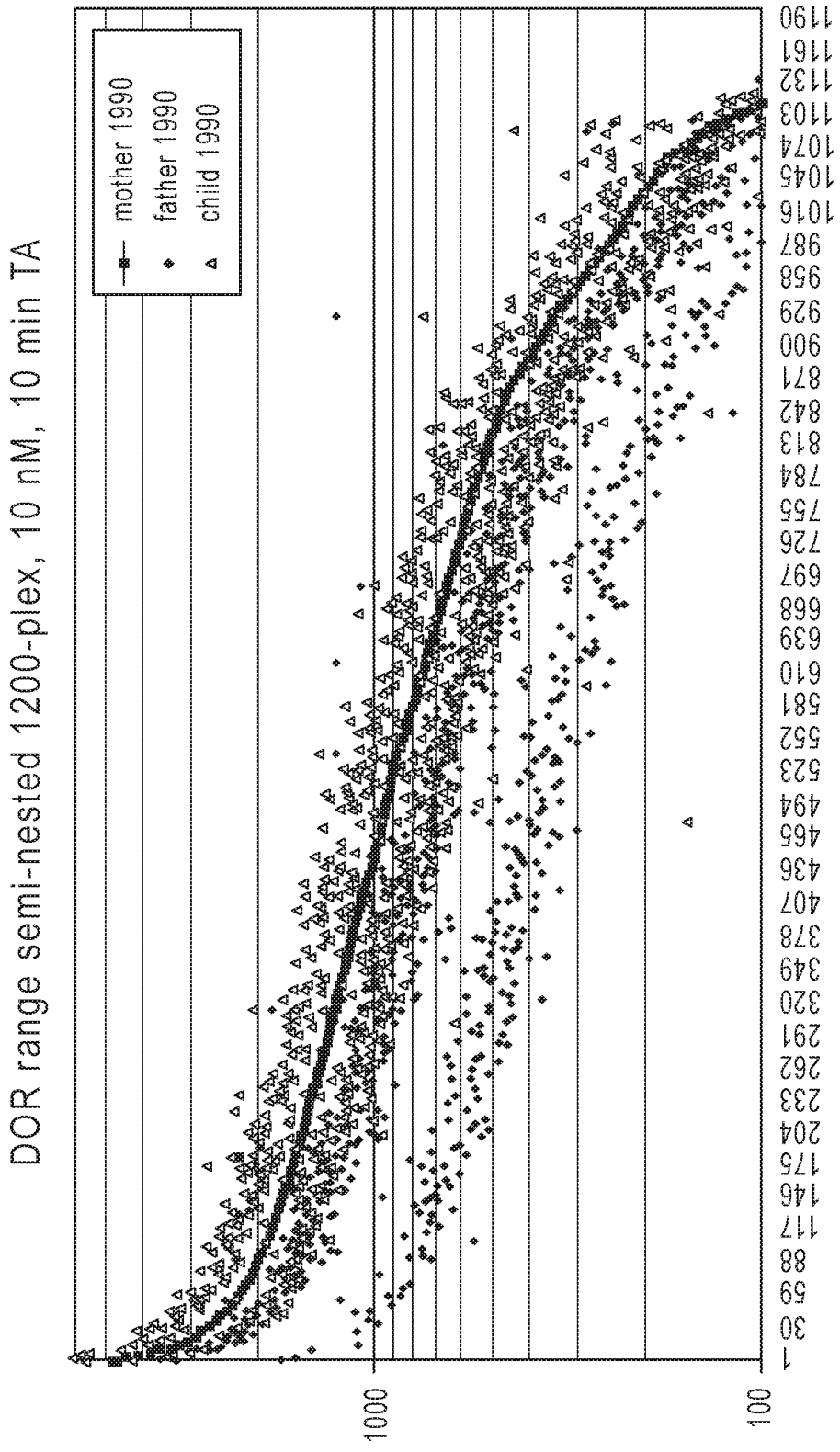

DOR range semi-nested 1200-plex, 10 nM, 10 min TA
mother 1990
father 1990
child 1990
1000
100
1
30
59
88
117
146
175
204
233
262
291
320
349
378
407
436
465
494
523
552
581
610
639
668
697
726
755
784
813
842
871
900
929
958
987
1016
1045
1074
1103
1132
1161
1190

FIG. 22

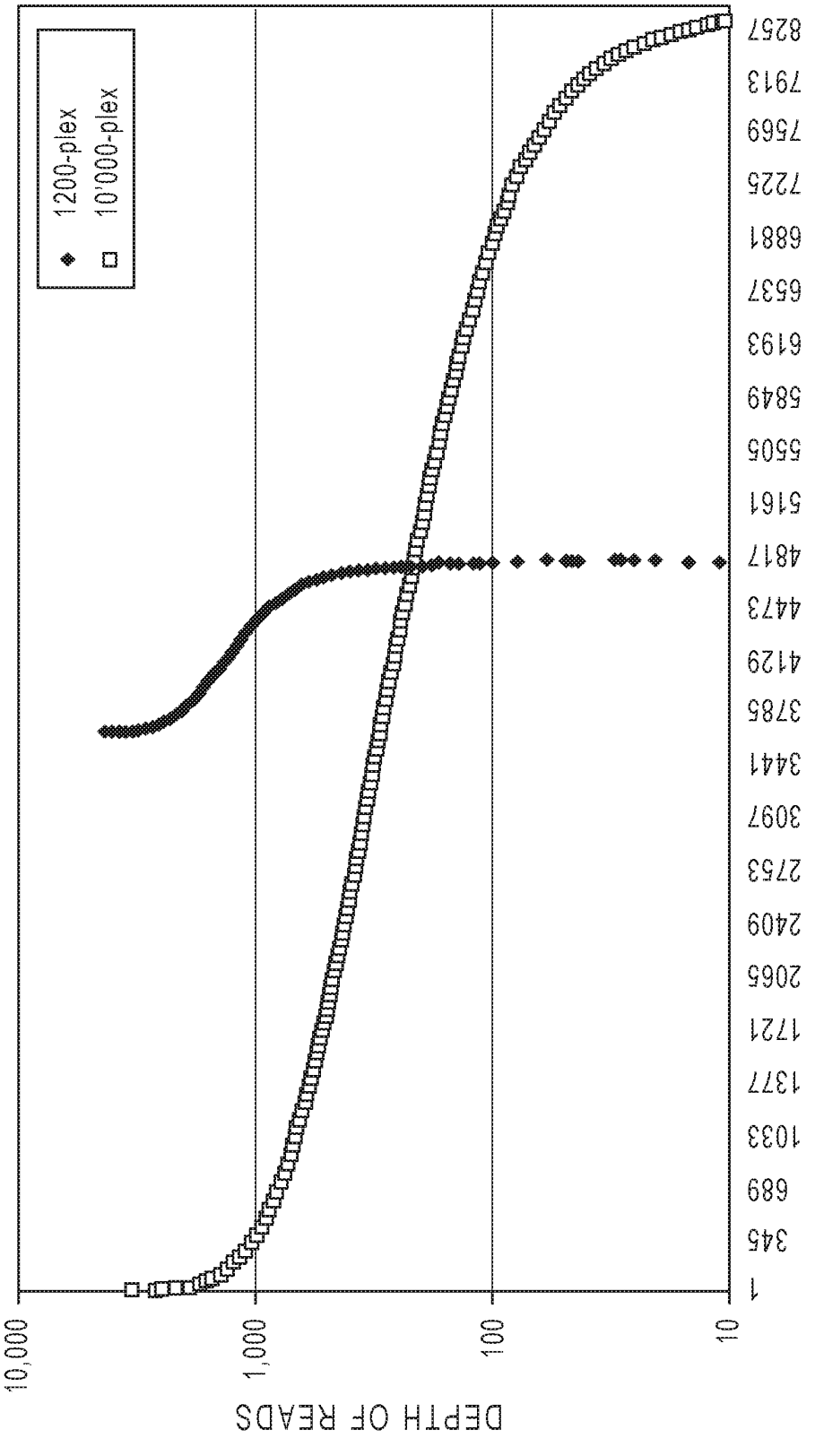

1200-plex
10'000-plex
10,000
1,000
100
10
DEPTH OF READS
1
345
689
1033
1377
1721
2065
2409
2753
3097
3441
3785
4129
4473
4817
5161
5505
5849
6193
6537
6881
7225
7569
7913
8257
RANKED ASSAY

FIG. 23

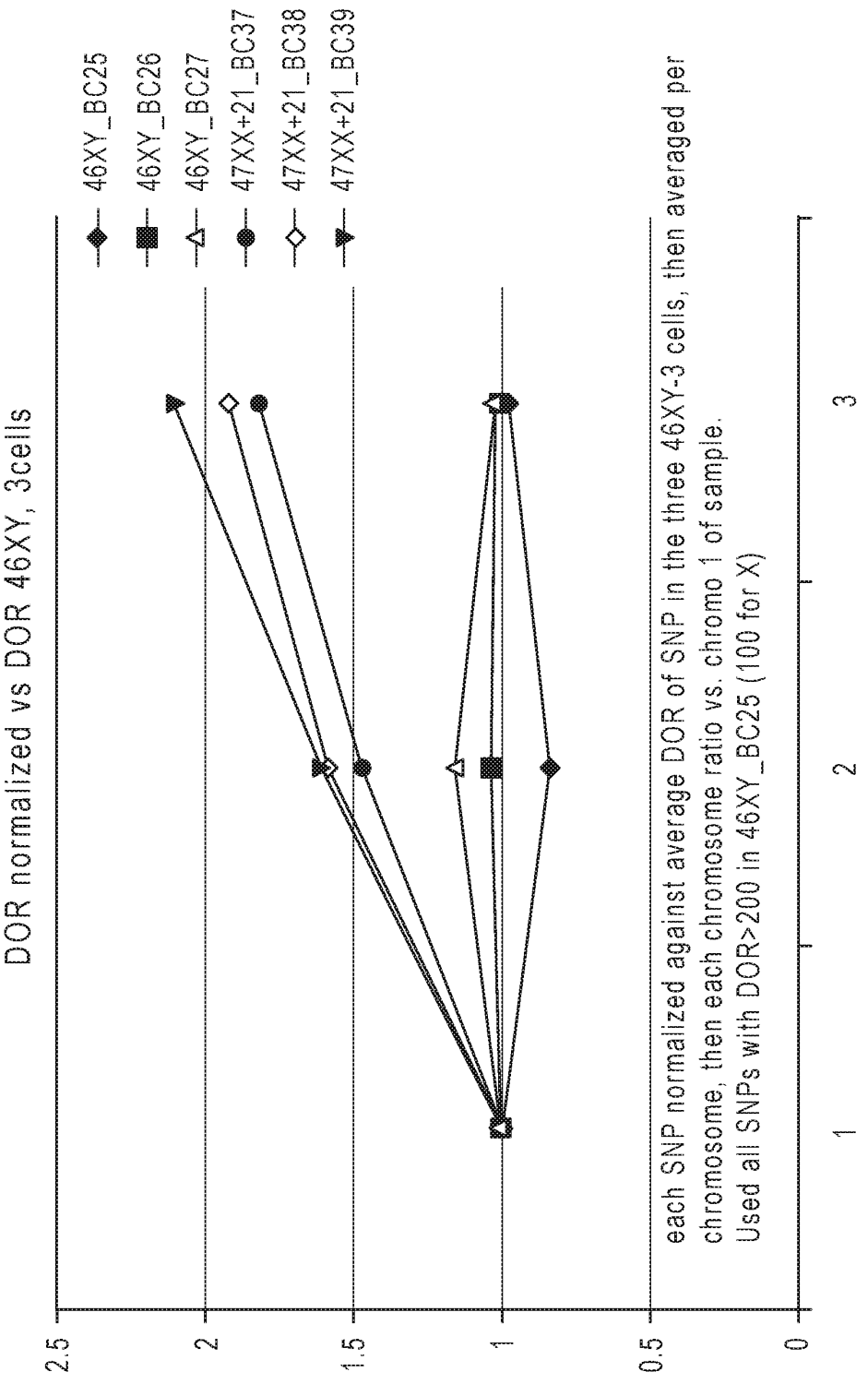

DOR normalized vs DOR 46XY, 3cells
46XY_BC25
46XY_BC26
46XY_BC27
47XX+21_BC37
47XX+21_BC38
47XX+21_BC39
2.5
2
1.5
1
0.5
0
1
2
3
each SNP normalized against average DOR of SNP in the three 46XY-3 cells, then averaged per chromosome, then each chromosome ratio vs. chromo 1 of sample.
Used all SNPs with DOR>200 in 46XY_BC25 (100 for X)

FIG. 24

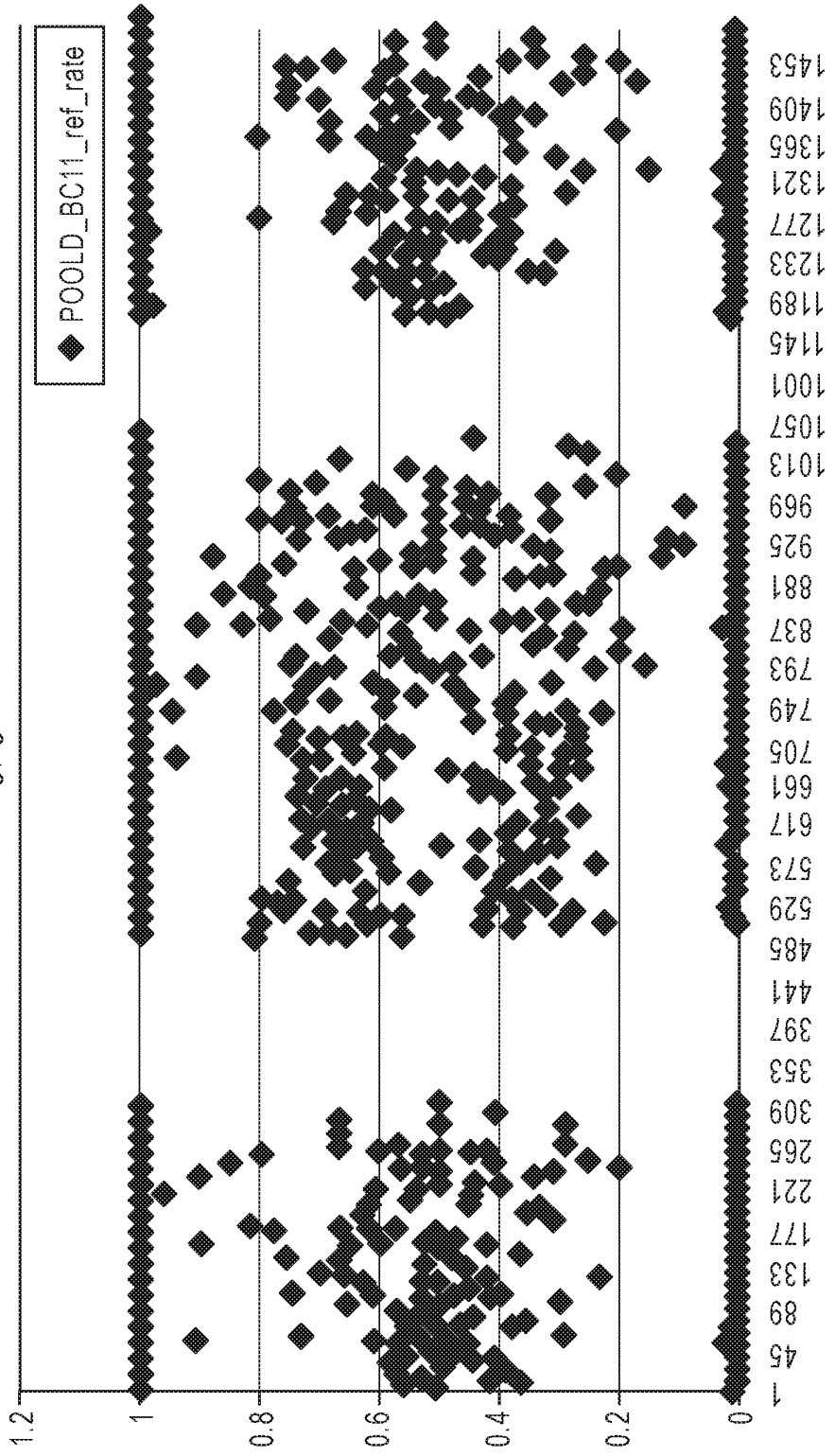

1 ng; gDNA T21
POOLD_BC11_ref_rate
1.2
1
0.8
0.6
0.4
0.2
0
1
45
89
133
177
221
265
309
353
397
441
485
529
573
617
661
705
749
793
837
881
925
969
1013
1057
1001
1145
1189
1233
1277
1321
1365
1409
1453

FIG. 25A

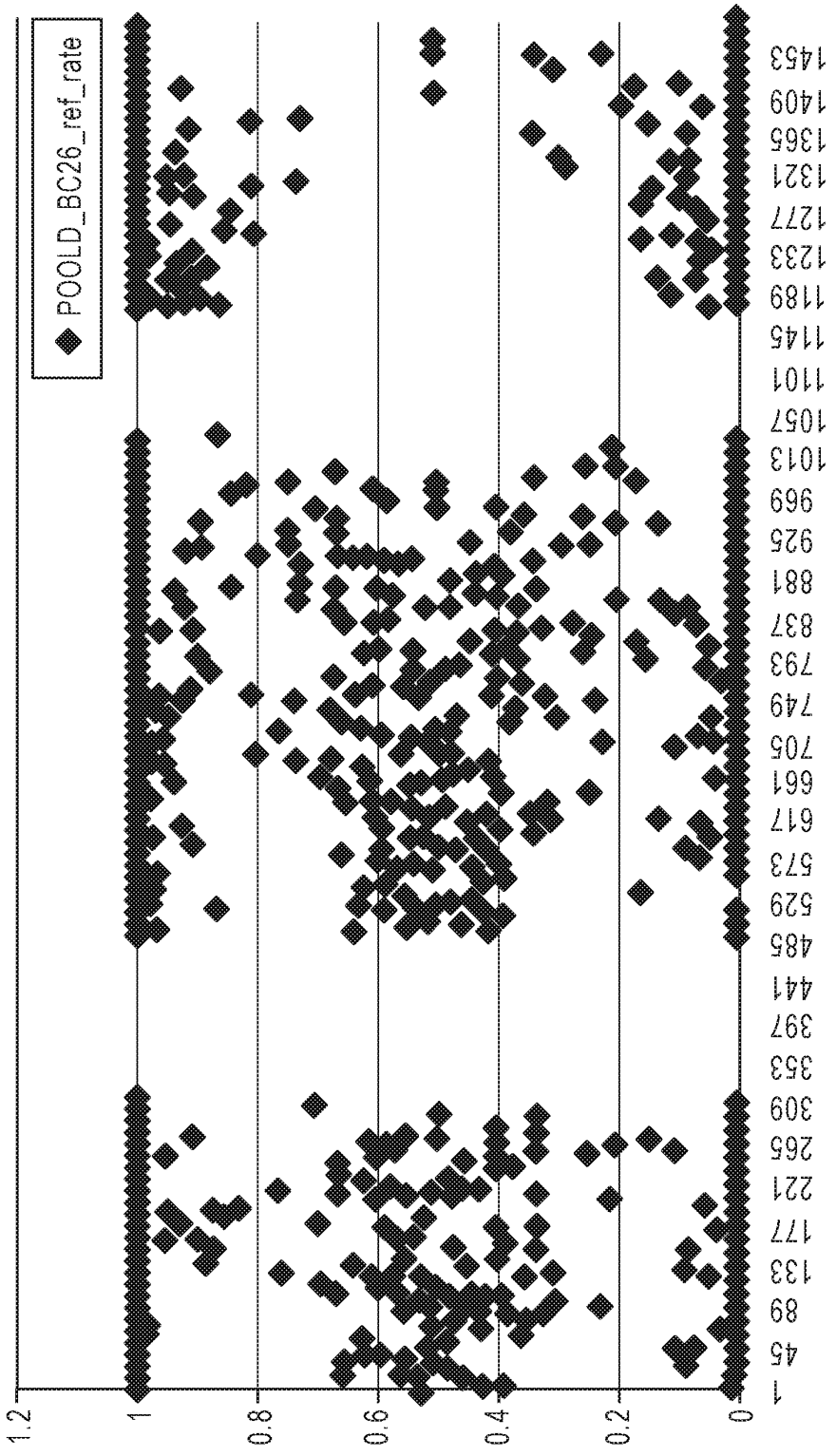

3 cells, Arcturus, GM07383 46XY
POOLD_BC26_ref_rate
1.2
1
0.8
0.6
0.4
0.2
0
1
45
89
133
177
221
265
309
353
397
441
485
529
573
617
661
705
749
793
837
881
925
969
1013
1057
1101
1145
1189
1233
1277
1321
1365
1409
1453

