PTO/AIA/15 (03-13)
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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	104371-5016-US08
First Named Inventor	Sydney Brenner
Title	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGE CELLS
Express Mail Label No.	

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. [✓] **Fee Transmittal Form** (PTO/SB/17 or equivalent)
2. [✓] **Applicant asserts small entity status.** See 37 CFR 1.27
3. [ ] **Applicant certifies micro entity status.** See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent.
4. [✓] **Specification** [*Total Pages* 42] Both the claims and abstract must start on a new page. *(See MPEP § 608.01(a) for information on the preferred arrangement)*
5. [✓] **Drawing(s)** (35 U.S.C. 113) [*Total Sheets* 13]
6. **Inventor's Oath or Declaration** [*Total Pages* ____] *(including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e))*
   a. [ ] Newly executed (original or copy)
   b. [ ] A copy from a prior application (37 CFR 1.63(d))
7. [✓] **Application Data Sheet** * *See note below.* See 37 CFR 1.76 (PTO/AIA/14 or equivalent)
8. **CD-ROM or CD-R** in duplicate, large table, or Computer Program (*Appendix*)
   [ ] Landscape Table on CD
9. **Nucleotide and/or Amino Acid Sequence Submission** (*if applicable, items a. – c. are required*)
   a. [ ] Computer Readable Form (CRF)
   b. [ ] Specification Sequence Listing on:
      i. [ ] CD-ROM or CD-R (2 copies); or
      ii. [ ] Paper
   c. [ ] Statements verifying identity of above copies

ADDRESS TO:

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

ACCOMPANYING APPLICATION PAPERS

10. [ ] **Assignment Papers** (cover sheet & document(s))
    Name of Assignee ____
11. [ ] **37 CFR 3.73(c) Statement** (*when there is an assignee*) [ ] **Power of Attorney**
12. [ ] **English Translation Document** (*if applicable*)
13. [ ] **Information Disclosure Statement** (PTO/SB/08 or PTO-1449)
    [ ] Copies of citations attached
14. [ ] **Preliminary Amendment**
15. [ ] **Return Receipt Postcard** (*MPEP § 503*) (*Should be specifically itemized*)
16. [ ] **Certified Copy of Priority Document(s)** (*if foreign priority is claimed*)
17. [ ] **Nonpublication Request** Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent.
18. [✓] **Other:** Track One Request

*Note: (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).
(2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

19. CORRESPONDENCE ADDRESS

[✓] The address associated with Customer Number: 43850 **OR** [ ] Correspondence address below

Name					
Address					
City		State		Zip Code	
Country		Telephone		Email	

Signature	Gargi Talukder	Date	Aug 15, 2017
Name (Print/Type)	Gargi Talukder	Registration No. (Attorney/Agent)	61,368

This collection of information is required by 37 CFR 1.53(b). 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 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.

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FEE TRANSMITTAL

Complete if known	
Application Number	
Filing Date	Herewith
First Named Inventor	Sydney Brenner
Examiner Name	
Art Unit	
Practitioner Docket No.	104371-5016-US08

[✓] 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.

TOTAL AMOUNT OF PAYMENT ($) 2,870

METHOD OF PAYMENT (check all that apply)

[ ] Check [ ] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[✓] Deposit Account Deposit Account Number: 50-0310 Deposit Account Name: Morgan, Lewis & Bockius LLP

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[✓] Charge fee(s) indicated below [ ] Charge fee(s) indicated below, **except for the filing fee**

[✓] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 [✓] Credit any overpayment of fee(s)

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.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	280	140*	70	600	300	150	720	360	180	730
Design	180	90	45	120	60	30	460	230	115	
Plant	180	90	45	380	190	95	580	290	145	
Reissue	280	140	70	600	300	150	2,160	1,080	540	
Provisional	260	130	65	0	0	0	0	0	0	

* The $140 small entity status filing fee for a utility application is further reduced to $70 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	80	40	20
Each independent claim over 3 (including Reissues)	420	210	105
Multiple dependent claims	780	390	195