FIG. 25B

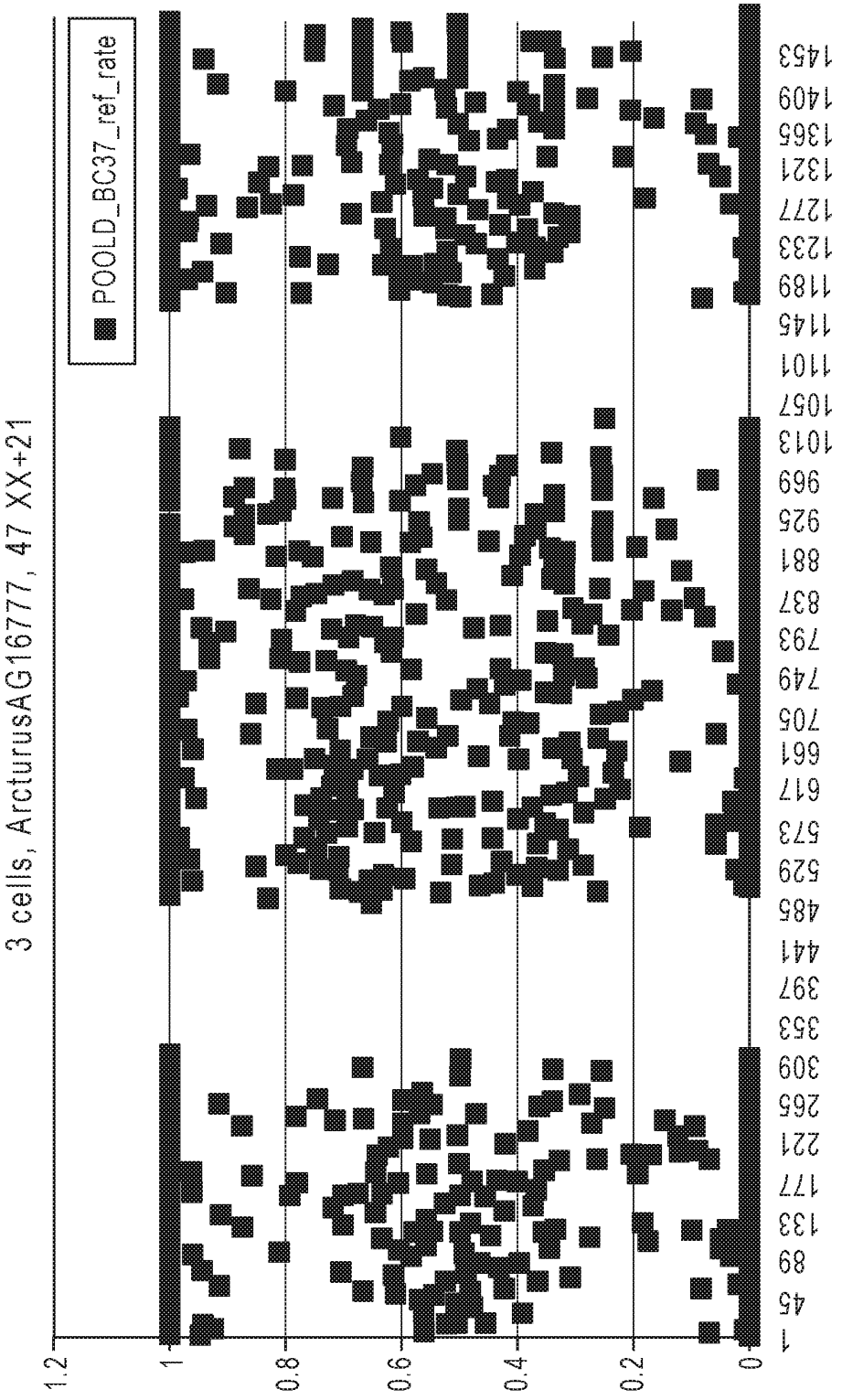

3 cells, ArcturusAG16777, 47 XX+21
POOLD_BC37_ref_rate
1.2
1
0.8
0.6
0.4
0.2
0
1
45
89
133
177
221
265
309
353
397
441
485
529
573
617
661
705
749
793
837
881
925
969
1013
1057
1101
1145
1189
1233
1277
1321
1365
1409
1453

FIG. 25C

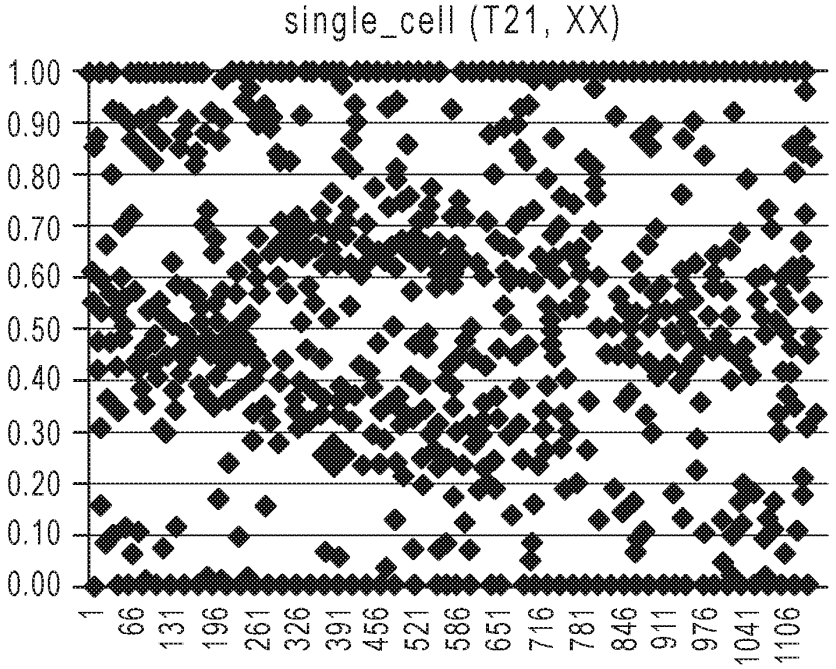


FIG. 26A

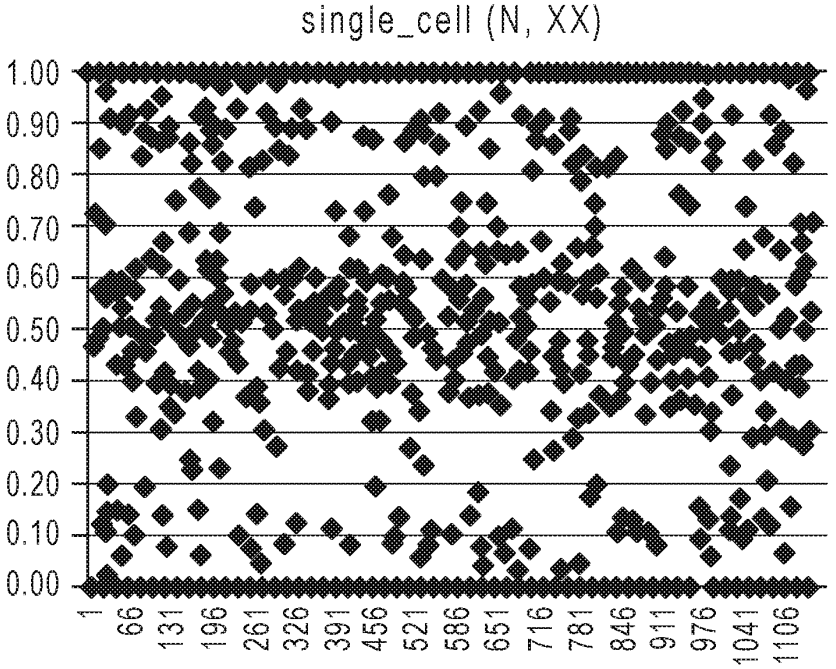


FIG. 26B

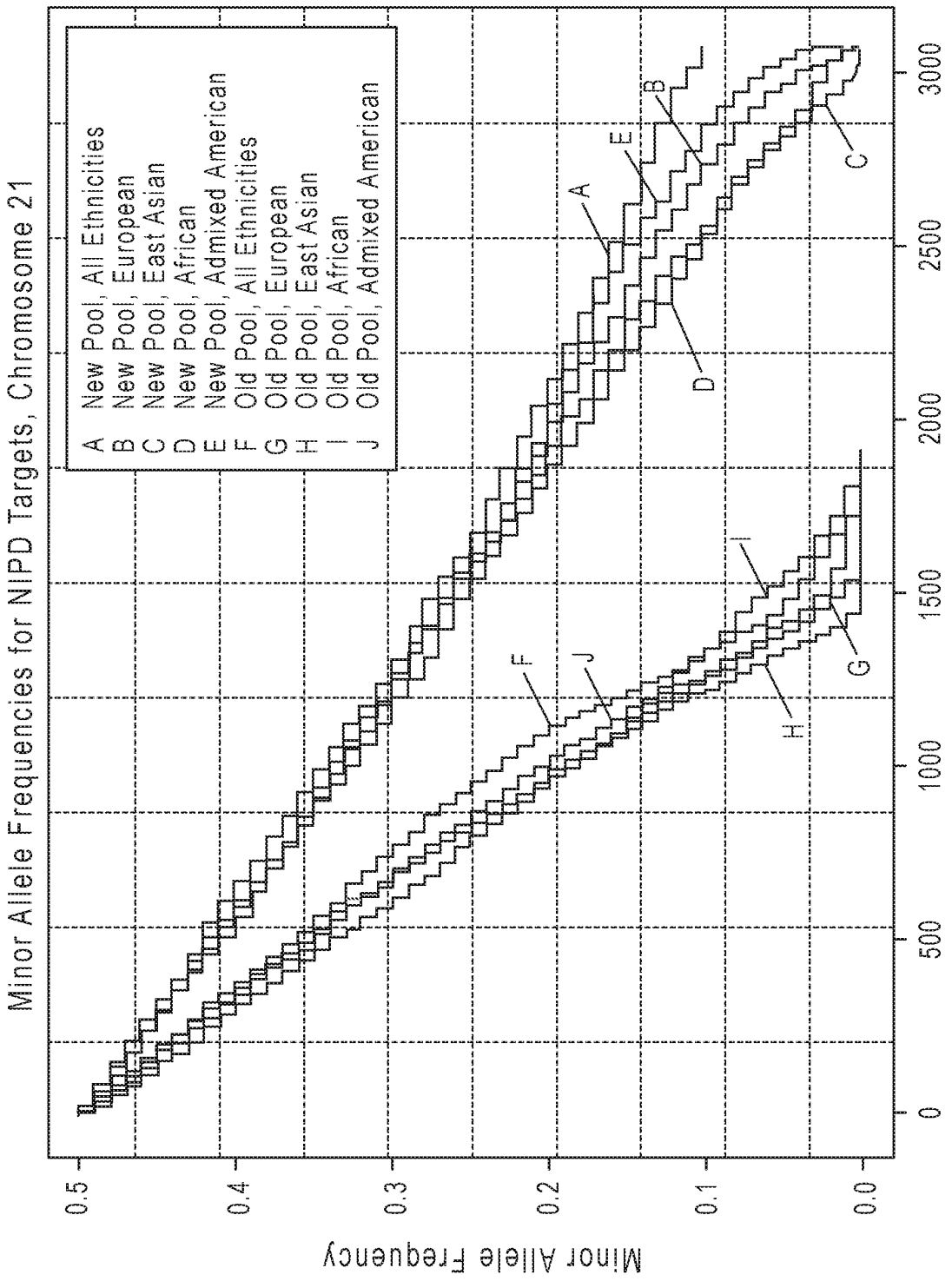

Minor Allele Frequencies for NIPD Targets, Chromosome 21
A New Pool, All Ethnicities
B New Pool, European
C New Pool, East Asian
D New Pool, African
E New Pool, Admixed American
F Old Pool, All Ethnicities
G Old Pool, European
H Old Pool, East Asian
I Old Pool, African
J Old Pool, Admixed American
Minor Allele Frequency
0.0
0.1
0.2
0.3
0.4
0.5
0
500
1000
1500
2000
2500
3000
Target Number

FIG. 27

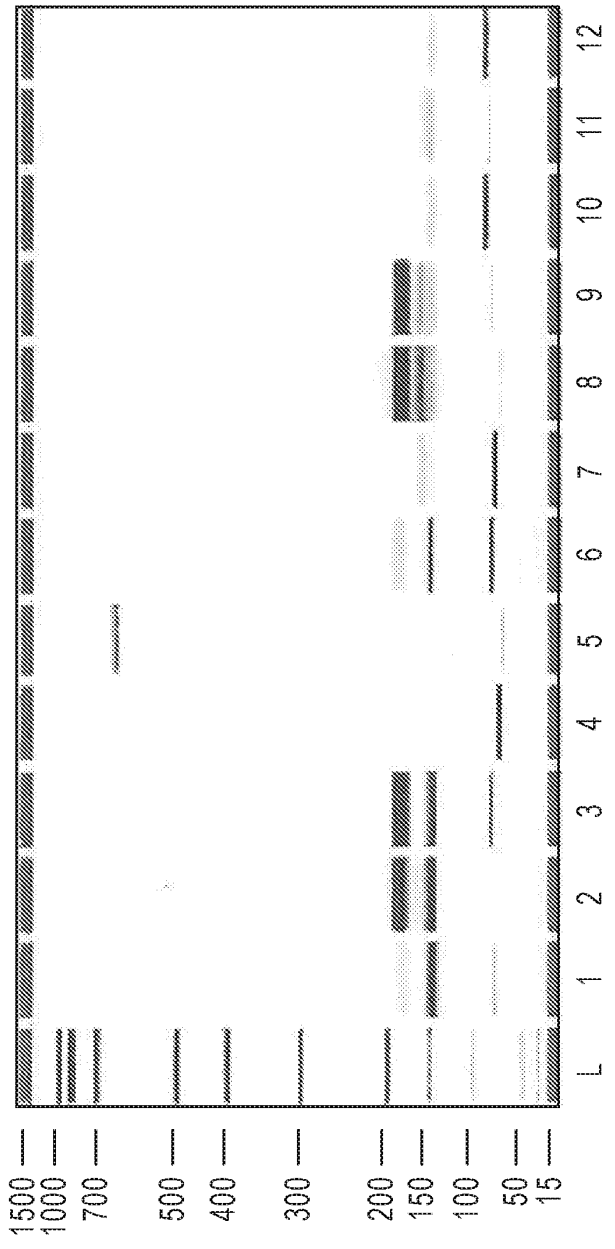


FIG. 28A

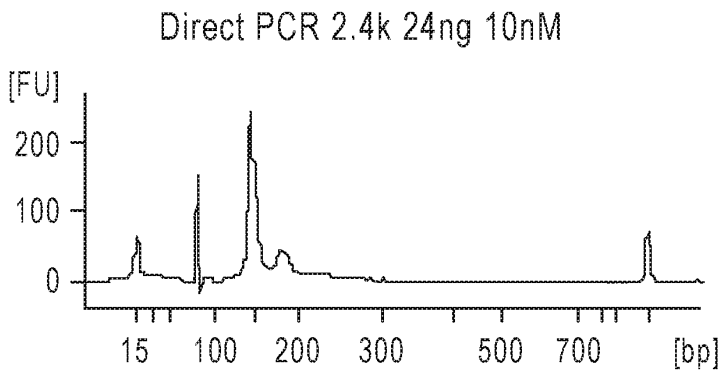


FIG. 28B

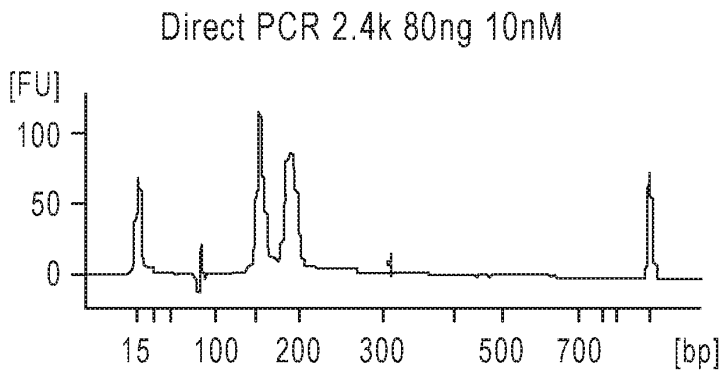


FIG. 28C

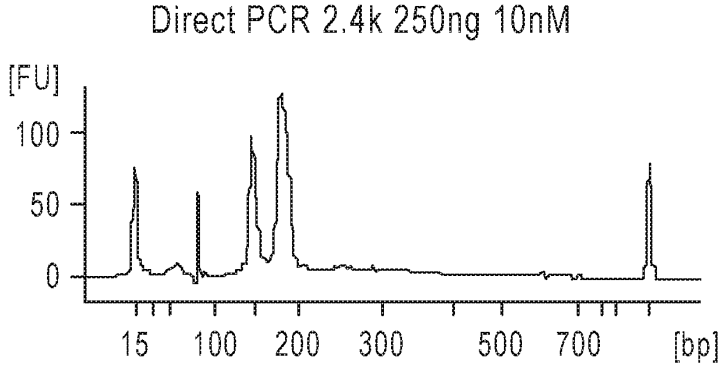


FIG. 28D

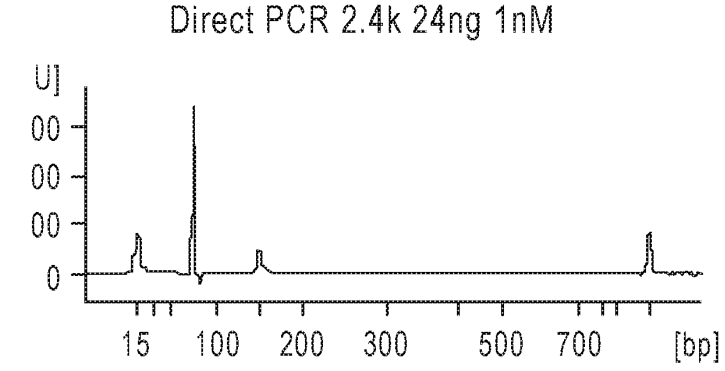


FIG. 28E

NeoGenomics
Exhibit 1003 Page 908

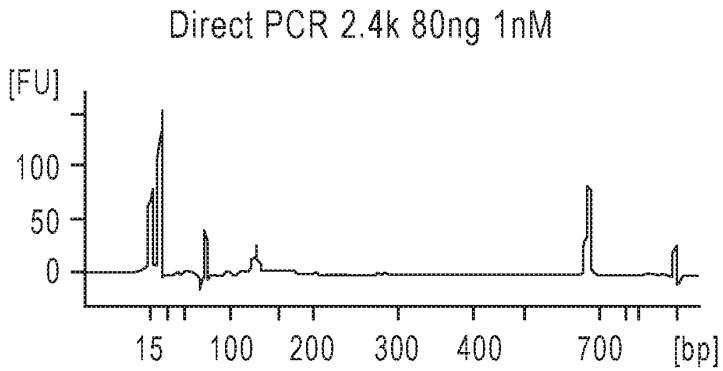


FIG. 28F

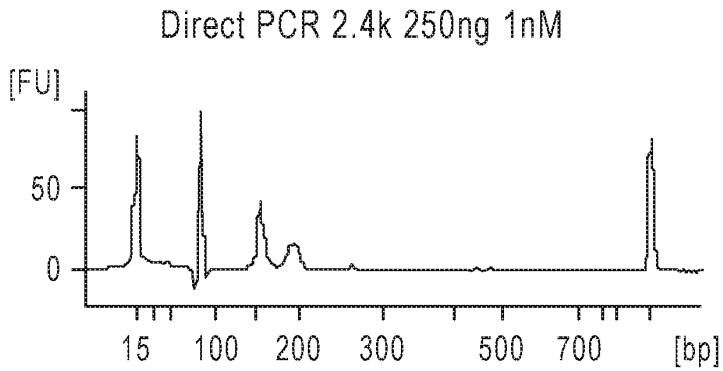


FIG. 28G

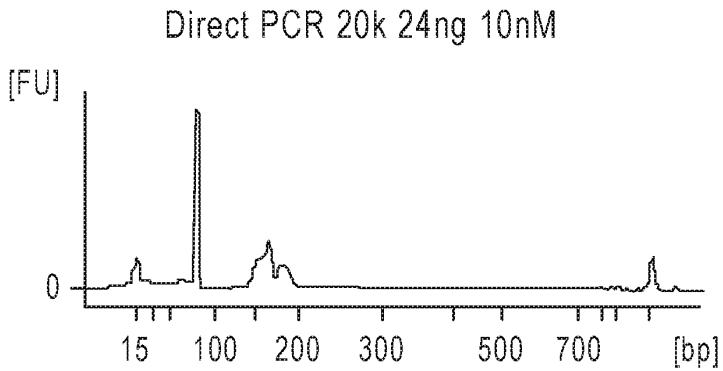


FIG. 28H

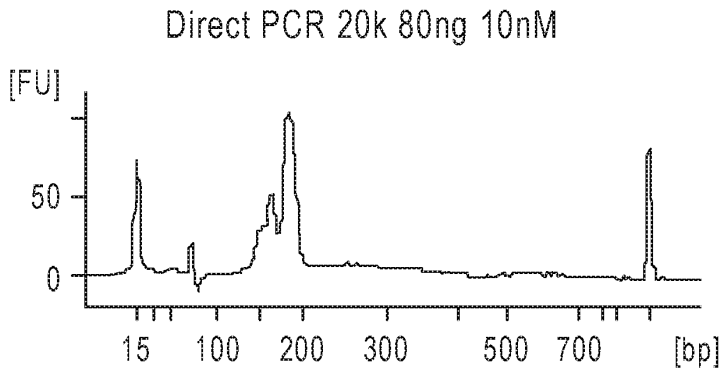


FIG. 28I

NeoGenomics
Exhibit 1003 Page 909

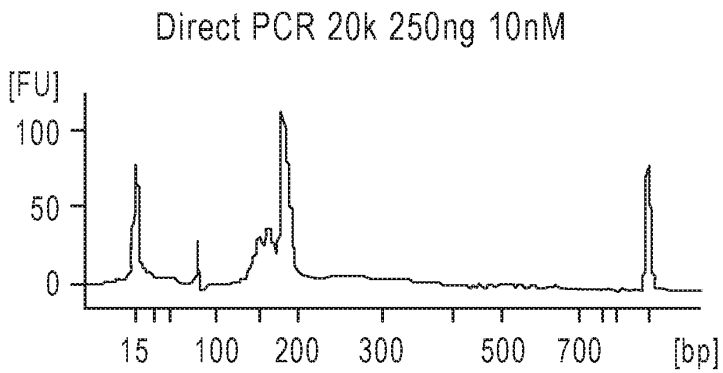


FIG. 28J

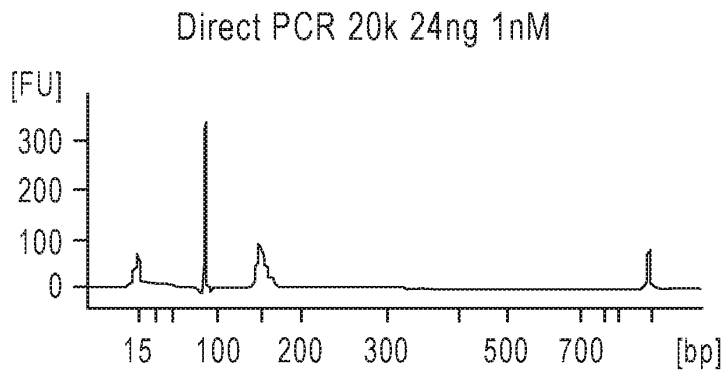


FIG. 28K

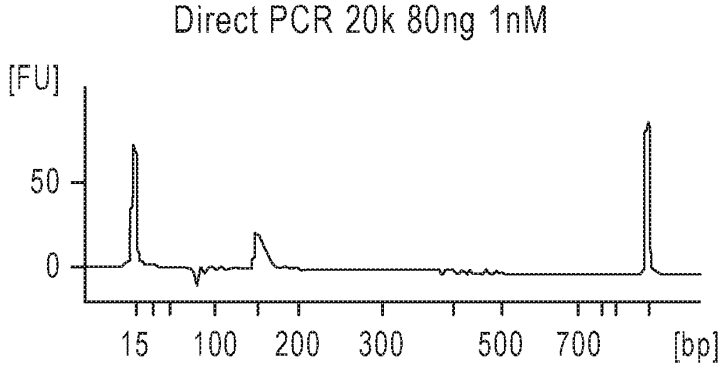


FIG. 28L

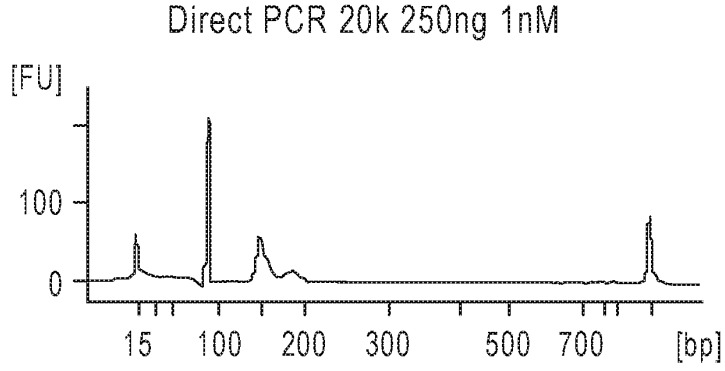


FIG. 28M

NeoGenomics
Exhibit 1003 Page 910

A
Maternal +/- Paternal Genotypic Data
Fetal + Fraction
B
Multiple Hypothesis for Each Chromosome
Crossover Frequency Data
C
Compare Predictions to Maternal Plasma Sequencing Data
D
Sum of Likelihood of Each Fetal Ploidy State
E
Correct Ploidy Call

FIG. 29

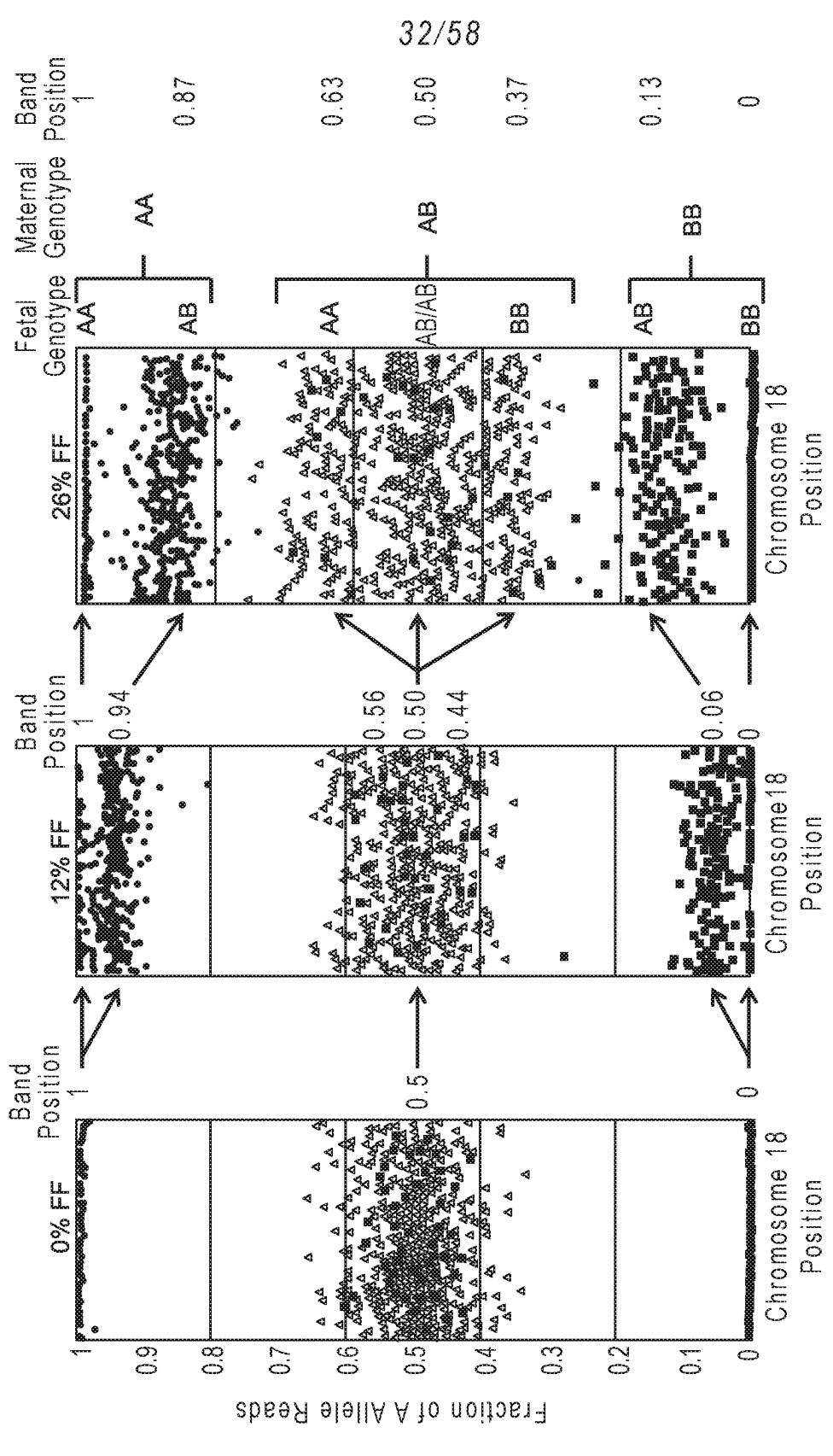

Fraction of A Allele Reads
0% FF
12% FF
26% FF
Chromosome 18 Position
Band Position
Fetal Genotype
Maternal Genotype
AA
AB
BB
0.94
0.56
0.50
0.44
0.06
0.87
0.63
0.37
0.13

FIG. 30

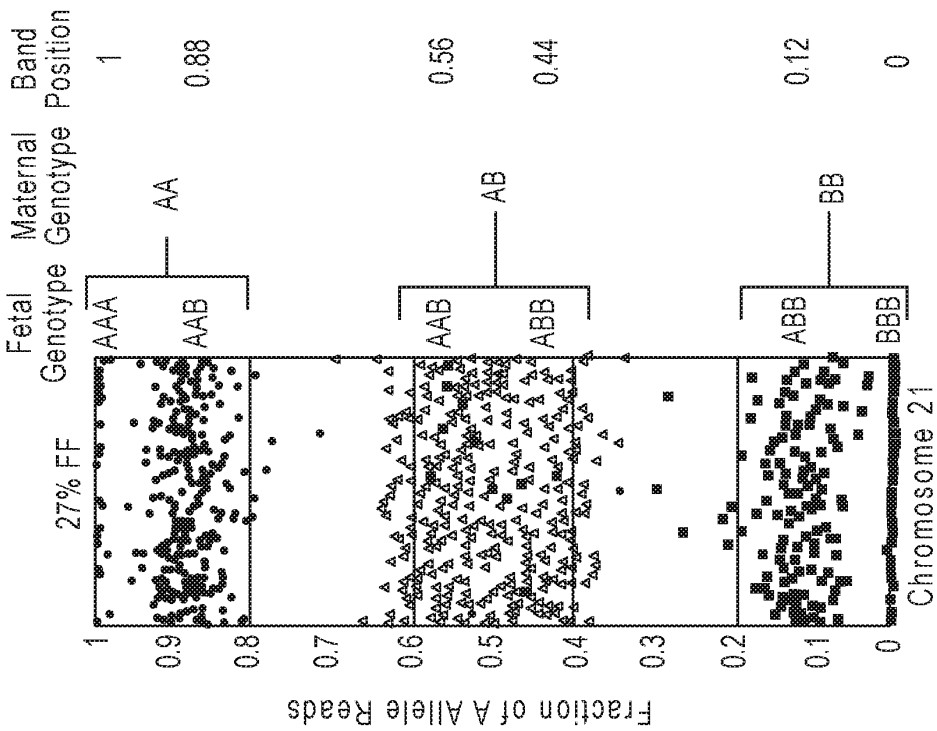


FIG. 30D

FIG. 30E

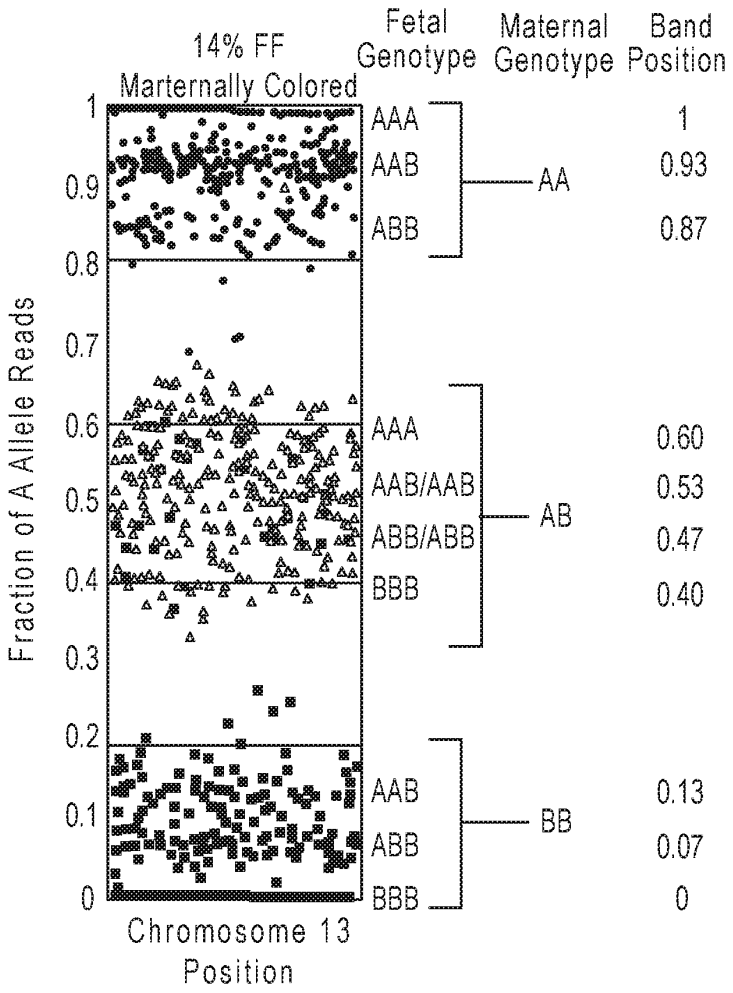


FIG. 30F

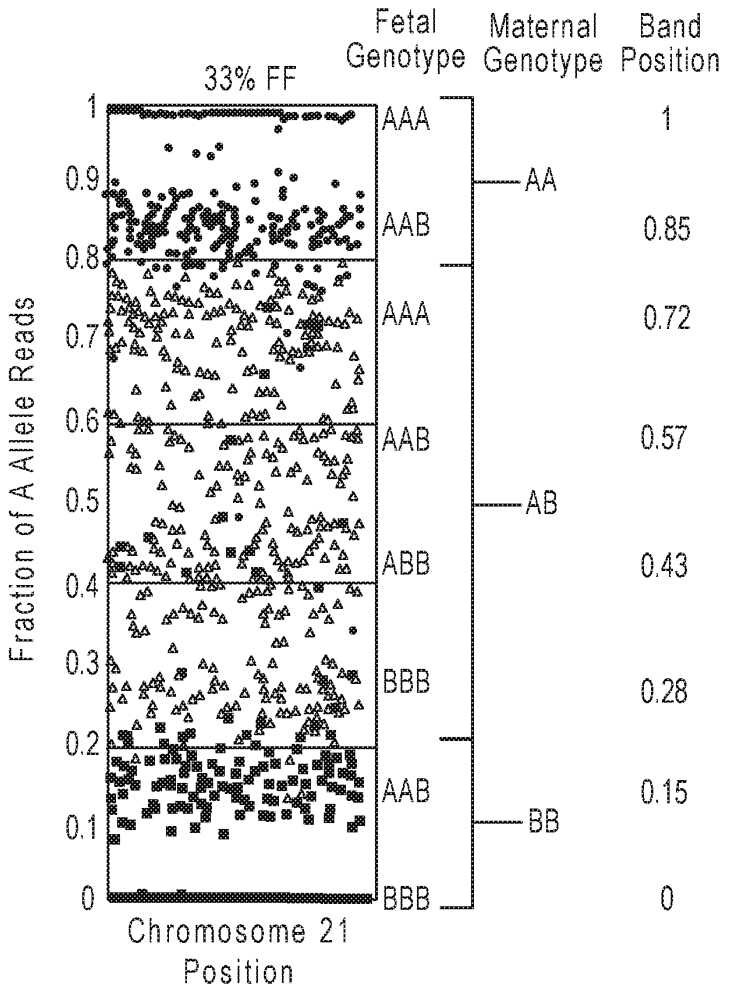


FIG. 30G

NeoGenomics
Exhibit 1003 Page 914

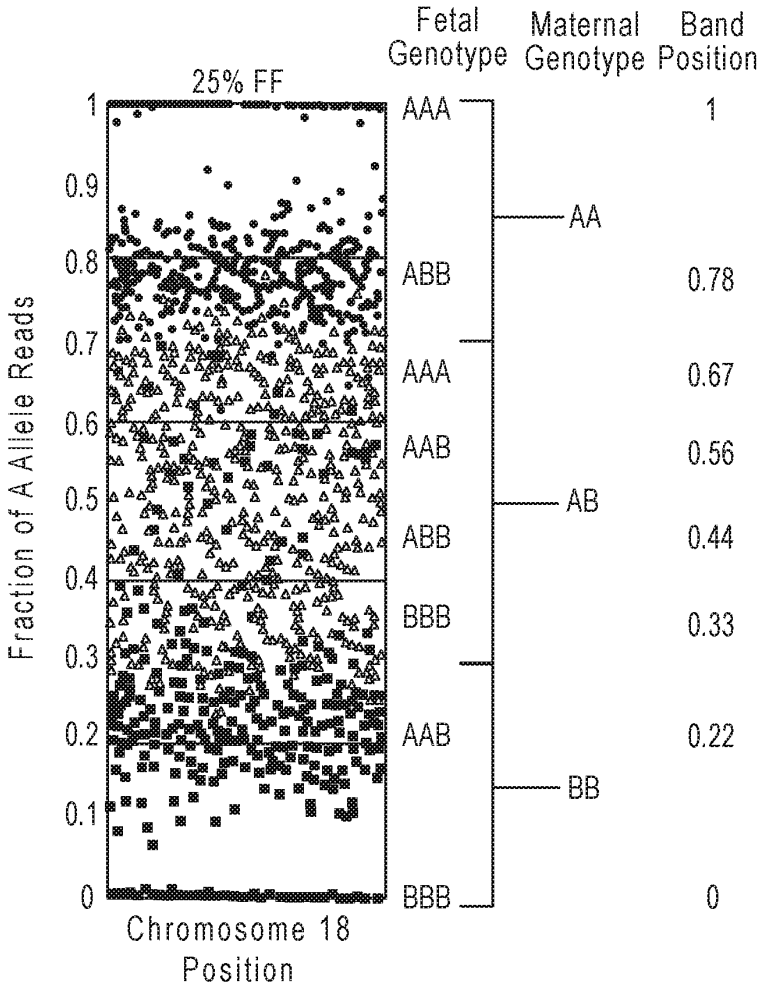

Fetal Genotype
Maternal Genotype
Band Position
25% FF
Fraction of A Allele Reads
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
AAA
ABB
AAA
AAB
ABB
BBB
AAB
BBB
AA
AB
BB
1
0.78
0.67
0.56
0.44
0.33
0.22
0
Chromosome 18 Position

FIG. 30H

FIG. 31A

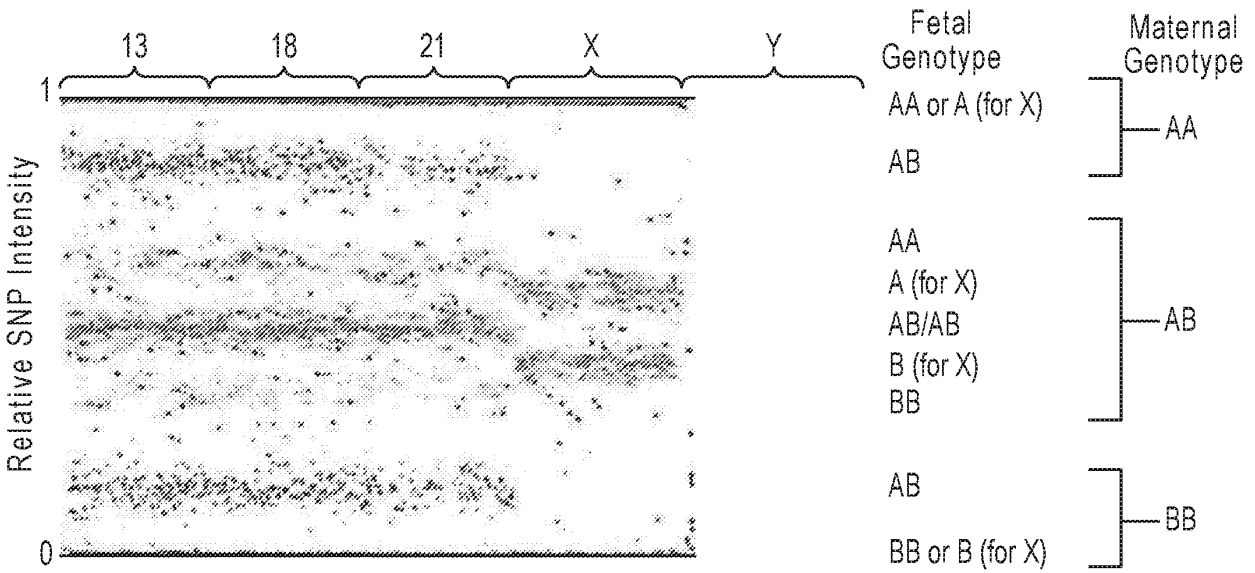
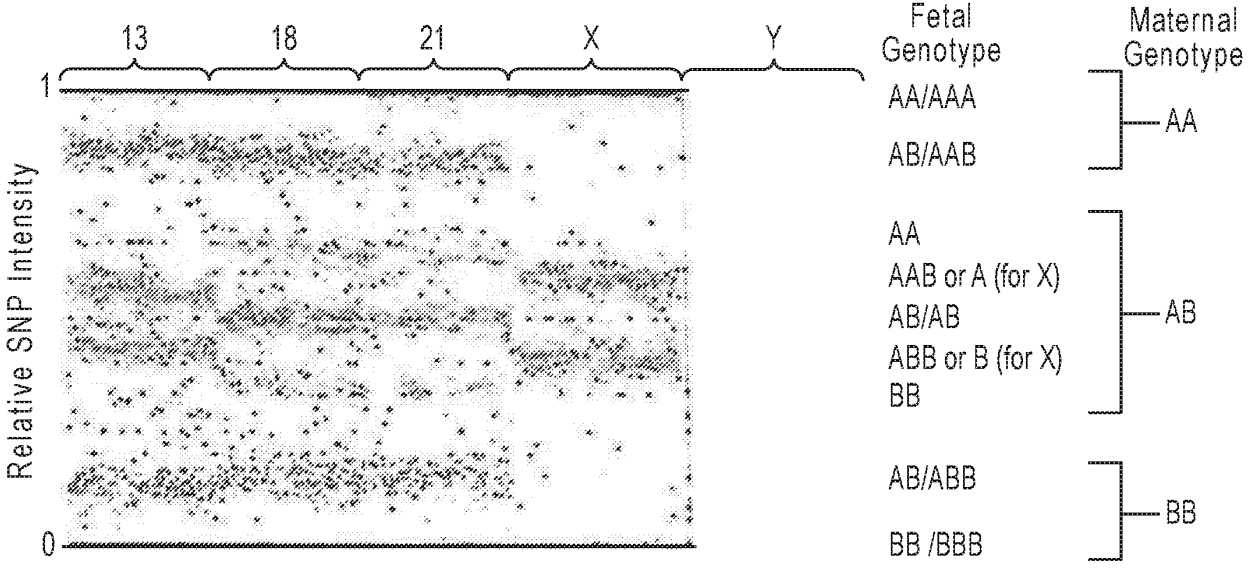