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
6	-20 or HP =	_____ x	_____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
1	-3 or HP =	_____ x	_____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**
_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**	**Fee ($)**		**Fee Paid ($)**
55	- 100 =	0	/ 50 =	_____ (round **up** to a whole number)	x _____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): late filing surcharge; Track One Request; processing fee	2,140

SUBMITTED BY

Signature	Gargi Talukder	Registration No. (Attorney/Agent) 61,368	Telephone 415.442.1000
Name (Print/Type)	Gargi Talukder		Date Aug 15, 2017

This collection of information is required by 37 CFR 1.136. 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, 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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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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
	Sydney		Brenner	

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

City	Ely	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	3 Barton Square		
Address 2			
City	Ely	**State/Province**	
Postal Code	CB7 4PJ	**Country** [i]	GB

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gi		Mikawa	

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

City	Great Shelford	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	104 High Street		
Address 2			
City	Great Shelford	**State/Province**	
Postal Code	CB1 6A3	**Country** [i]	GB

Inventor 3 Remove

Legal Name

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		Osborne	

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

City	Great Chesterford	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	38 Pilgrim Close		
Address 2			
City	Great Chesterford	**State/Province**	
Postal Code	CB10 1QB	**Country** [i]	GB

Inventor 4 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Andrew		Slatter	

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

City	Lindon	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	65a Huddleston Road		
Address 2			
City	London	**State/Province**	
Postal Code	N7 0AE	**Country** [i]	GB

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	43850		
Email Address	sfipdocketing@morganlewis.com	Add Email	Remove Email

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Application Information:

Title of the Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS		
Attorney Docket Number	104371-5016-US08	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	13	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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

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

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

Publication Information:

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

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

Representative Information:

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

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	43850		

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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		Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)

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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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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	10X Genomics, Inc.

Mailing Address Information For Applicant:

Address 1	7068 Koll Center Parkway, Suite 401		
Address 2			
City	Pleasanton	**State/Province**	CA
Country	US	Postal Code	94566
Phone Number		Fax Number	
Email Address			

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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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

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

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

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	Gargi Talukder			Date (YYYY-MM-DD)	2017-08-15
First Name	Gargi	Last Name	Talukder	Registration Number	61368

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

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	104371-5016-US08
	Application Number	
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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.**