FIG. 31B



NeoGenomics
Exhibit 1003 Page 916

T13
13% FF
XY

FIG. 31C

T21
20% FF
XX

FIG. 31D

FIG. 31E

FIG. 31F

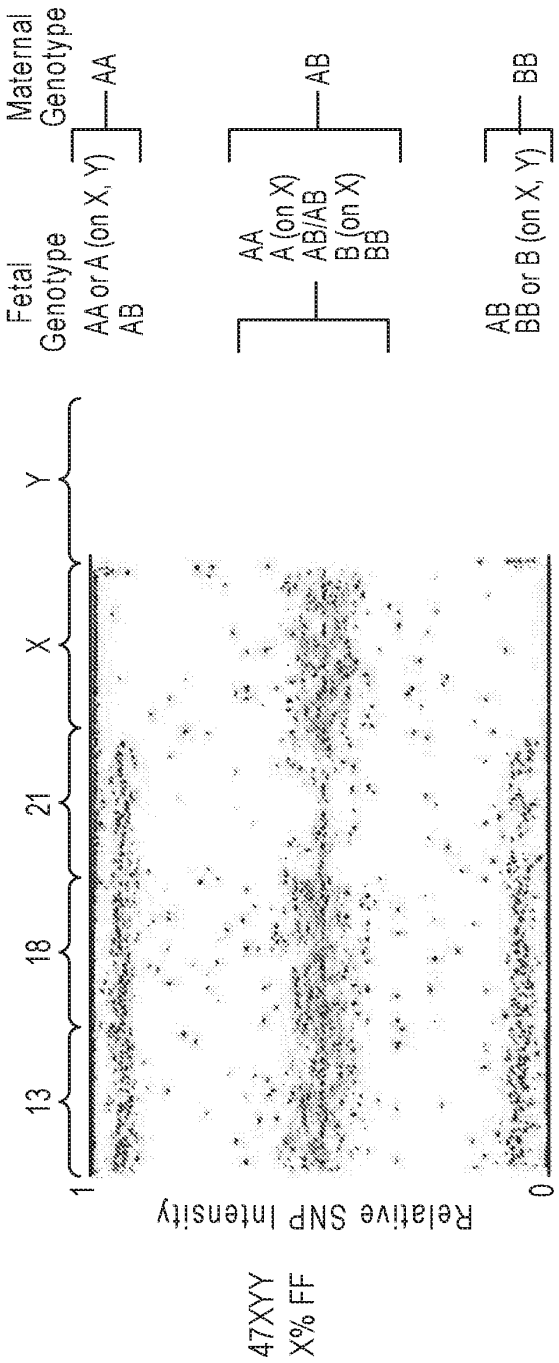

47XYY
X% FF
Relative SNP Intensity
1
0
13
18
21
X
Y
Fetal Genotype
AA or A (on X, Y)
AB
Maternal Genotype
AA
AB
AA
A (on X)
AB/AB
B (on X)
BB
AB
BB or B (on X, Y)
BB

FIG. 31G

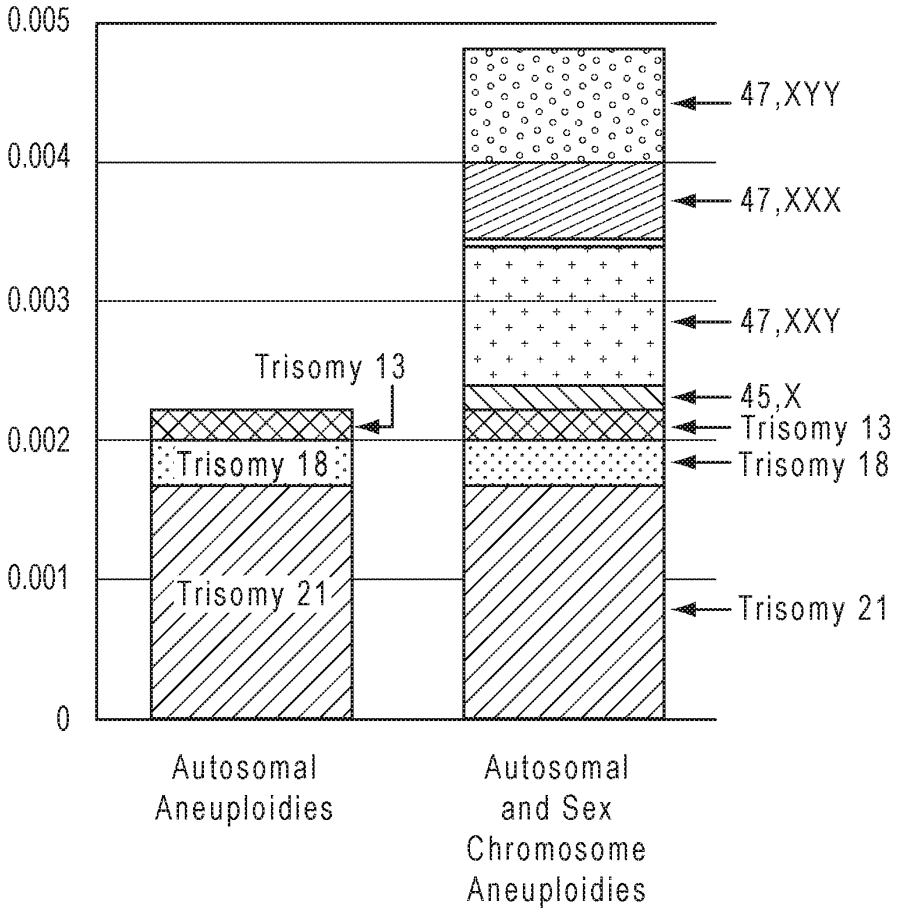

0.005
0.004
0.003
0.002
0.001
0
Trisomy 13
Trisomy 18
Trisomy 21
47,XYY
47,XXX
47,XXY
45,X
Trisomy 13
Trisomy 18
Trisomy 21
Autosomal Aneuploidies
Autosomal and Sex Chromosome Aneuploidies

FIG. 32

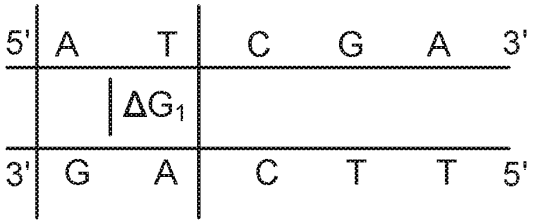
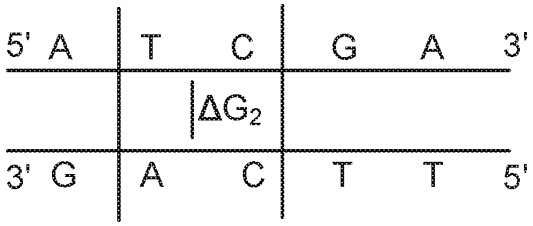


FIG. 33A



$$\Delta G = \Delta G_1 + \Delta G_2 + \ldots + \Delta G_x$$

FIG. 33B

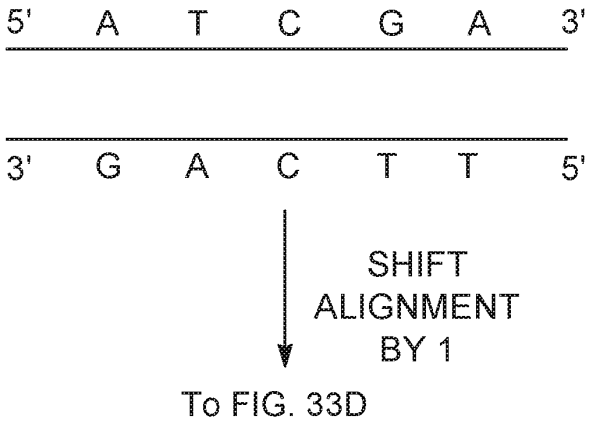


FIG. 33C

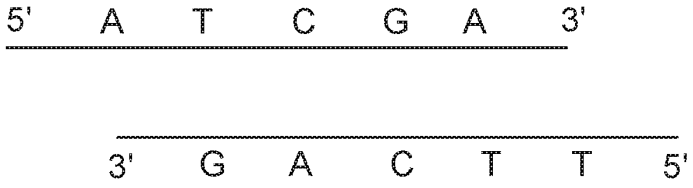


FIG. 33D

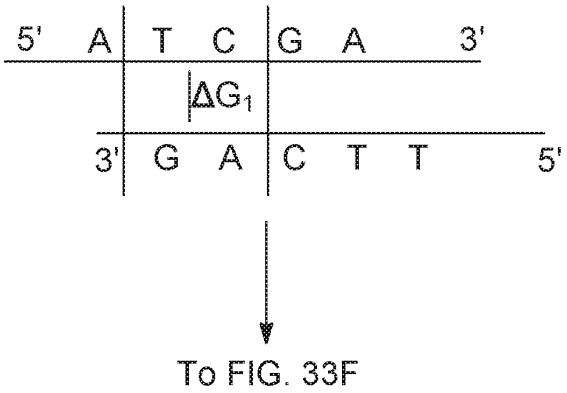


FIG. 33E

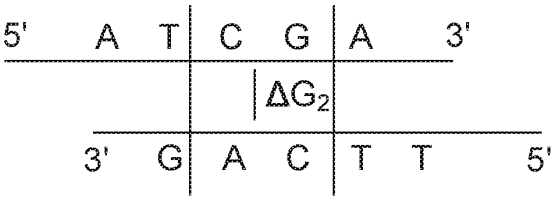


FIG. 33F

Description	MAPPED_READS	TOTAL_READS	%Mapped Reads
gMother	3,633,900	3,647,446	100%
gMother	3,567,685	3,578,549	100%
gMother	3,733,706	3,747,692	100%
gChild	3,725,554	3,737,742	100%
gChild	3,816,989	3,829,450	100%
gChild	3,524,956	3,536,569	100%
1 mother	3,467,493	7,564,869	46%
1 mother	3,868,210	7,107,028	54%
1 mother	4,918,140	7,613,240	65%
1 child	361,390	6,507,434	6%
1 child	1,885,864	6,496,348	29%
1 child	2,789,647	6,259,288	45%

FIG. 34

NeoGenomics
Exhibit 1003 Page 924

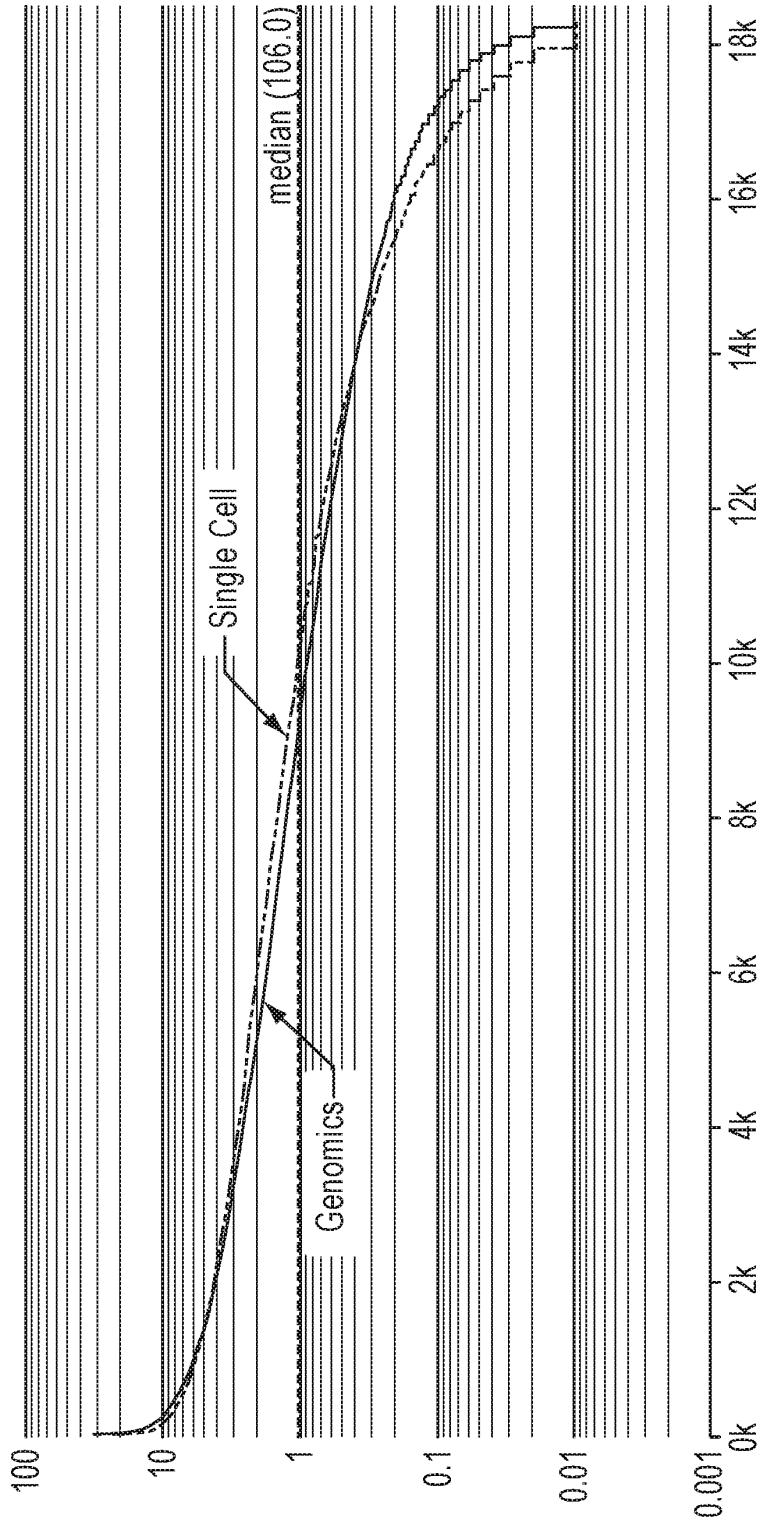

100
10
1
0.1
0.01
0.001
0k
2k
4k
6k
8k
10k
12k
14k
16k
18k
SNP INDEX
median (106.0)
Single Cell
Genomics

FIG. 35

Description	MAPPED_READS	TOTAL_READS	%Mapped Reads	
case 1 blastoceol	68,123	8,470,872	1%	
case 1 cell 1	4,340,613	8,248,598		53%
case 1 cell 2	5,480,580	8,230,870		67%
case 1 cell 3	4,664,577	7,846,040		59%
case 2 blastoceol	45,794	6,302,957	1%	
case 2 cell 1	6,988,854	8,622,495		81%
case 2 cell 2	7,083,600	8,843,495		80%
case 2 cell 3	5,811,364	8,256,310		70%

FIG. 36

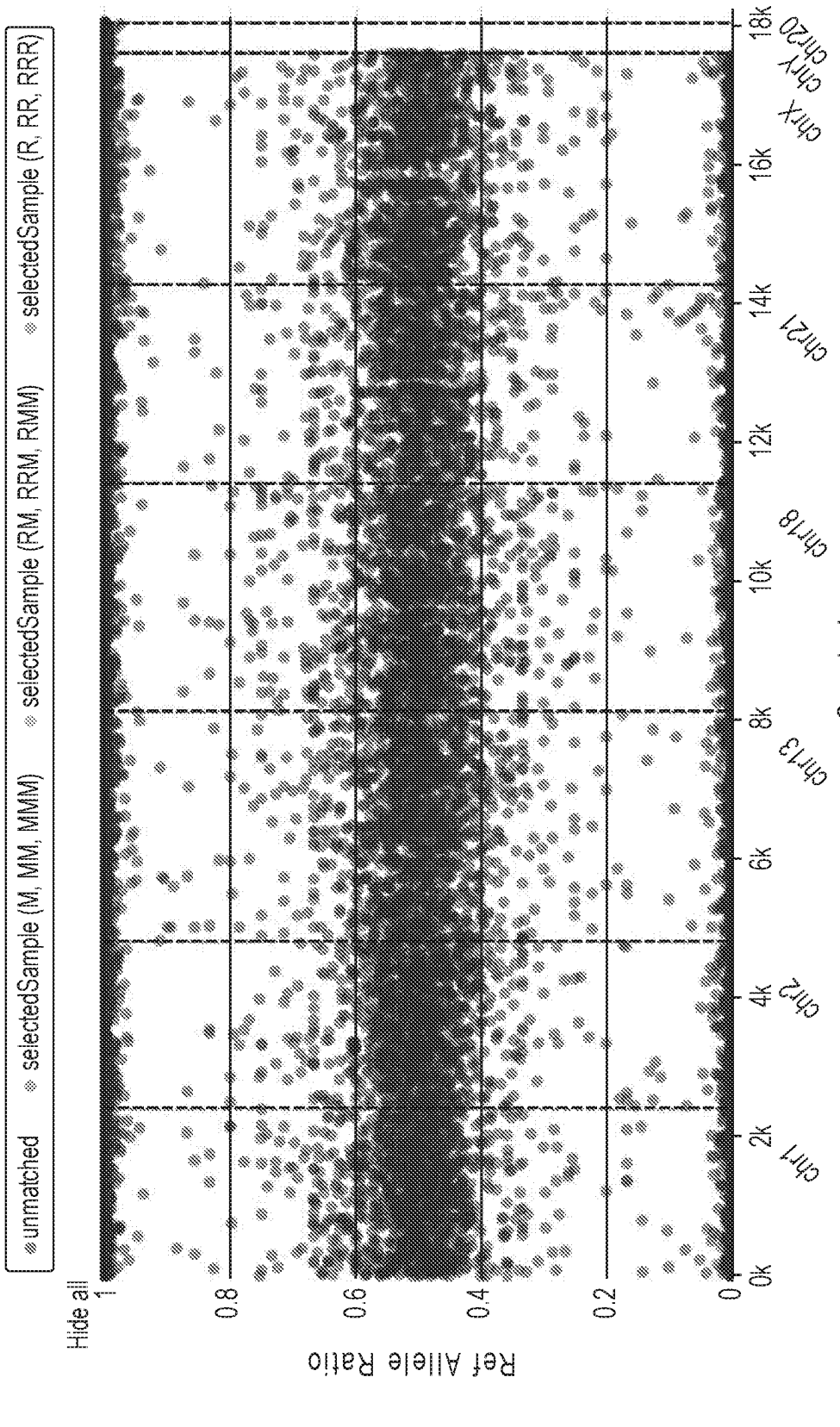

unmatched
selectedSample (M, MM, MMM)
selectedSample (RM, RRM, RMM)
selectedSample (R, RR, RRR)
Hide all
Ref Allele Ratio
1
0.8
0.6
0.4
0.2
0
0k
2k
4k
6k
8k
10k
12k
14k
16k
18k
chr1
chr2
chr13
chr18
chr21
chrX
chrY
chr20
Snp Index