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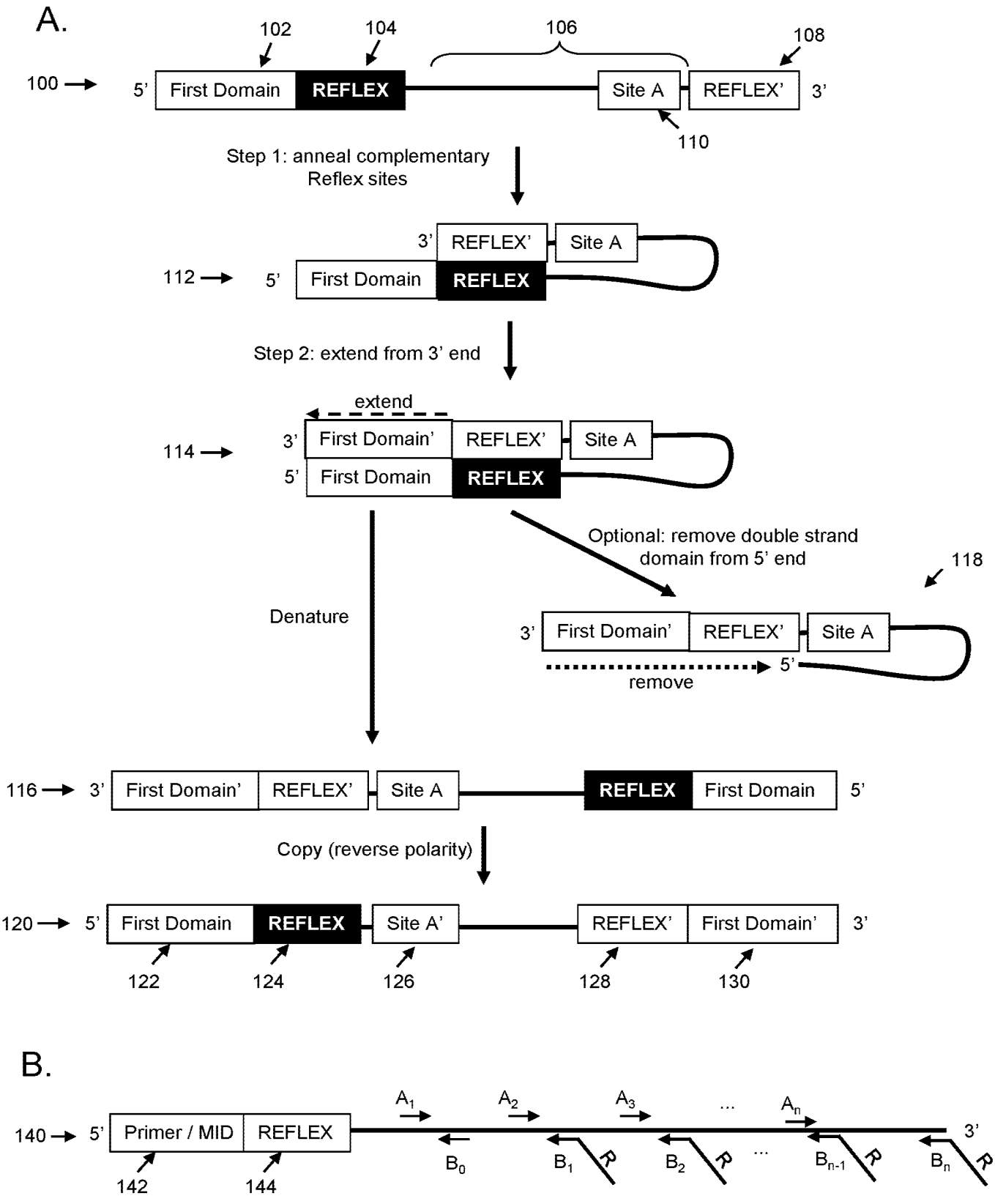

A.
102
104
106
108
100
5'
First Domain
REFLEX
Site A
REFLEX'
3'
110
Step 1: anneal complementary Reflex sites
3'
REFLEX'
Site A
112
5'
First Domain
REFLEX
Step 2: extend from 3' end
extend
114
3'
First Domain'
REFLEX'
Site A
5'
First Domain
REFLEX
Optional: remove double strand domain from 5' end
118
Denature
3'
First Domain'
REFLEX'
Site A
5'
remove
116
3'
First Domain'
REFLEX'
Site A
REFLEX
First Domain
5'
Copy (reverse polarity)
120
5'
First Domain
REFLEX
Site A'
REFLEX'
First Domain'
3'
122
124
126
128
130
B.
140
5'
Primer / MID
REFLEX
142
144
A1
A2
A3
...
An
3'
B0
B1
R
B2
R
...
Bn-1
R
Bn
R

Fig. 1

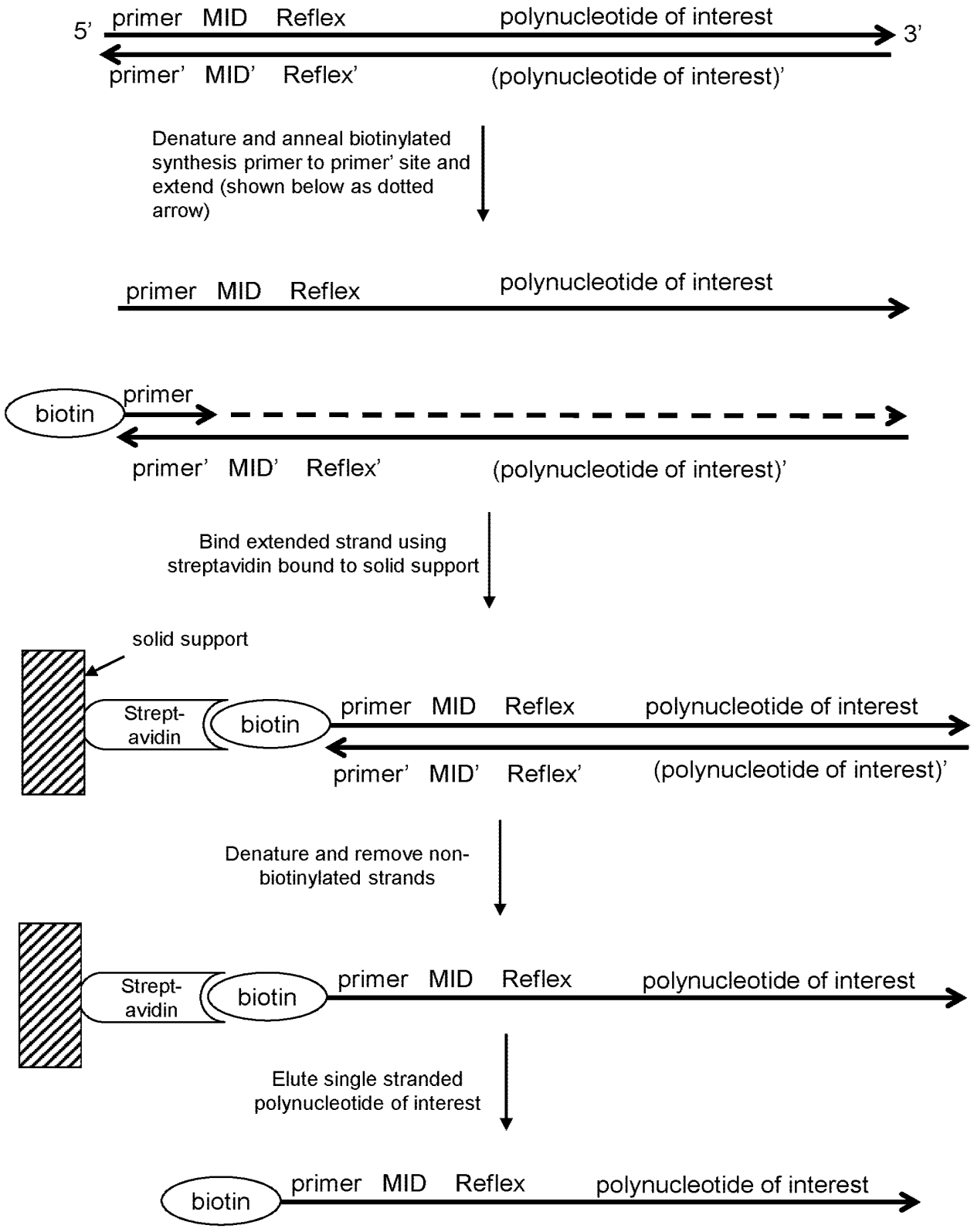