FIG. 37

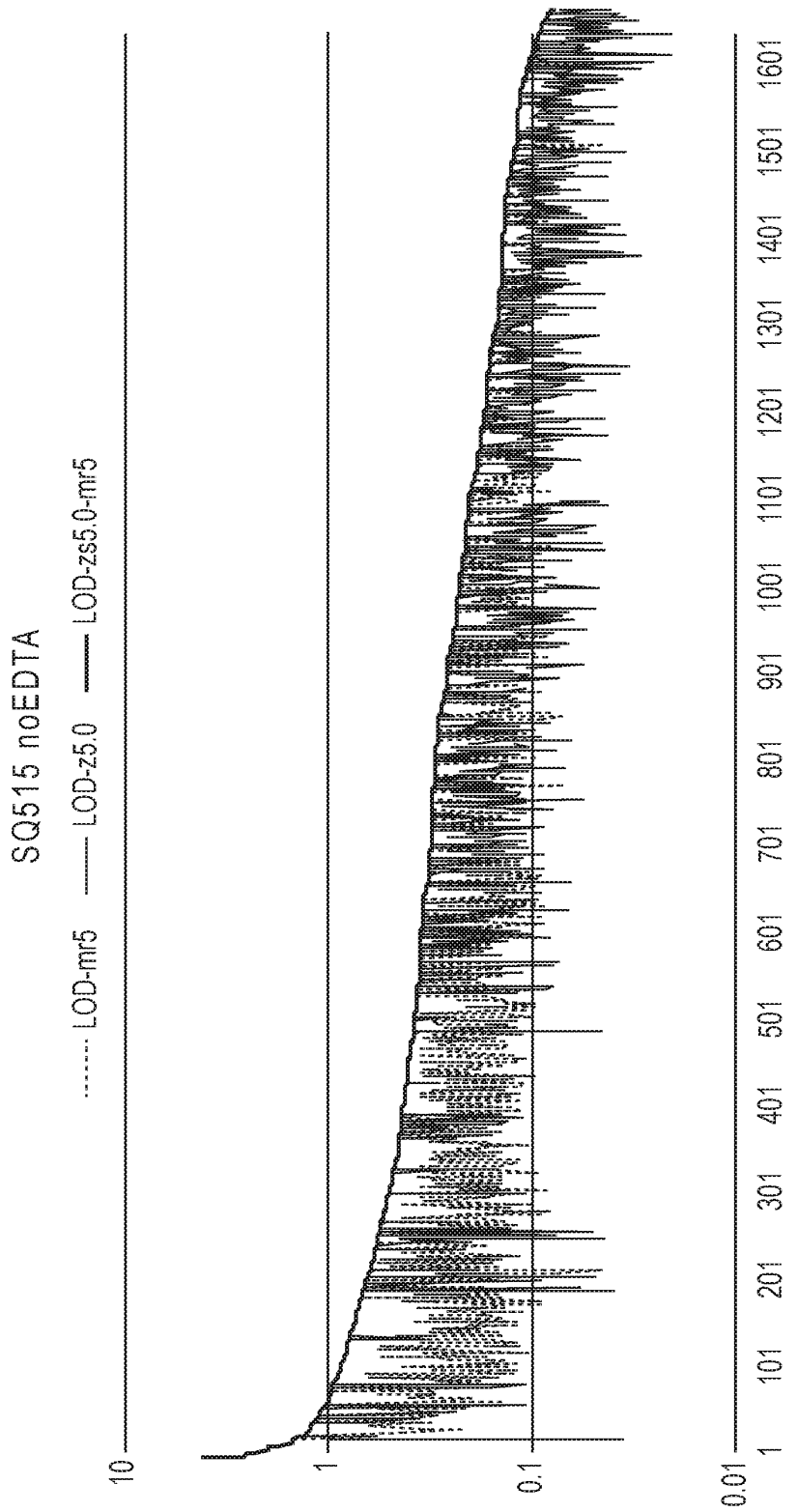

SQ515 noEDTA
LOD-mr5
LOD-z5.0
LOD-zs5.0-mr5
10
1
0.1
0.01
1
101
201
301
401
501
601
701
801
901
1001
1101
1201
1301
1401
1501
1601

FIG. 38

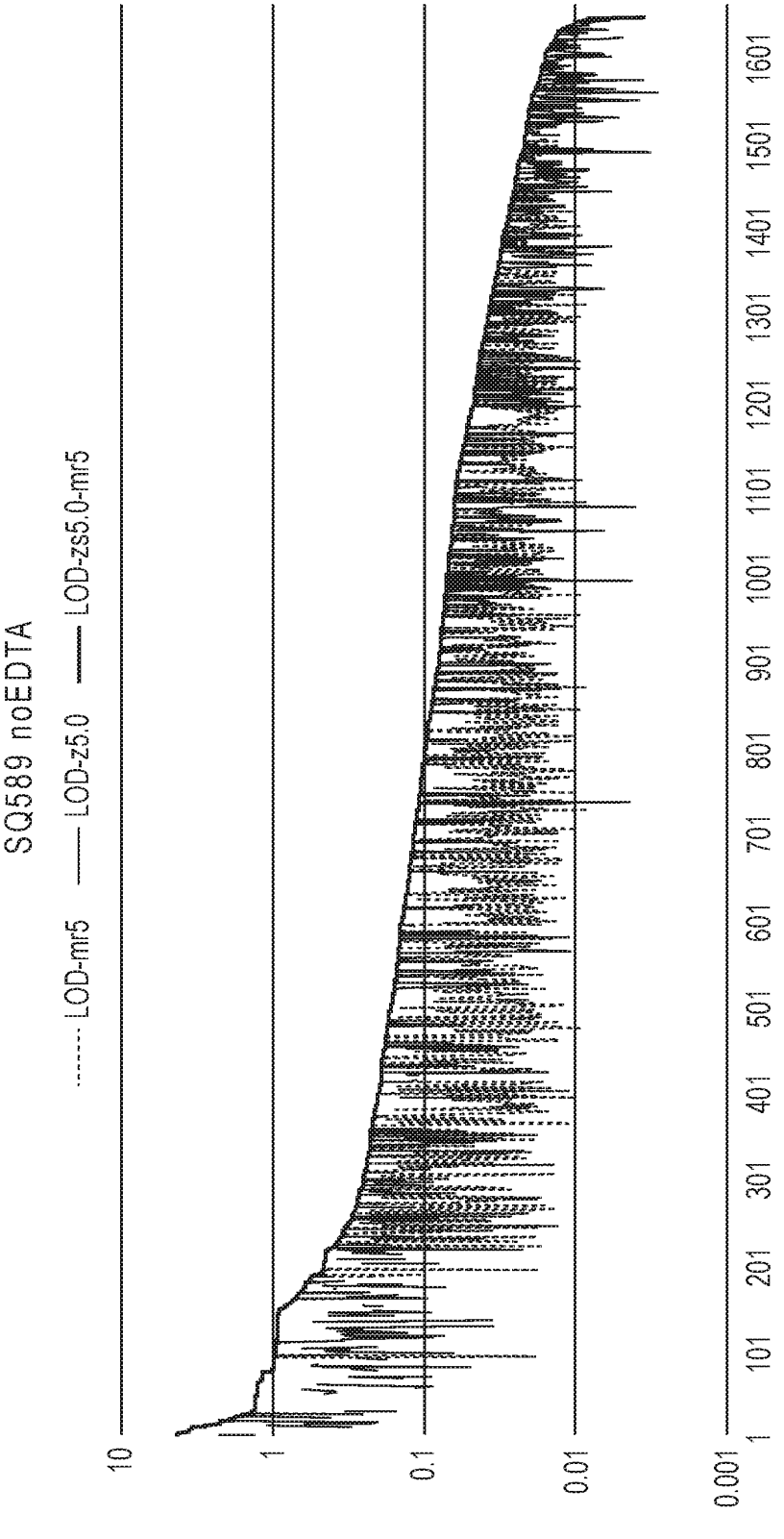

SQ589 noEDTA
LOD-mr5
LOD-z5.0
LOD-zs5.0-mr5
10
1
0.1
0.01
0.001
1
101
201
301
401
501
601
701
801
901
1001
1101
1201
1301
1401
1501
1601

FIG. 39

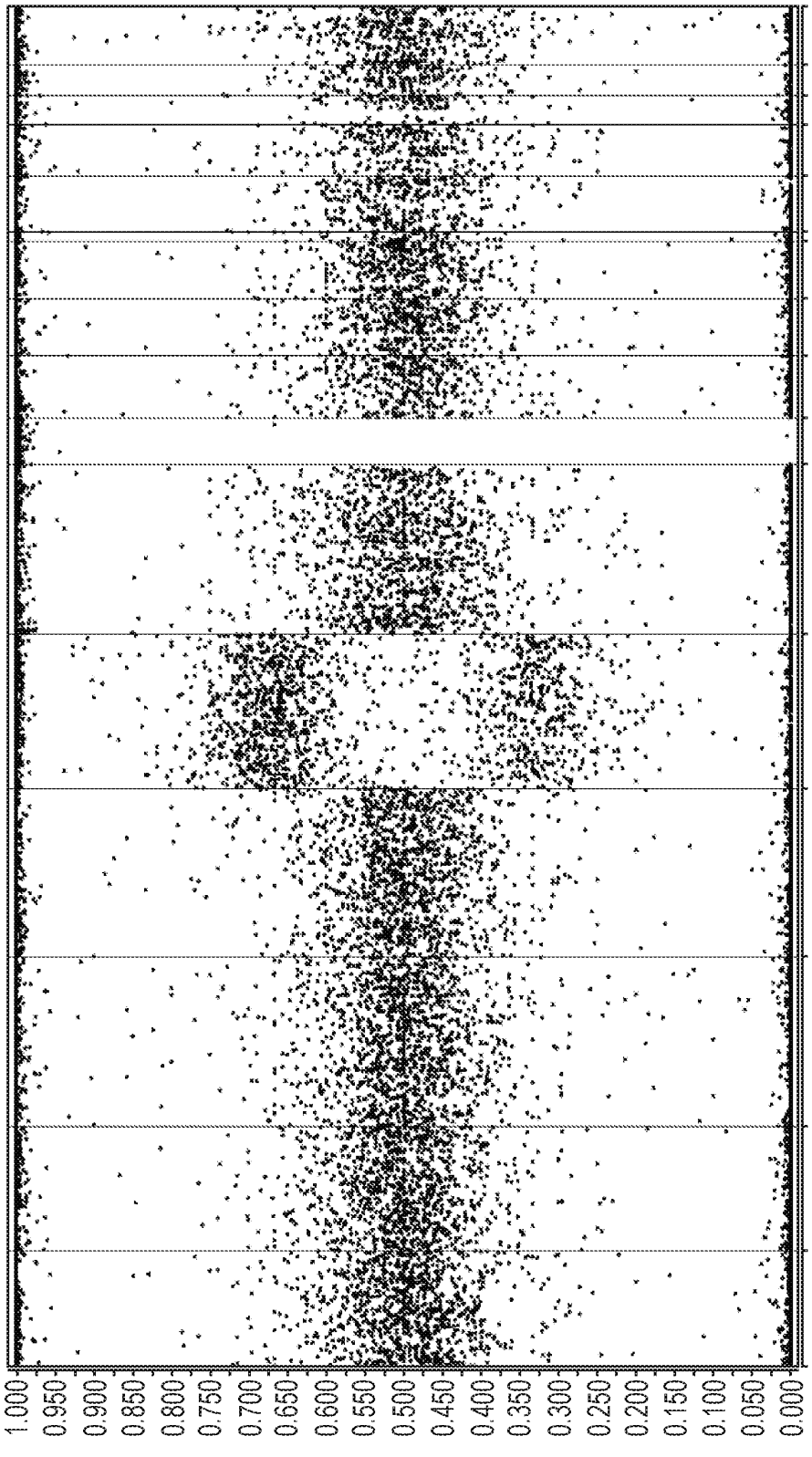

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
chr13
chr18
chr21
chrX
chr26
Genomics

FIG. 40A

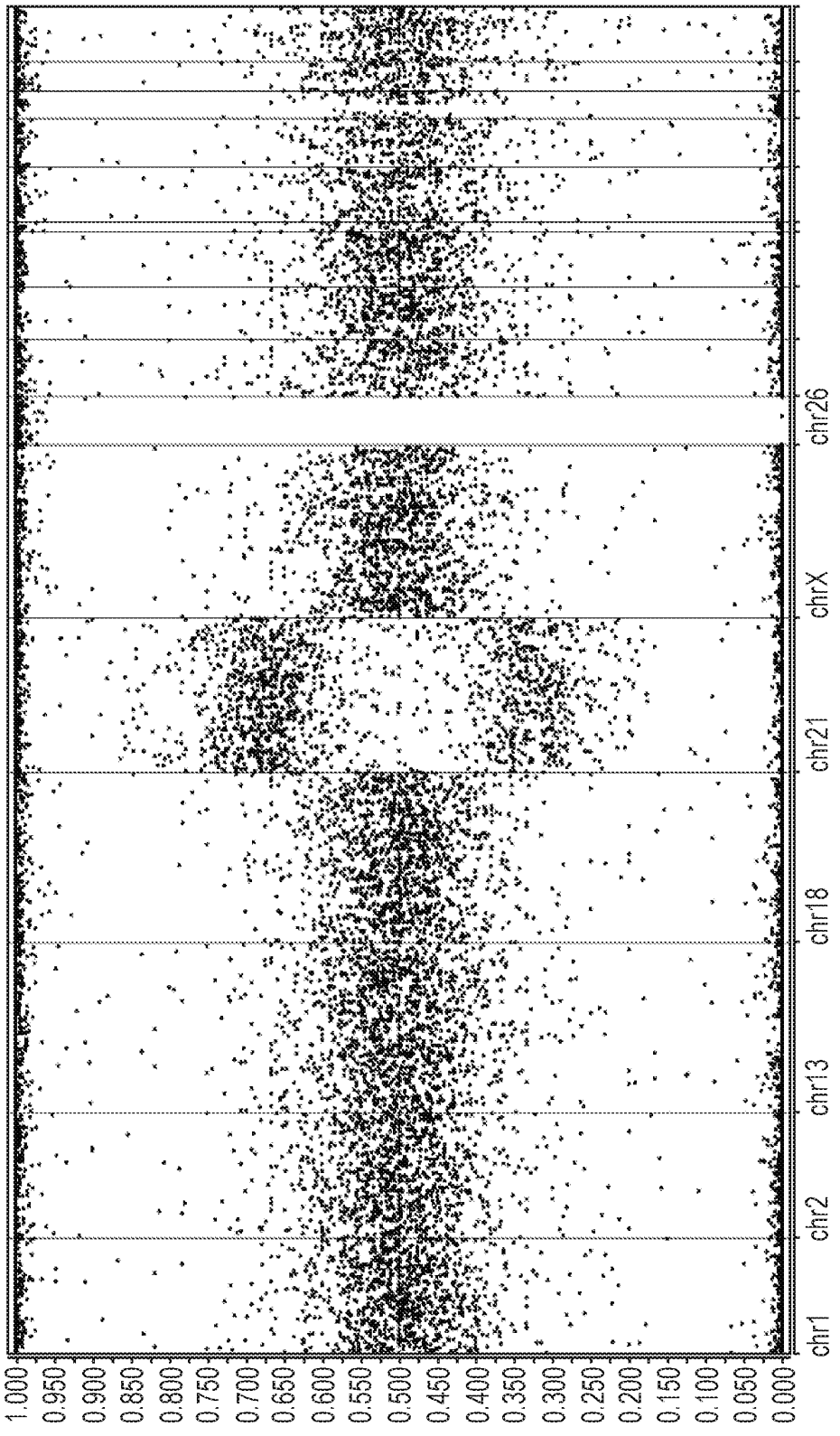

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
chr13
chr18
chr21
chrX
chr26
Single Cell

FIG. 40B

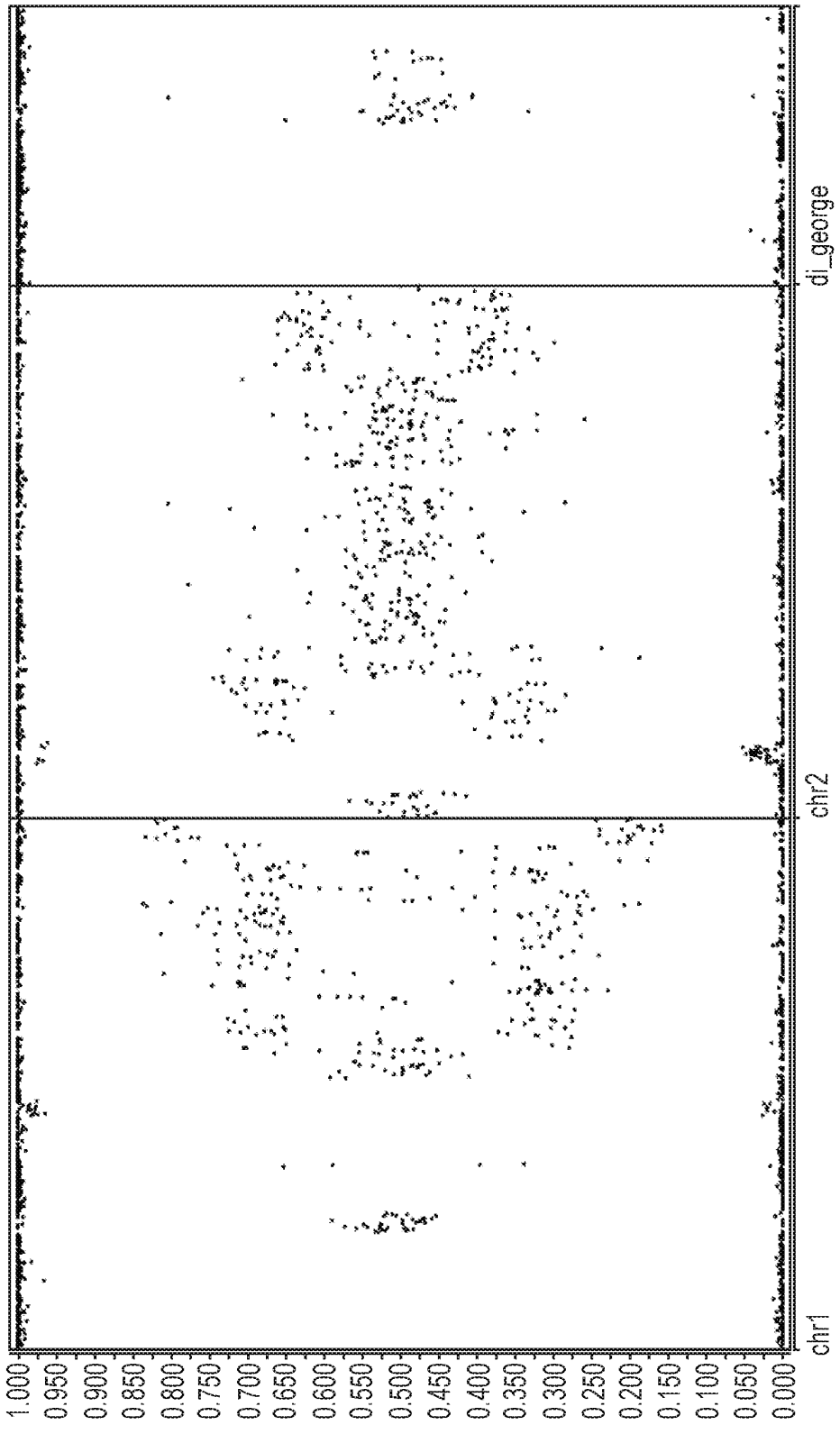

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
di_george
Genomics

FIG. 41A

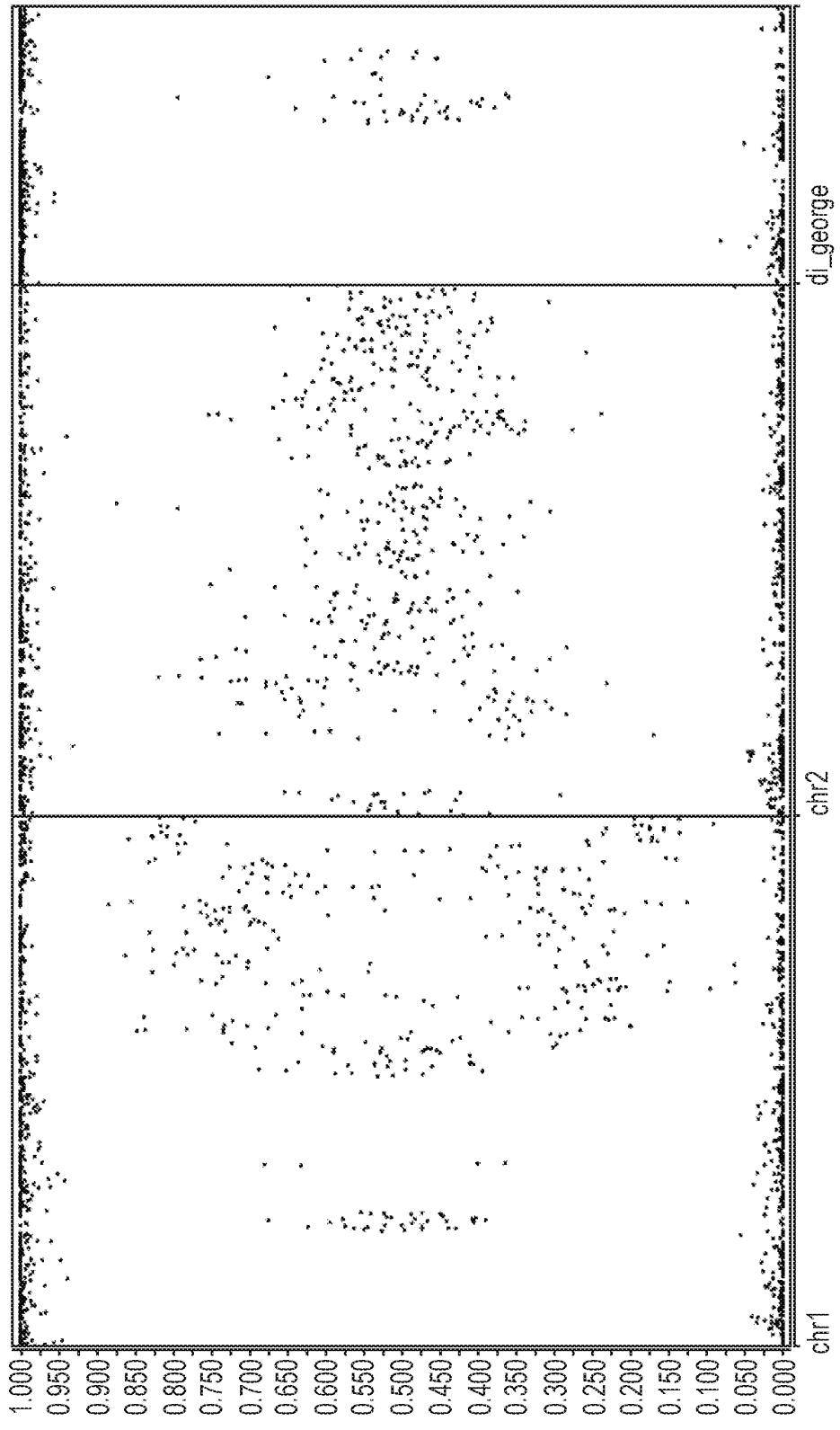

1.000
0.950
0.900
0.850
0.800
0.750
0.700
0.650
0.600
0.550
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
chr1
chr2
di_george
Single Cell