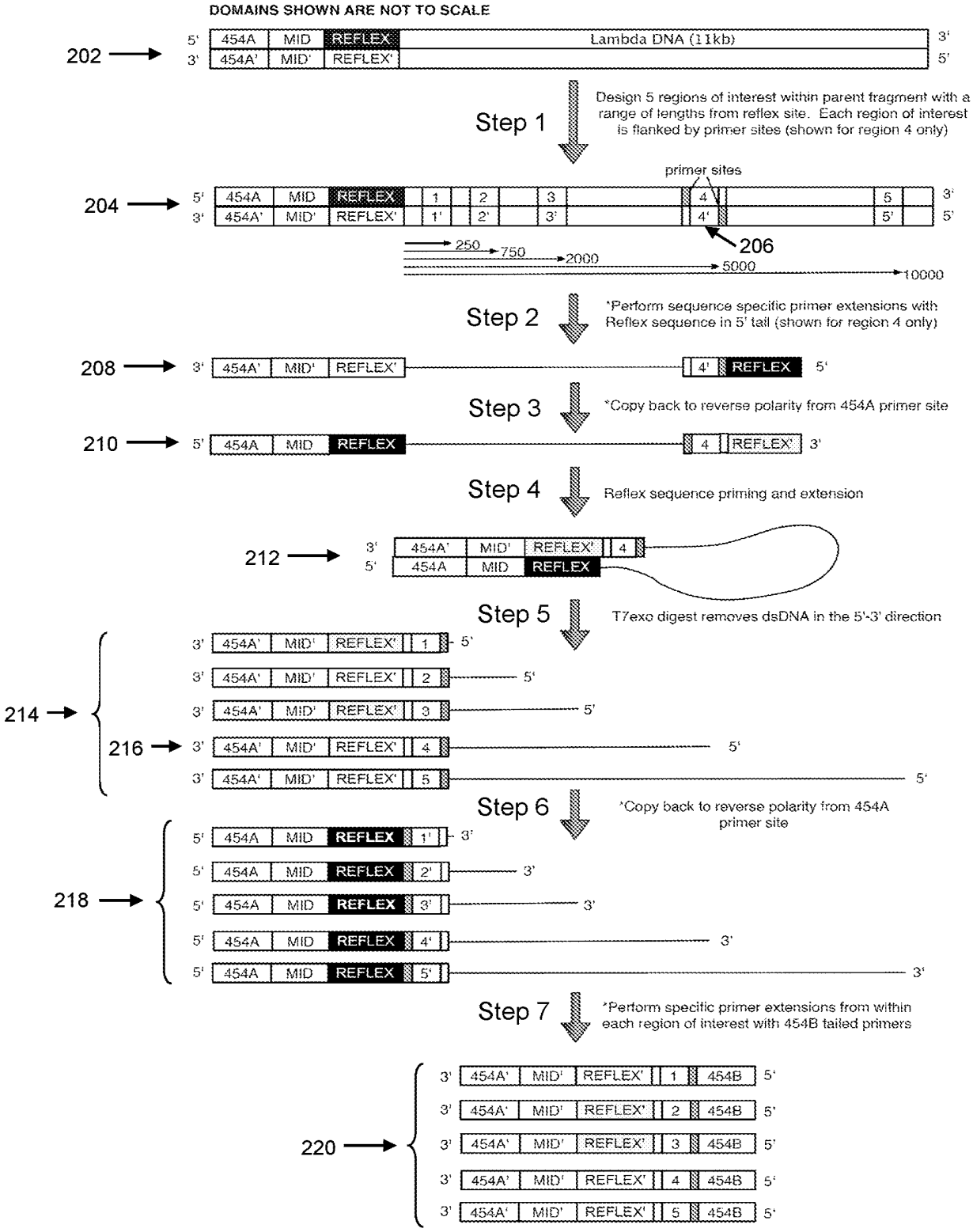