FIG. 41B

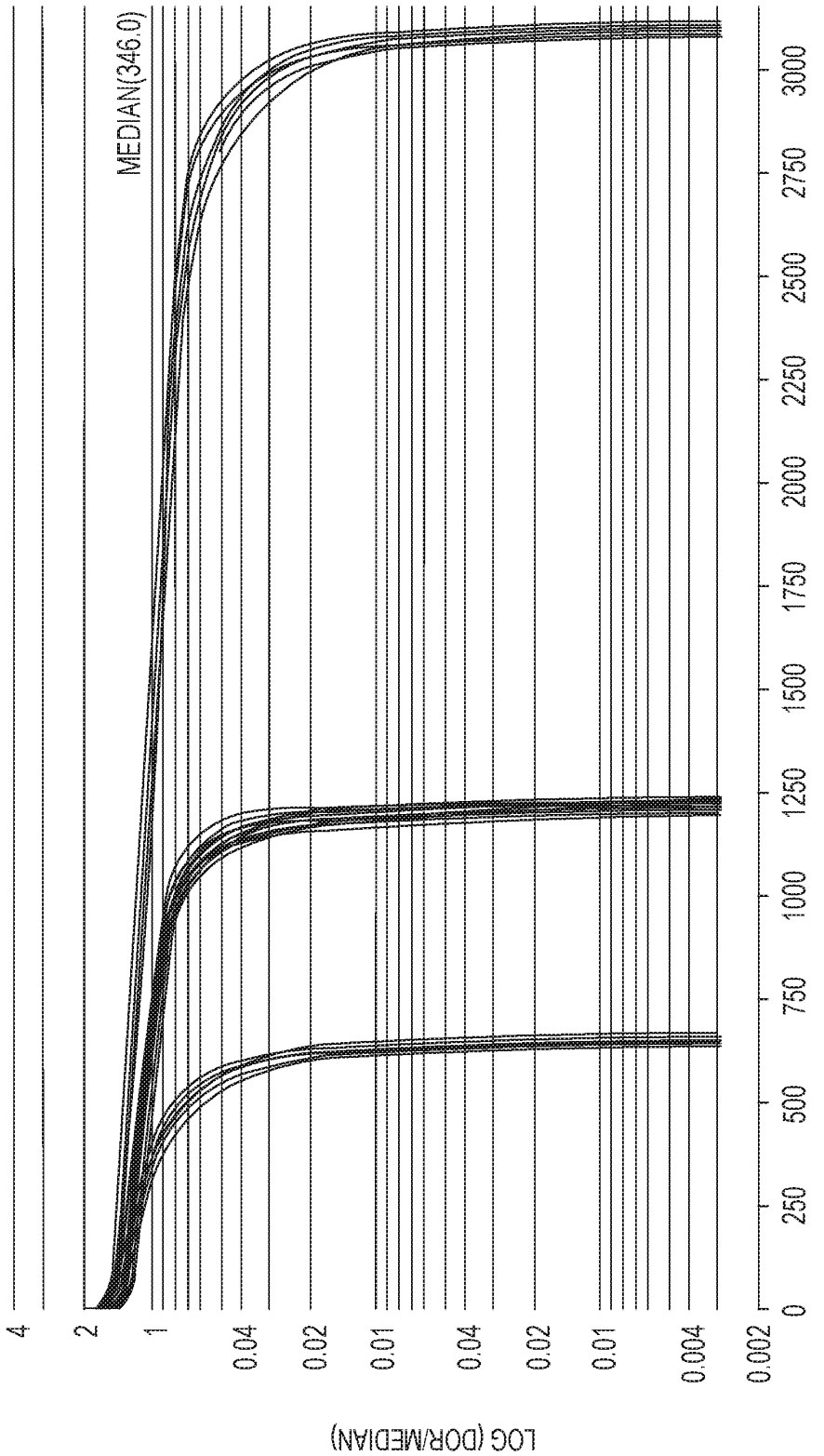

MEDIAN(346.0)
4
2
1
0.04
0.02
0.01
0.04
0.02
0.01
0.004
0.002
LOG (DOR/MEDIAN)
0
250
500
750
1000
1250
1500
1750
2000
2250
2500
2750
3000
SNP INDEX

FIG. 42

	gDNA	Single Cell
Count	75	510
Mean	0.15 %	0.51 %
Median	0.09 %	0.33 %
Max	1.03 %	10 %
Standard Deviation	0.16%	0.79 %
95th percentile	0.43 %	1.22 %
90th percentile	0.37 %	0.92 %

FIG. 43

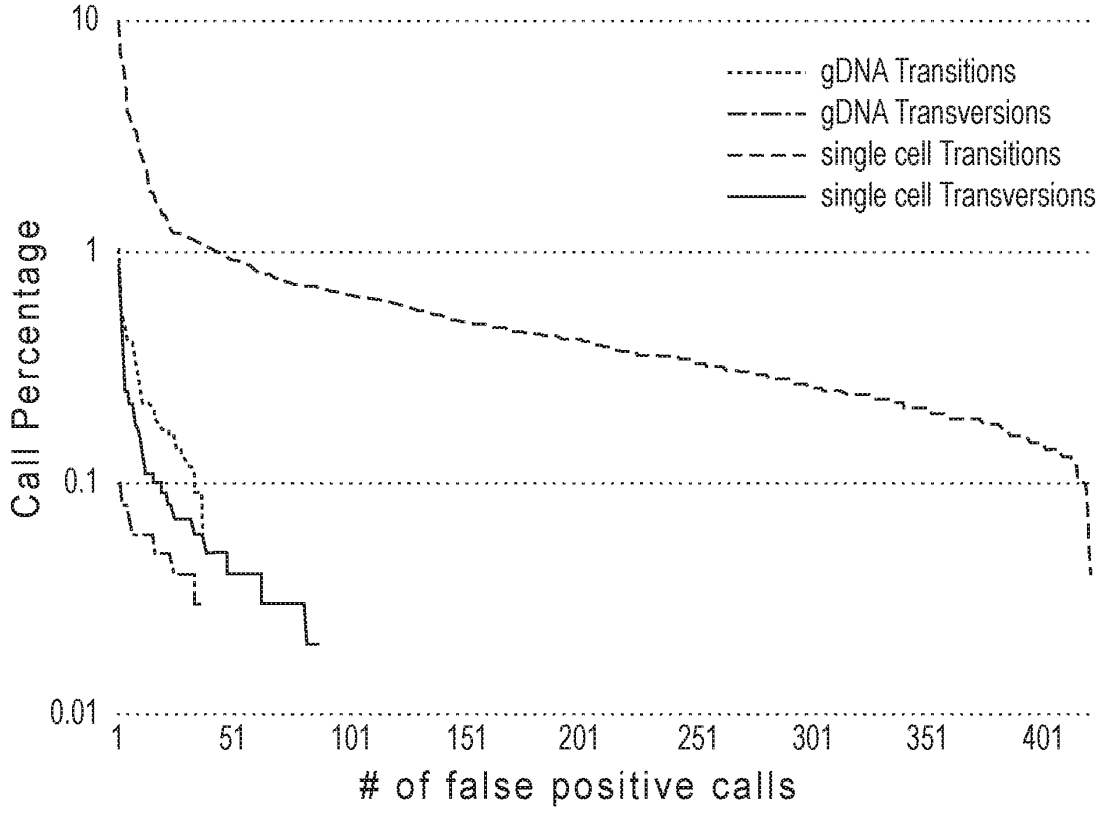


FIG. 44

DOE1	Mapped READS	TOTAL READS	% Mapped	Dropout Count	Median DOR All	NOR	Error Rate (%)
1xMM	1,112,007	1,262,558	80.0%	436	26.25	1,043,539	0.107%
2xMM	3,412,593	3,615,347	94.4%	105	147.75	3,206,478	0.141%
F-A	449,074	635,571	70.6%	1379	9.625	421,228	0.077%
F-B	3,293,944	3,519,378	93.7%	105	142.5	3,106,520	0.072%
F-D	4,028,128	4,109,448	98.0%	122	142.5	3,796,213	0.064%
F-J	3,676,617	3,922,330	93.7%	102	159.25	3,461,304	0.079%
F-A is : 25 mM Tris pH 7.8, 3 mM $MgCl_2$, **0 mM KCl, 10 mM $(NH_4)_2SO_4$, 50 U/mL Taq Gold** aka F-A Gold							
F-B is : 75 mM Tris pH 7.8, 6 mM $MgCl_2$, 0 mM KCl, 40 mM $(NH_4)_2SO_4$, 150 U/mL Taq Gold aka F-B Gold							
F-D is : 25 mM Tris **pH 8.2**, 3 mM $MgCl_2$, 30 mM KCl, 40 mM $(NH_4)_2SO_4$, 150 U/mL Taq Gold							
F-J is : 75 mM Tris pH 7.8, 6 mM $MgCl_2$, 0 mM KCl, 40 mM $(NH_4)_2SO_4$, 150 U/mL **Qiagen HS Taq** aka F-B Qiagen							

FIG. 45

NeoGenomics
Exhibit 1003 Page 936

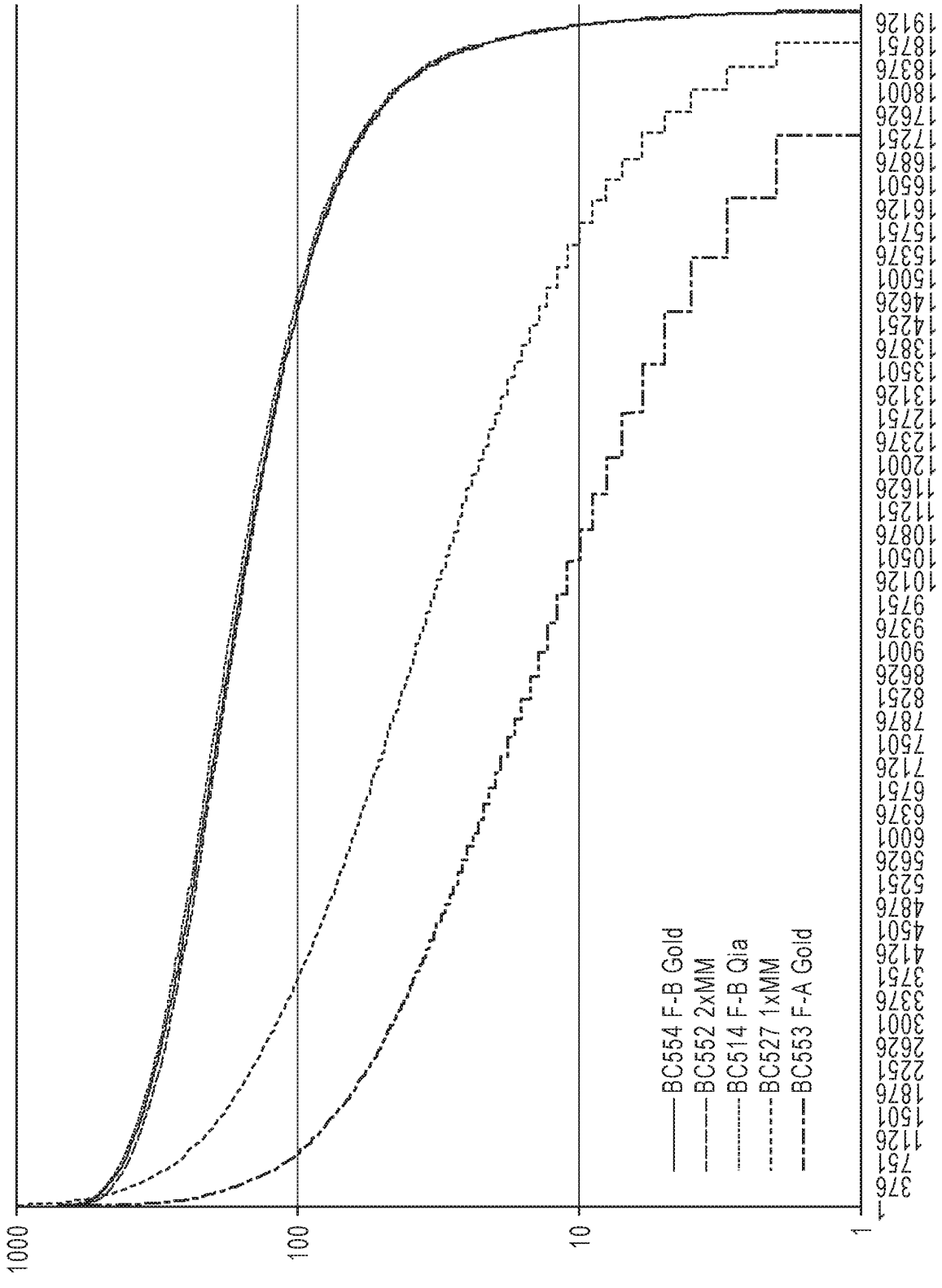

1000
100
10
1
BC554 F-B Gold
BC552 2xMM
BC514 F-B Qia
BC527 1xMM
BC553 F-A Gold

FIG. 46

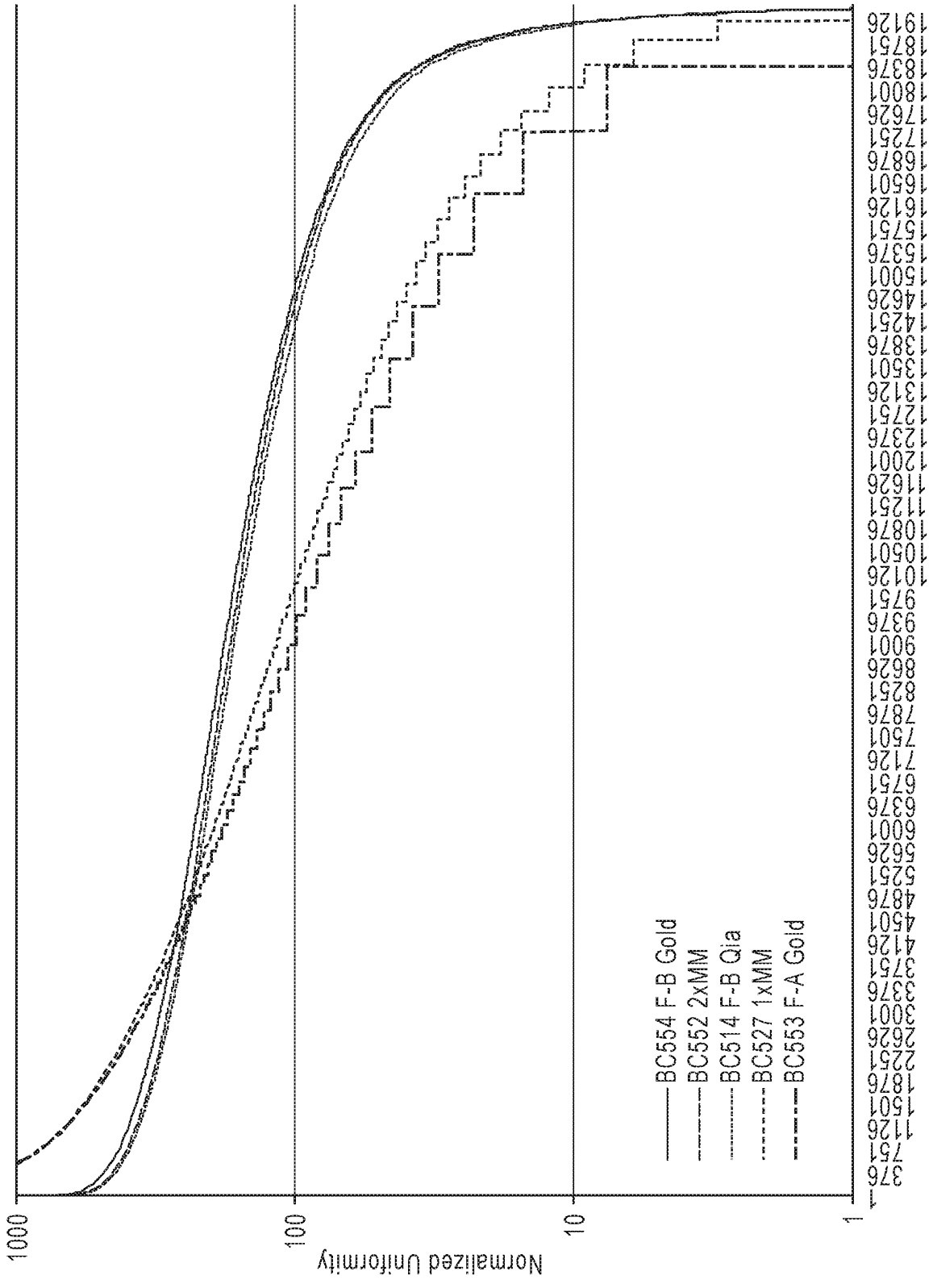

Normalized Uniformity
1000
100
10
1
BC554 F-B Gold
BC552 2xMM
BC514 F-B Qia
BC527 1xMM
BC553 F-A Gold

FIG. 47

Electronic Acknowledgement Receipt

EFS ID:	40616743
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	21-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	15:46:03
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	01_N012US32_Response_to_Notice_to_Comply_dated_18SEPT2020_SIGNED.pdf	19256 b0f8b7ab9f58e05a55c4c366a186abc05aa791e2	no	1

Warnings:

Information:					
2	Drawings-other than black and white line drawings	02_N012US32_Replacement_Drawings.pdf	1968283 5da4d97f84236802255cbcce7ccda2f3138b109f	no	58
Warnings:					
Information:					
		Total Files Size (in bytes):	1987539		

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

New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 16/934,407

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	300
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	660
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	760
TOTAL CLAIMS (37 CFR 1.16(i))	15 minus 20 =	*			OR	x 100 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*				x 460 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						2000
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	3720

APPLICATION AS AMENDED - PART II

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

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

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32

CONFIRMATION NO. 2396

110711
Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

FORMALITIES LETTER

OC000000119977212

Date Mailed: 09/18/2020

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Filing Date Granted

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to comply with the sequence rules, 37 CFR §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR §1.821(g). Extension of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR §1.136.

Items 1) and 2) provide general guidance related to requirements for sequence disclosures.

1) 37 CFR 1.821(c) requires that patent applications which contain disclosures of nucleotide and/or amino acid sequences that fall within the definitions of 37 CFR 1.821(a) must contain a "Sequence Listing", *as a separate part of the disclosure*, which presents the nucleotide and/or amino acid sequences and associated information using the symbols and format in accordance with the requirements of 37 CFR 1.821-1.825. This "Sequence Listing" part of the disclosure may be submitted:
   a) via EFS-Web (see Section I.1 of the Legal Framework for EFS-Web (https://www.uspto.gov/patents-application-process/filing-online/legal-framework-efs-web), hereinafter "Legal Framework") as an ASCII text file, together with an incorporation-by-reference of the material in the ASCII text file in a separate paragraph of the specification identifying:
      i) the name of the ASCII text file;
      ii) the date of creation; and
      iii) the size of the ASCII text file in bytes;
   b) on compact disc(s) in duplicate according to 37 CFR 1.52(e)(1)(ii) and (4), labeled according to 37 CFR 1.52(e)(6), together with a statement that the duplicate compact discs are identical and an incorporation-by-reference of the material in the ASCII text file according to 37 CFR 1.52(e)(5) in a separate paragraph of the specification identifying:
      i) the name of the ASCII text file;
      ii) the date of creation; and
      iii) the size of the ASCII text file in bytes;
   c) via EFS-Web as a PDF (not recommended); or
   d) on paper.
2) 37 CFR 1.821(e) requires that a *copy* of the "Sequence Listing" must also be submitted in computer readable form (CRF) in accordance with the requirements of 37 CFR 1.824.
   a) If a "Sequence Listing" ASCII text file submitted via EFS-Web on the application filing date complies with the requirements of 37 CFR 1.824(a)(2)-(6) and (b), and applicant has not filed a "Sequence Listing" as

a PDF, the text file will serve as both the "Sequence Listing" required by 37 CFR 1.821(c) and the CRF required by 37 CFR 1.821(e), and the statement of identity under the "Legal Framework" is not required.

b) If the "Sequence Listing" required by 37 CFR 1.821(c) is filed via EFS-Web as a PDF, then the "Legal Framework" requires submission of a statement that the "Sequence Listing" content of the PDF copy and the ASCII text file copy submitted via EFS-Web are identical.

c) If the "Sequence Listing" required by 37 CFR 1.821(c) is filed on paper or compact disc, then 37 CFR 1.821(f) requires submission of a statement that the "Sequence Listing" content of the paper or compact disc copy and the CRF are identical.

Specific deficiencies and the required response to this notice are as follows:

- Sequences appearing in the drawings must be identified by sequence identifiers in accordance with 37 CFR 1.821(d). Sequence identifiers for sequences must appear either in the drawings or in the Brief Description of the Drawings. Applicant must provide:
  - Replacement and annotated drawings in accordance with 37 CFR 1.121(d) inserting the required sequence identifiers;

  AND/OR

  - A substitute specification in compliance with 37 CFR 1.121(b)(3) and 1.125 inserting the required sequence identifiers into the Brief Description of the Drawings, consisting of:
    - A copy of the previously-submitted specification, with deletions shown with strikethrough or brackets and insertions shown with underlining (marked-up version);
    - A copy of the amended specification without markings (clean version); and
    - A statement that the substitute specification contains no new matter.

For questions regarding compliance to these requirements, please contact:

- **For Rules interpretation, call (571) 272-2510**
- **For CRF submission help, call (571) 272-2510**
- **For PatentIn software program support technical assistance, call (866) 217-9197.**
- **Send e-mail correspondence for PatentIn software program help to ebc@uspto.gov**
- **PatentIn software is available at http://www.uspto.gov/patents/resources/tools/checker/patentinrel.jsp .**

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

NeoGenomics
Exhibit 1003 Page 943

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice". https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

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

/ygizaw/

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/934,407	07/21/2020	1637	3720	N.012.US.32	15	1

CONFIRMATION NO. 2396

110711
Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

FILING RECEIPT

OC000000119377211

Date Mailed: 09/18/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

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Applicant(s)

Natera, Inc., San Carlos, CA;

Assignment For Published Patent Application

Natera, Inc., San Carlos, CA

Power of Attorney: The patent practitioners associated with Customer Number 110711

Domestic Priority data as claimed by applicant

This application is a CON of 16/743,724 01/15/2020 PAT 10731220
which is a CON of 16/399,268 04/30/2019 PAT 10538814
which is a CON of 16/140,298 09/24/2018
which is a CON of 14/918,544 10/20/2015 PAT 10316362
which is a CIP of 14/877,925 10/07/2015 ABN

and is a CIP of 14/692,703 04/21/2015 PAT 10179937
and is a CIP of 14/538,982 11/24/2014 PAT 9677118
and claims benefit of 62/148,173 04/15/2015
and claims benefit of 62/147,377 04/14/2015
and claims benefit of 62/146,188 04/10/2015
and claims benefit of 62/066,514 10/21/2014
and said 14/877,925 10/07/2015
is a CIP of 14/225,356 03/25/2014 ABN
and is a CIP of 13/780,022 02/28/2013 ABN
and is a CON of 13/683,604 11/21/2012 ABN
and said 14/692,703 04/21/2015
claims benefit of 62/148,173 04/15/2015
and claims benefit of 62/147,377 04/14/2015
and claims benefit of 62/146,188 04/10/2015
and claims benefit of 62/066,514 10/21/2014
and claims benefit of 61/994,791 05/16/2014
and claims benefit of 61/987,407 05/01/2014
and claims benefit of 61/982,245 04/21/2014
and said 14/538,982 11/24/2014
claims benefit of 62/066,514 10/21/2014
and claims benefit of 61/994,791 05/16/2014
and claims benefit of 61/987,407 05/01/2014
and claims benefit of 61/982,245 04/21/2014
and said 14/225,356 03/25/2014
is a CON of PCT/US2012/058578 10/03/2012
and said 13/780,022 02/28/2013
is a CIP of 13/683,604 11/21/2012 ABN
and is a CIP of PCT/US2012/058578 10/03/2012
and is a CIP of 13/335,043 12/22/2011 PAT 10113196
which is a CIP of 13/300,235 11/18/2011 PAT 10017812
which is a CIP of 13/110,685 05/18/2011 PAT 8825412
and said 13/780,022 02/28/2013
claims benefit of 61/634,431 02/29/2012
and said 13/683,604 11/21/2012
is a CIP of 13/300,235 11/18/2011 PAT 10017812
and is a CIP of 13/110,685 05/18/2011 PAT 8825412
and claims benefit of 61/675,020 07/24/2012
and said PCT/US2012/058578 10/03/2012
is a CIP of 13/300,235 11/18/2011 PAT 10017812
and claims benefit of 61/683,331 08/15/2012
and claims benefit of 61/542,508 10/03/2011
and said 13/335,043 12/22/2011
is a CIP of 13/300,235 11/18/2011 PAT 10017812
and is a CIP of 13/110,685 05/18/2011 PAT 8825412
and claims benefit of 61/426,208 12/22/2010
and said 13/300,235 11/18/2011
is a CIP of 13/110,685 05/18/2011 PAT 8825412
and claims benefit of 61/542,508 10/03/2011
and claims benefit of 61/571,248 06/23/2011
and said 13/110,685 05/18/2011
claims benefit of 61/516,996 04/12/2011

and claims benefit of 61/448,547 03/02/2011
and claims benefit of 61/448,547 03/02/2011
and claims benefit of 61/462,972 02/09/2011
and claims benefit of 61/398,159 06/21/2010
and claims benefit of 61/395,850 05/18/2010

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

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

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

If Required, Foreign Filing License Granted: 07/27/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/934,407**

Projected Publication Date: 11/05/2020

Non-Publication Request: No

Early Publication Request: No
Title

METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

Preliminary Class

435

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

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

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

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

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

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

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

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

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

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

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

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed

from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32

CONFIRMATION NO. 2396

110711
Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

WITHDRAWAL NOTICE

OC000000119977012

Date Mailed: 09/18/2020

Letter Regarding a New Notice and/or the Status of the Application

If a new notice or Filing Receipt is enclosed, applicant may disregard the previous notice mailed on 07/29/2020. The time period for reply runs from the mail date of the new notice. Within the time period for reply, applicant is required to file a reply in compliance with the requirements set forth in the new notice to avoid abandonment of the application.

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web. https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at **1-866-217-9197** or visit our website at http://www.uspto.gov/ebc.

If the reply is not filed electronically via EFS-Web, the reply must be accompanied by a copy of the new notice.

If the Office previously granted a petition to withdraw the holding of abandonment or a petition to revive under 37 CFR 1.137, the status of the application has been returned to pending status.

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

/ygizaw/

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/934,407	07/21/2020	Joshua BABIARZ	N.012.US.32	2396

110711 7590 09/16/2020

Natera, Inc.
201 Industrial Road
Suite 410
San Carlos, CA 94070

EXAMINER	
MUMMERT, STEPHANIE KANE	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
09/16/2020	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):

IP@natera.com

Office Action Summary	Application No. 16/934,407	Applicant(s) BABIARZ et al.	
	Examiner STEPHANIE K MUMMERT	Art Unit 1637	AIA (FITF) Status Yes

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

Period for Reply

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

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

Status

1)☐ Responsive to communication(s) filed on _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

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

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

Disposition of Claims*

5) ☑ Claim(s) 1-15 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) 1-15 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 _____ 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: sequence routing sheet.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

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

Claims 1-15 are pending.

Claim Rejections - 35 USC § 112

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.

Claims 4-5. 8, 13-15 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

In each of the rejected claims, the phrasing of the claim either includes additional words, (e.g. “the”) or are missing words like “step”. For example, claim 4 recites “wherein the amplifying the tagged products”. Should it read “wherein amplifying the tagged products”? Again in claim 5, the claim recites “wherein the second amplifying comprises”. Should this read “wherein the second amplifying step”? The same issues apply to claims 8 and 13-15. Clarification is requested.

Sequence Compliance - Notice to Comply

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Figure 12 includes nucleic acid sequences that are 10 or more nucleotide residues in length and require corresponding sequence identifiers (SEQ ID NOs).

Applicant is given a period within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Double Patenting

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 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 § 2146 *et seq.* 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 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.

Claim 1-2 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1, 3, 5, 22 of U.S. Patent No. 1,0731,220 (‘220 patent). Although the claims at issue are not identical, they are not patentably distinct from each other because while

the patents are not identical, they are drawn to very similar subject matter. The instant claims require tagging adaptors on to cell free DNA with universal tails, followed by amplification, introducing a barcode and sequencing tag and then sequencing the products. The final step of the method includes high throughput sequencing.

The claims differ in that the '220 patent includes very similar steps in a different order, and includes a step of multiplexed amplification. The '220 patent includes universal and barcode sequences, amplification and high throughput sequencing. The ligation step is included in claim 3 of '220 and the multiplex sequencing is recited in claim 5 and 22 of '220.

Therefore, while the claims are not the same they are also not patentably distinct.

Claim 1-2 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1, 3-4, 22 of U.S. Patent No. 10,538,814 ('814 patent). Although the claims at issue are not identical, they are not patentably distinct from each other because while the patents are not identical, they are drawn to very similar subject matter. The instant claims require tagging adaptors on to cell free DNA with universal tails, followed by amplification, introducing a barcode and sequencing tag and then sequencing the products. The final step of the method includes high throughput sequencing.

The claims differ in that the '814 patent includes very similar steps in a different order and includes a step of multiplexed amplification. The '814 patent includes universal sequences, amplification and high throughput sequencing. The ligation and barcode features are present in the dependent claims of '814, see claims 3, 4.

Therefore, while the claims are not the same they are also not patentably distinct.

Claim 1-2 and 6 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1, 3-4, 22 of U.S. Patent No. 10,557,172 ('172 patent). Although the claims at issue are not identical, they are not patentably distinct from each other because while the patents are not identical, they are drawn to very similar subject matter. The instant claims require tagging adaptors on to cell free DNA with universal tails, followed by amplification, introducing a barcode and sequencing tag and then sequencing the products. The final step of the method includes high throughput sequencing.

The claims differ in that the '172 patent includes very similar steps in a different order and includes a step of multiplexed amplification. The '172 patent includes universal and barcode sequences, amplification and high throughput sequencing. The ligation step is included in claim 3 of '172 patent. Also the nested feature of instant claim 6 is present in claim 22 of the '172 patent.

Therefore, while the claims are not the same they are also not patentably distinct.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 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 –
>
> (a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.
>
> (a)(2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

Claim(s) 1-5 and 10-15 is/are rejected under 35 U.S.C. 102(a)(1) as being anticipated by Fan et al. (US PgPub 20100112575; May 2010).

With regard to claim 1, Fan teaches a method for amplifying and sequencing DNA, comprising:

tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject (paragraph 79, where universal adaptors are included with tagging of cell free sequences);

amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplifying steps introduces a barcode and one or more sequencing tags (paragraph 76, where samples are amplified); and

sequencing a plurality of loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of loci comprises 25-2,000 loci (paragraph 79, where sequencing occurs).

With regard to claim 2, Fan teaches a method of claim 1, wherein the tagging the cell free DNA comprises ligating the one or more universal tail adaptors to the cell free DNA (Example 3, where it is exemplified where the adaptors are ligated).

With regard to claim 3, Fan teaches a method of claim 2, wherein the one or more universal tail adaptors each comprise a first strand and a second strand, wherein a first end of each of the universal tail adaptors comprises a double-stranded section comprising the 5' portion of the first strand and the 3' portion of the second strand, wherein the first end is ligated to the cell free DNA (Example 3, where it is exemplified where the adaptors are ligated).

With regard to claim 4, Fan teaches a method of claim 3, wherein the amplifying the tagged products comprises a first amplifying and a second amplifying, wherein the first amplifying comprises a first target- specific primer that specifically anneals to a target sequence

and a first adaptor primer having a nucleotide sequence identical to a first portion of the first strand to generate a first amplification product (paragraph 76, where samples are amplified).

With regard to claim 5, Fan teaches a method of claim 4, wherein the second amplifying comprises a second target- specific primer that specifically anneals to the first amplification product and a second adaptor primer having a nucleotide sequence identical to a second portion of the first strand to generate the final amplification product (paragraph 76, where samples are amplified).

With regard to claim 10, Fan teaches a method of claim 1, wherein the one or more universal tail adaptors comprise a second barcode (Example 3, where it is exemplified where the adaptors are ligated; paragraph 76, where samples are amplified).

With regard to claim 11, Fan teaches a method of claim 1, wherein the one or more universal tail adaptors comprise a second sequencing tag (Example 3, where it is exemplified where the adaptors are ligated).

With regard to claim 12, Fan teaches a method of claim 1, wherein the one or more universal tail adaptors comprise a first universal tail adaptor and a second universal tail adaptor (Example 3, where it is exemplified where the adaptors are ligated).

With regard to claim 13, Fan teaches a method of claim 12, wherein the tagging the cell free DNA comprises amplifying the cell free DNA with a first primer comprising the first universal tail adaptor and a second primer comprising the second universal tail adaptor (Example 3, where it is exemplified where the adaptors are ligated; paragraph 76, where samples are amplified).

With regard to claim 14, Fan teaches a method of claim 12, wherein the amplifying the tagged products comprises a single amplifying (paragraph 76, where samples are amplified).

With regard to claim 15, Fan teaches a method of claim 14, wherein the amplifying the tagged products comprises a third primer and a fourth primer, wherein the third primer comprises a first sequencing tag and wherein the fourth primer comprises a second sequencing tag (paragraph 76, where samples are amplified).

Claim Rejections - 35 USC § 103

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

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

This application currently names joint inventors. In considering patentability of the claims the examiner presumes that the subject matter of the various claims was commonly owned as of the effective filing date of the claimed invention(s) absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and effective filing dates of each claim that was not commonly owned as of the effective filing date of the later invention in order for the examiner to consider the applicability of 35 U.S.C. 102(b)(2)(C) for any potential 35 U.S.C. 102(a)(2) prior art against the later invention.

Claim 6 is/are rejected under 35 U.S.C. 103 as being unpatentable over Fan et al. (US PgPub 20100112575; May 2010) as applied over claims 1-5 and 10-15 above and further in view of Wright et al. (Hum Reprod Updt, 2009, 15(1):139-151).

With regard to claim 6, Wright teaches a method of claim 5, wherein the second adaptor primer is nested relative to the first adaptor primer (Table 1, where nested amplification occurs, p. 141, col. 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Fan to include a nested primer as taught by Wright to arrive at the claimed invention with a reasonable expectation for success. Wright teaches "A number of different types of PCR have been explored, of which the most popular is real-time quantitative PCR (Traeger-Synodinos, 2006), as it combines high sensitivity with a closed detection system, thereby minimiz-ing the risk of contamination. Nested PCR (Al-Yatama et al., 2001) and pyrophosphorolysis-activated polymerization PCR (Boon et al., 2007) have also been investigated in this context. Higher precision of measure-ment may be possible through the application of digital PCR, which allows the exact number of original template DNA molecules to be counted (Fan and Quake, 2007; Lo et al., 2007a)" (p. 141, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have adjusted the teachings of Fan to include a nested primer as taught by Wright to arrive at the claimed invention with a reasonable expectation for success.

Claim 7-9 is/are rejected under 35 U.S.C. 103 as being unpatentable over Fan et al. (US PgPub 20100112575; May 2010) as applied over claims 1-5 and 10-15 above and further in view of Cronn et al. (Nucleic Acids Research 2008, 36(19):e122).

With regard to claim 7, Cronn teaches a method of claim 6, wherein the second target-specific primer comprises an index tag (Abstract, p. 2 and p. 6).

With regard to claim 8, Cronn teaches a method of claim 7, wherein the second amplifying further comprises an index primer comprising a sequence complementary to the index tag (Abstract, p. 2 and p. 6).

With regard to claim 9, Cronn teaches a method of claim 8, wherein the index primer comprises the barcode and a first sequencing tag (Abstract, p. 2 and p. 6).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Fan to include the index tag as taught by Cronn to arrive at the claimed invention with a reasonable expectation for success. Cronn teaches "To gain maximal access to the historical record contained within chloroplast genomes, we have adapted multiplex sequencing-by-synthesis (MSBS) to simultaneously sequence multiple genomes using the Illumina Genome Analyzer. We PCR-amplified ~120 kb plas-tomes from eight species (seven Pinus, one Picea)in 35 reactions. Pooled products were ligated to mod-ified adapters that included 3 bp indexing tags and samples were multiplexed at four genomes per lane. Tagged microreads were assembled by de novo and reference-guided assembly methods, using pre-viously published Pinus plastomes as surrogate references" (Abstract). Therefore, one of ordinary skill in the art at the time the invention was made would have adjusted the teachings of Fan to include the index tag as taught by Cronn to arrive at the claimed invention with a reasonable expectation for success.

Conclusion

No claims are allowed. All claims stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE KANE MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F 9:00-5:30.

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, Gary Benzion can be reached on 571-272-0782. 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 https://ppair-my.uspto.gov/pair/PrivatePair. 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.

/STEPHANIE K MUMMERT/
Primary Examiner, Art Unit 1637

SKM

Notice of References Cited	Application/Control No. 16/934,407	Applicant(s)/Patent Under Reexamination BABIARZ et al.	
	Examiner STEPHANIE K MUMMERT	Art Unit 1637	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20100112575-A1	05-2010	Fan; Hei-Mun Christina	C12Q1/6883	435/6.11
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Wright et al. (Hum Reprod Updt, 2009, 15(1):139-151) (Year: 2009)
	V	Cronn et al. (Nucleic Acids Research 2008, 36(19):e122) (Year: 2008)
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/934,407	BABIARZ et al.
	Examiner	Art Unit
	STEPHANIE K MUMMERT	1637

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
inventor search - all names searched - PALM	08/31/2020	SKM
search Google/Scholar	09/03/2020	SKM
searched PE2E tool	09/03/2020	SKM
searched Google/Scholar	09/04/2020	SKM

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

NeoGenomics
Exhibit 1003 Page 965

Sequence Compliance Review for U.S. Applications (35 U.S.C. 111 and 371)	**Application No.** 16/934,407	**Applicant(s)** BABIARZ et al.	
	Examiner STEPHANIE K MUMMERT	**Art Unit** 1637	**AIA Status** Yes

1. Check the appropriate Box for the application type

☑ U.S. National Application (35 U.S.C. 111) ☐ PCT National Stage Application (35 U.S.C. 371)

SEQUENCE RULE COMPLIANCE REVIEW

2. Check the appropriate Box

☐ CRF, paper copy of sequence listing, and statement that both are same missing

☐ CRF contains error(s) according to STIC Report

☐ CRF damaged or unreadable according to STIC Report

☐ CRF transferred from prior application is not complaint

DOES NOT COMPLY WITH THE SEQUENCE RULES. See reasons below:
Figure 12 needs sequence identifiers.

/STEPHANIE K MUMMERT/ Primary Examiner, Art Unit 1637	

Bibliographic Data

Application No: 16/934,407

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☑ No ☐ Met After Allowance

Verified and Acknowledged: /STEPHANIE K MUMMERT/ (Examiner's Signature) | (Initials)

Title: METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
07/21/2020	435	1637	N.012.US.32
RULE			

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CONTINUING DATA

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FOREIGN APPLICATIONS

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07/27/2020

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FILING FEE RECEIVED

$7,860

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	92	(multiplex SAME tagg$3 SAME barcode SAME universal)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:05 AM
L2	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:07 AM
L3	0	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3 SAME "cell free")	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:08 AM
L4	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3),clm.	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:08 AM
L5	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail) SAME sequenc$3)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:09 AM
L6	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail)) AND sequenc$3	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:09 AM
L7	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequenc$3	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:11 AM
L8	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequencing	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:11 AM
L9	3	(multiplex SAME (universal NEAR tail)) AND tagged AND barcode AND sequencing	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:12 AM
L10	3711884	(universal adaptor) multiplex AND sequencing AND "cell free" AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 10:54 PM

L11	527	(universal SAME adaptor) AND multiplex AND sequencing AND "cell free" AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 10:56 PM
L12	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 10:57 PM
L13	0	(universal SAME adaptor) AND (multiplex NEAR sequencing NEAR "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:02 PM
L14	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:02 PM
L15	91	(universal SAME adaptor) AND (multiplex SAME sequencing SAME "cell free") AND tagging	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:11 PM
L16	12948	"L19" NOT L14	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:11 PM
L17	26547	"L15" NOT L14	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:11 PM
L18	0	L15 NOT L14	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:12 PM
L19	472	(universal SAME adaptor) AND (multiplex SAME sequencing) AND "cell free" AND tagging	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/02 11:12 PM
L20	580	(universal SAME adaptor) AND (sequencing) AND "cell free" AND tagging AND barcode	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/03 09:11 PM
L21	22	((universal SAME adaptor) SAME sequencing SAME "cell free") AND tagging AND	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/09/03 09:11 PM

		barcode					

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

NeoGenomics
Exhibit 1003 Page 972

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	92	(multiplex SAME tagg$3 SAME barcode SAME universal)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:05 AM
L2	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:07 AM
L3	0	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3 SAME "cell free")	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:08 AM
L4	85	(multiplex SAME tagg$3 SAME barcode SAME universal SAME sequenc$3),clm.	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:08 AM
L5	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail) SAME sequenc$3)	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:09 AM
L6	0	(multiplex SAME tagg$3 SAME barcode SAME (universal NEAR tail)) AND sequenc$3	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:09 AM
L7	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequenc$3	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:11 AM
L8	0	(multiplex SAME tagged SAME barcode) AND (universal NEAR tail) AND sequencing	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:11 AM
L9	3	(multiplex SAME (universal NEAR tail)) AND tagged AND barcode AND sequencing	US-PGPUB; USPAT; USOCR; FIT (CN, FR, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	ON	2020/08/31 10:12 AM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

Web Search History

date, time	web site	search string
9/4/2020 9:14:40 PM	Google Scholar	[before:2010] "index primer" and sequencing
9/4/2020 9:35:10 PM	Google Scholar	[before:2010] "index tag" and sequencing

NeoGenomics
Exhibit 1003 Page 974

Web Search History

date, time	web site	search string
8/31/2020 10:14:48 AM	Google	(universal tail) multiplex and sequencing and "cell free"
8/31/2020 10:14:53 AM	Google Scholar	(universal tail) multiplex and sequencing and "cell free"
8/31/2020 10:15:01 AM	Google Scholar	(universal tail) multiplex and sequencing and "cell free" [before:2010]

NeoGenomics
Exhibit 1003 Page 975

Electronic Acknowledgement Receipt

EFS ID:	40483807
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	10-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	18:00:49
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	WO2011041485.pdf	10430373 089fe432316e3985c8f39ca357549ed732058b0b	no	78
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5	Foreign Reference	WO2011146632.pdf	17804009 e2b81a75d034f031b85fdc741e3a36ceb6ac5e27	no	141
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6	Foreign Reference	WO2012019200A2.pdf	1328559 1a90c68e4a4473ffd483be4e97c65b693f50a18c	no	147
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7	Foreign Reference	WO2012028746A1.pdf	5599952 1d9e65e81a3faa46398197162c0a0d421378b093	no	128
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8	Foreign Reference	WO2012083250.pdf	3866594 9823d19a0dc29b777a48d5edd522efeb659c37a8	no	71
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

Electronic Acknowledgement Receipt

EFS ID:	40483805
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	10-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	18:01:29
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	HARTWELL_2004_441_NPL.pdf	12872473 95a097b32e566a2067c74383dd568a2d6bb59203	no	48

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

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Electronic Acknowledgement Receipt

EFS ID:	40483802
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	10-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	18:02:04
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

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New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

Electronic Acknowledgement Receipt

EFS ID:	40483798
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	10-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	18:00:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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50	Non Patent Literature	ZIMMERMANN_Supplemental_Information_2012_7pgs_NPL.pdf	254972 e6f49aab80a3631c6adf1e5f2ab57e042da88636	no	7
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New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

Electronic Acknowledgement Receipt

EFS ID:	40483785
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	10-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	17:56:58
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

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1	Foreign Reference	WO2007117256A1.pdf	348317 396393aa6d222daf72c2902b3a8a6703984 8c7fd	no	41

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<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Electronic Acknowledgement Receipt

EFS ID:	40483796
Application Number:	16934407
International Application Number:	
Confirmation Number:	2396
Title of Invention:	METHODS FOR SIMULTANEOUS AMPLIFICATION OF TARGET LOCI
First Named Inventor/Applicant Name:	Joshua BABIARZ
Customer Number:	110711
Filer:	Anton John Bokal/Angela McGowan
Filer Authorized By:	Anton John Bokal
Attorney Docket Number:	N.012.US.32
Receipt Date:	10-SEP-2020
Filing Date:	21-JUL-2020
Time Stamp:	17:59:43
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Information:					
27	Non Patent Literature	SHEN.pdf	1179650 60191f1ccb150a05d25e388027a13ece9791d1d5	no	6
Warnings:					
Information:					
28	Non Patent Literature	SHEN_2005_70_NPL.pdf	1056120 5843d07758da64f183e74b0e585da6399fb3d781	no	13
Warnings:					
Information:					
29	Non Patent Literature	SHEN_ZHIYONG.pdf	1182060 79a5ff6a5bfdd369a4962595f37aff7e3ce5d76f	no	7
Warnings:					
Information:					

30	Non Patent Literature	SHERLOCK_1998.pdf	3288413 0dfefd468b0c35ce3dba00d80a879a1fce21c8b8	no	15
Warnings:					
Information:					
31	Non Patent Literature	SHIROGUCHI_2012.pdf	810357 627602220bae89256dcf49abad1e0550c313d73d	no	6
Warnings:					
Information:					
32	Non Patent Literature	SIGDEL_2018_17pgs_NPL.pdf	2668118 874af75a4b1de030dc666e10f93bedca88b37ae0	no	17
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
33	Non Patent Literature	SIGDEL_2018_S178_NPL.pdf	196049 8c68ed9215f428bb64077c177ca21a4c5cabfcb7	no	2
Warnings:					
Information:					
34	Non Patent Literature	SIMPSON.pdf	1319318 2d4b42dae8e185c021d8538b357fb01ad9d20deb	no	8
Warnings:					
Information:					
35	Non Patent Literature	Sint.pdf	345187 c288aafbaf1d3c65421f800489586da5599ab92c	no	8
Warnings:					
Information:					
36	Non Patent Literature	SLATER.pdf	3164031 a51116ad7d2b5d2bd8df5ffdf95e1d5cf354e940	no	18
Warnings:					
Information:					

37	Non Patent Literature	Snijders_2001_Nat_Genet.pdf	232553 01e581607669eb9b4cb05a16bd4cadf684195e0e	no	2
Warnings:					
Information:					
38	Non Patent Literature	SNYDER_2011_6229_NPL.pdf	581475 f1c485be2a5ce6b74e6bfe07b2ef50429b5a695b	no	6
Warnings:					
Information:					
39	Non Patent Literature	SPARKS_Noninvasive.pdf	1982020 702b347b791afa132e2f519d14a9f4589275fdb8	no	9
Warnings:					
Information:					
40	Non Patent Literature	SPARKS_Selective.pdf	1293058 00081ec6ee199e3c02448a88ffb4255e04eb27f0	no	7
Warnings:					
Information:					
41	Non Patent Literature	Spiro2000.pdf	2166720 4277fd951b01f3065ef0007b3da21531ea6be452	no	9
Warnings:					
Information:					
42	Non Patent Literature	Spits.pdf	245539 cdb5a3496d2bf916961e75a3a7ca5daecfb90c09	no	8
Warnings:					
Information:					
43	Non Patent Literature	SRINIVASAN.pdf	972313 ba02ea07c339a83e652b543a26be26425d2b4488	no	10
Warnings:					
Information:					

44	Non Patent Literature	STEPHENS.pdf	1607496 55cf92655d04b84f8951b241e8a375b239c15e05	no	8
Warnings:					
Information:					
45	Non Patent Literature	STEVENS.pdf	1758134 c9aea6b4588d0284b52d8048508f237484755e6f	no	17
Warnings:					
Information:					
46	Non Patent Literature	STEYERBERG.pdf	1850858 c54197a5cb6f17110b5d225bd4a303d141a68701	no	13
Warnings:					
Information:					
47	Non Patent Literature	StimulantWikipedia.pdf	1374191 7be444f04f656f5b1f5f128986bf2c9c75fd9fd2	no	17
Warnings:					
Information:					
48	Non Patent Literature	STROM_1998.pdf	1513582 3b55edffb2a6dcb25f85a4527e520b251fd42e62	no	9
Warnings:					
Information:					
49	Non Patent Literature	STROM_2000.pdf	1219951 ee53d94fc65594c2a7956d99ff47305fa386c0d4	no	5
Warnings:					
Information:					
50	Non Patent Literature	STROUN.pdf	1504000 d4114f2111dc3ce1277bb49afcceef339ebfb1f3	no	11
Warnings:					
Information:					

51	Non Patent Literature	SU_2010.pdf	436236 6db348fdff15225a6f017853dcad3902f0396327	no	9
Warnings:					
Information:					
52	Non Patent Literature	SUN_2009.pdf	1451265 b4a66b6e31eca9d7560e7847c44b628ccadd8253	no	12
Warnings:					
Information:					
53	Non Patent Literature	SWEETKIND-SINGER.pdf	204563 261332f068462458782O7c645b4dd67ba0cd52fd	no	1
Warnings:					
Information:					
54	Non Patent Literature	TALIUN_2014.pdf	9492510 81f8dc05686ef0cfcc4c7f3ac319a5f2805ca57b	no	18
Warnings:					
Information:					
55	Non Patent Literature	TAMURA.pdf	599598 d6b66b467b315ae9b7a8611594b766c0f7838dc9	no	8
Warnings:					
Information:					
56	Non Patent Literature	TANG1999.pdf	72819 1832d29de3f7600ad7962392562271c5b9506db0	no	3
Warnings:					
Information:					
57	Non Patent Literature	tang2009.pdf	173320 4d307b8f8739439d50796e15d4d091265fa0c6c6	no	5
Warnings:					
Information:					

58	Non Patent Literature	TEBBUTT_2004_977_NPL.pdf	383309 5f5b42555332bca17b22f4ae9bd2db0caee25ce8	no	9
Warnings:					
Information:					
59	Non Patent Literature	ten_BOSCH_2008_NPL.pdf	695428 82dfe138c9fad1546c7251f229a6226bc4acea99	no	9
Warnings:					
Information:					
60	Non Patent Literature	TEWHEY_2011.pdf	470261 b5db83f76b86af421a373a3a49d35736ba0dab81	no	9
Warnings:					
Information:					
		Total Files Size (in bytes):	76595466		

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

New Applications Under 35 U.S.C. 111

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

National Stage of an International Application under 35 U.S.C. 371

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

New International Application Filed with the USPTO as a Receiving Office

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

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
VICKI L. HEALY
NATERA, INC.
201 INDUSTRIAL ROAD
SUITE 410
SAN CARLOS, CA 94070

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing *(day/month/year)*	18 FEB 2014
Applicant's or agent's file reference W16	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 13/57924	International filing date *(day/month/year)* 04 September 2013 (04.09.2013)
Applicant NATERA, INC.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 338 82 70

   For more detailed instructions, see *PCT Applicant's Guide*, International Phase, paragraphs 9.004 – 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. Following the expiration of 30 months from the priority date, these comments will also be made available to the public.

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer Lee W. Young PCT Helpdesk: 571-272-4300 Telephone No. PCT OSP: 571-272-7774

Form PCT/ISA/220 (July 2010)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference W16	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 13/57924	International filing date *(day/month/year)* 04 September 2013 (04.09.2013)	(Earliest) Priority Date *(day/month/year)* 04 September 2012 (04.09.2012)
Applicant NATERA, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (see Box No. II).

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the drawings to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 13/57924

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 5-29
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 13/57924

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C40B 20/00 (2013.01)
USPC - 506/2,12; 702/1,19; 435/6.1,7.2
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) -C40B 20/00 (2013.01)
USPC - 506/2,12; 702/1,19; 435/6.1,7.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Patents, non-patent literature, search term limited

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Patbase (pgpb, uspt, usoc, epab, jpab, dwpi, tdbd), Dialog Proquest (npl), Google Patents (pl, npl), Google scholar (pl, npl); WIPO (npl); Search Terms: enrich, fetal, increase, fraction, dna, pregnant, prenatal, maternal, blood, serum, plasma, noninvasive, non-invasive, carbohydrate, diet, drink, food, stimulant, natera, nutritious, testing, conc

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- A	US 5,716,776 A (BOGART) 10 February 1998 (10.02.1998) entire document, especially pg 3, ln 64-pg 4, ln 4, 34-38	31 --- 1-4, 30-34
A	US 2011/0251149 A1 (PERRINE, et al.) 13 October 2011 (13.10.2011) entire document, especially para [0008]	1-4, 30-34
A	US 2008/0138809 A1 (KAPUR, et al.) 12 June 2008 (12.06.2008) entire document, para [0005], [0009]	1-4, 30-34
A	Ashoor, Ghalia, et al. "Fetal fraction in maternal plasma cell-free DNA at 11-13 weeks' gestation: effect of maternal and fetal factors." Fetal diagnosis and therapy May 4, 2012, 237-243.	1-4, 30-34

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 January 2014 (23.01.2014)	18 FEB 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: VICKI L. HEALY
NATERA, INC.
201 INDUSTRIAL ROAD
SUITE 410
SAN CARLOS, CA 94070

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	18 FEB 2014
Applicant's or agent's file reference: W16	FOR FURTHER ACTION: See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 13/57924	04 September 2013 (04.09.2013)	04 September 2012 (04.09.2012)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - C40B 20/00 (2013.01)
USPC - 506/2,12; 702/1,19; 435/6.1,7.2

Applicant NATERA, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 *bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	23 January 2014 (23.01.2014)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/237 (cover sheet) (July 2011)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 13/57924

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. (means)

   ☐ on paper

   ☐ in electronic form

   b. (time)

   ☐ in the international application as filed

   ☐ together with the international application in electronic form

   ☐ subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US 13/57924

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 5-29

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 5-29 are so unclear that no meaningful opinion could be formed *(specify)*:

Claims 5-29 are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 5-29

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 13/57924

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-4, 30, 32-34	YES
	Claims	31	NO
Inventive step (IS)	Claims	1-4, 30, 32-34	YES
	Claims	31	NO
Industrial applicability (IA)	Claims	1-4, 30-34	YES
	Claims	None	NO

2. Citations and explanations:

Claim 31 lacks novelty under PCT Article 33(2) as being anticipated by US 5,716,776 A (Bogart).

As to claim 31, Bogart discloses the use of (ii) a stimulant (col 4, ln 34-38) for increasing the fetal fraction in the blood, plasma, or serum of a pregnant woman (col 3, ln 64 to pg 4, ln 4).

Claims 1-4, 30 and 32-34 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed subject matter, specifically increasing the fetal fraction in the blood, plasma, serum of a pregnant woman by administering a nutritious composition or stimulant prior to obtaining the sample.

The best prior art on record that discloses increased fetal fractions in prenatal testing are below:

US 5,716,776 A (Bogart) discloses the use of a stimulant (pg 4, ln 34-38) to increase the fetal fraction in the blood of a pregnant woman (col 3, ln 64 to pg 4, ln 4), but does not disclose wherein the administration of the stimulant occurs before the blood is taken from the pregnant woman.

US 2011/0251149 A1 to Perrine, et al. (hereinafter 'Perrine') discloses increasing the percentage of fetal hemoglobin in the blood of subject by administering a substance to the subject (para [0008]), but does not disclose wherein the substance is a stimulant or a nutritious composition or wherein the increase is used in prenatal testing.

US 2008/0138809 A1 to Kapur, et al. (hereinafter 'Kapur') discloses the enrichment of fetal cells from blood samples that are used in prenatal testing (para [0005] and [0009]), but does not disclose wherein the increase occurs before the blood is taken from the pregnant woman.

The article titled "Fetal fraction in maternal plasma cell-free DNA at 11-13 weeks' gestation: Effect of maternal and fetal factors" by Ashoor, et al. (hereinafter 'Ashoor') discloses wherein the fetal fraction in maternal plasma cfDNA increases with serum PAPP-A and free B-hCG and decreases with maternal weight and wherein (pg 1, 1st paragraph) and wherein the fetal fraction is used in prenatal testing (pg 1, 2nd paragraph), but does not disclose administering any substance to a pregnant woman to increase the fetal fraction before the sample is taken. There is no prior art on record that discloses the claimed subject matter, specifically increasing the fetal fraction in the blood, plasma, serum of a pregnant woman by administering a nutritious composition or stimulant prior to obtaining the sample. Thus, claims 1-4, 30 and 32-34 meet the criteria set out in PCT Article 33(2)-(3).

Claims 1-4 and 30-34 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in the industry.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: Ivor R. Elrifi
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC
One Financial Center
Boston, Massachusetts 02111

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	28 SEP 2007

Applicant's or agent's file reference	FOR FURTHER ACTION
35506-501-061	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 06/45281	22 November 2006 (22.11.2006)	26 November 2005 (26.11.2005)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - G06F 19/00 (2007.01)
USPC - 702/20

Applicant Gene Security Network, LLC

1. This opinion contains indications relating to the following items:

- [x] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [x] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	02 May 2007 (02.05.2007)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 06/45261

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing

      ☐ contained in the international application as filed

      ☐ filed together with the international application in electronic form

      ☐ furnished subsequently to this Authority for the purposes of search

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

NeoGenomics
Exhibit 1003 Page 1045

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 06/45281

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	5, 15, 18, 26-27, 29, 32-35, 43	YES
	Claims	1-4, 6-14, 16-17, 19-25, 28, 30-31, 36-42, 44-61	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-61	NO
Industrial applicability (IA)	Claims	1-61	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-4, 6-14, 16-17, 19-25, 28, 30-31, 36-42 and 44 lack novelty under PCT Article 33(2) as being anticipated by WO 03/031646 A1 to Findlay et al. (hereinafter 'Findlay).

As to claims 1 and 28, Findlay teaches a method for determining genetic data of a target individual based on the imperfect knowledge of the target individual's genetic data, and knowledge of the genetic data of one or more individuals genetically related to the target (see pg 14, ln 1 - pg 16, ln 27), the method comprising:
(i) creating a set of one or more hypotheses concerning which segments of which chromosomes from the related individual(s) correspond to those segments found in the target individual's genome (appropriate chromosome) (see pg 8, ln 16-19).
(ii) determining the probability of each of the hypotheses (genetic identification, human embryo identification, forensics, genetic identification by DNA fingerprinting) given the measurements of the target individual's genetic data and of the related individual's genetic data (see pg 9, ln 1-4 and pg 12, ln 26-28); and
(iii) using the probabilities associated with each hypothesis to determine the most likely state of the actual genetic material (heterozygosity index, genetic marker selection) of the target individual (see pg 7, ln 25 pg 8, in4).

As to claim 2, Findlay teaches the method of claim 1, wherein the method involves determining which regions of the parental chromosomes have the maximum likelihood of having contributed to the formation of the gametes that contributed to the target individual, based on the measurements of genetic data of the target and determination of the likelihood of those particular measurements given the genetic data of the parents (see pg 7, ln 25 - pg 8, ln 4).

As to claim 3, Findlay teaches the haplotypes of at least one of the parents have been determined by using genetic data measured from the parent's diploid sample, and the genetic data measured from a haploid sample from the parent which is used to determine which alleles measured from the diploid sample belong to which haplotype (see table 6b).

As to claim 4, Findlay teaches the genetic data from genetically related individuals are taken from a group comprising genetic data from a diploid maternal sample, a haploid maternal sample, a diploid paternal sample, and a haploid paternal sample (see pg 20, ln 11-24).

As to claim 6-7, Findlay teaches the method of claim 1, wherein the genetic data from the genetically related individual are taken from a group comprising genetic data from diploid maternal cell, diploid paternal cells, and diploid cells from a related individual known to be a carrier of the phenotype in question (see Fig 4-7 and pg 6, ln 23 - pg 7, ln 3).

As to claim 8-11, Findlay teaches:
the genetically related individuals are taken from a group consisting of the father, mother, twin1, twin2 (see table 6a, 6b and pg 6, ln 8-12);
the target individual is a human embryo (see pg 9, ln 1-2);
one or more of the individual's genetic data has been amplified using tools and/or techniques taken from the group comprising Polymerase Chain Reaction (PCR) (see pg 9, ln 6-8);
the individual's genetic data has been measured using fluorescent in-situ hybridization (FISH) (see pg 17, ln 1-2).

As to claim 12, Findlay teaches the method of claim 1, where one or more of the individual's genetic data has been measured by analyzing substances taken from the group comprising the individual's bulk diploid tissue, one or more diploid cells taken from the individual, one or more blastocysts taken from the individual, the individual's semen, the individual's egg, extra cellular genetic material from the individual found in maternal blood, genetic material known to have originated from the individual and combinations thereof (nucleic acids isolated from fetal cells) (see pg 14, ln 1-7).

As to claims 13-14 Findlay teaches one or more of the related individual's genetic data is partly or wholly known in silico, or is provided by parties other than those determining the target individual's genetic data; and where the haploid genetic data of one or more of the individuals is partly or wholly generated in silico by means of a computer algorithm that simulates haploid data from diploid data (forensic, pathology, genetic diagnosis, and evolutionary genetics) (see pg 22, ln 18-19).

(See Supplemental Box - Reasoned Statement)

NeoGenomics
Exhibit 1003 Page 1046