5'
primer
MID
Reflex
polynucleotide of interest
3'
primer'
MID'
Reflex'
(polynucleotide of interest)'
Denature and anneal biotinylated synthesis primer to primer' site and extend (shown below as dotted arrow)
primer
MID
Reflex
polynucleotide of interest
biotin
primer
primer'
MID'
Reflex'
(polynucleotide of interest)'
Bind extended strand using streptavidin bound to solid support
solid support
Strept-avidin
biotin
primer
MID
Reflex
polynucleotide of interest
primer'
MID'
Reflex'
(polynucleotide of interest)'
Denature and remove non-biotinylated strands
Strept-avidin
biotin
primer
MID
Reflex
polynucleotide of interest
Elute single stranded polynucleotide of interest
biotin
primer
MID
Reflex
polynucleotide of interest

Fig. 2



Primer extension reactions with * may be performed such that isolation of single strand species is facilitated (e.g., using primers with binding moieties and/or multiple cycles of extension)

Fig. 3

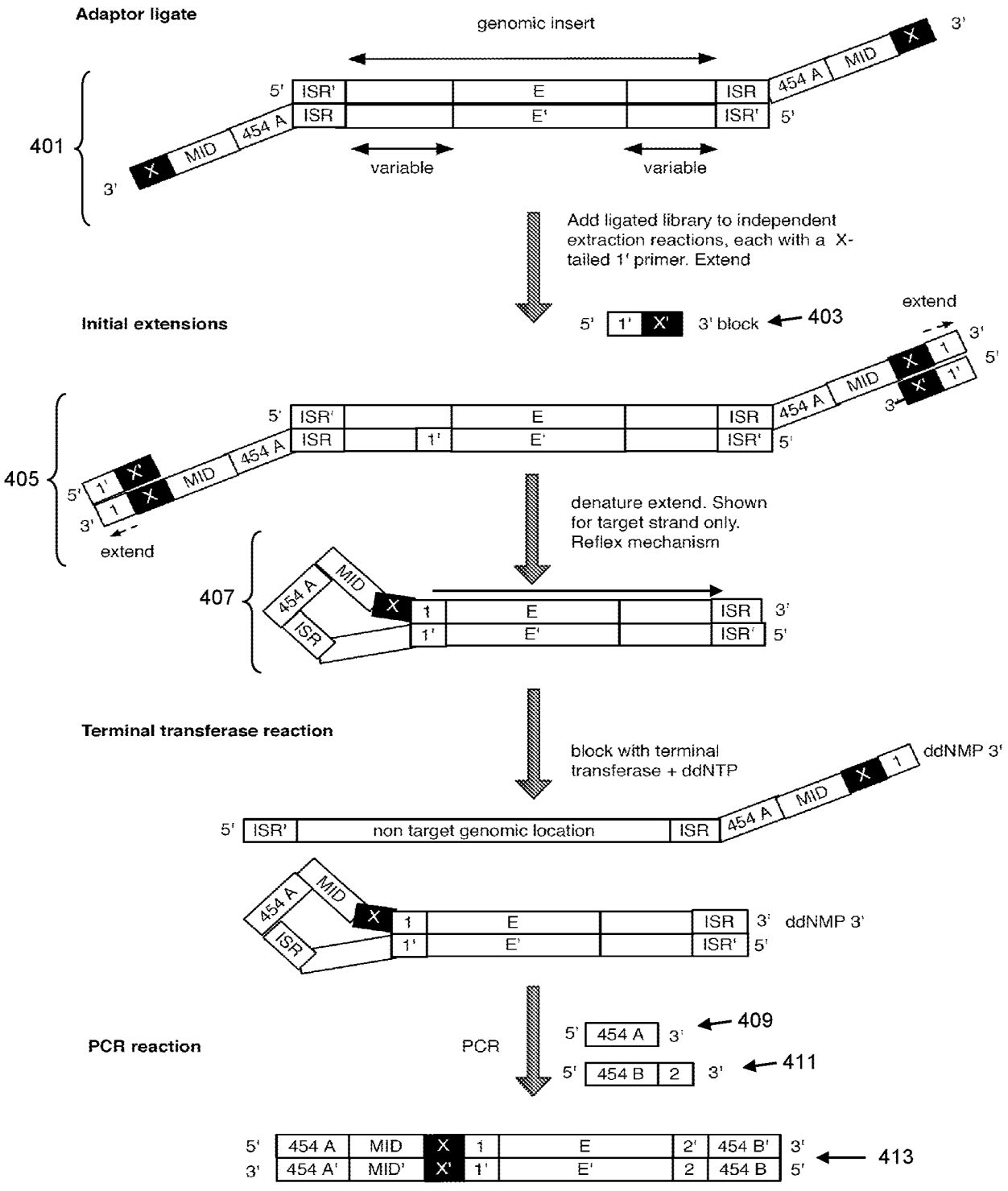

Adaptor ligate
genomic insert
401
5'
ISR'
E
ISR
454 A
MID
X
3'
ISR
E'
ISR'
variable
variable
Add ligated library to independent extraction reactions, each with a X-tailed 1' primer. Extend
Initial extensions
5' 1' X' 3' block
403
extend
405
1
1'
extend
denature extend. Shown for target strand only. Reflex mechanism
407
Terminal transferase reaction
block with terminal transferase + ddNTP
ddNMP 3'
non target genomic location
PCR reaction
PCR
409
411
454 B
2
413

Fig. 4

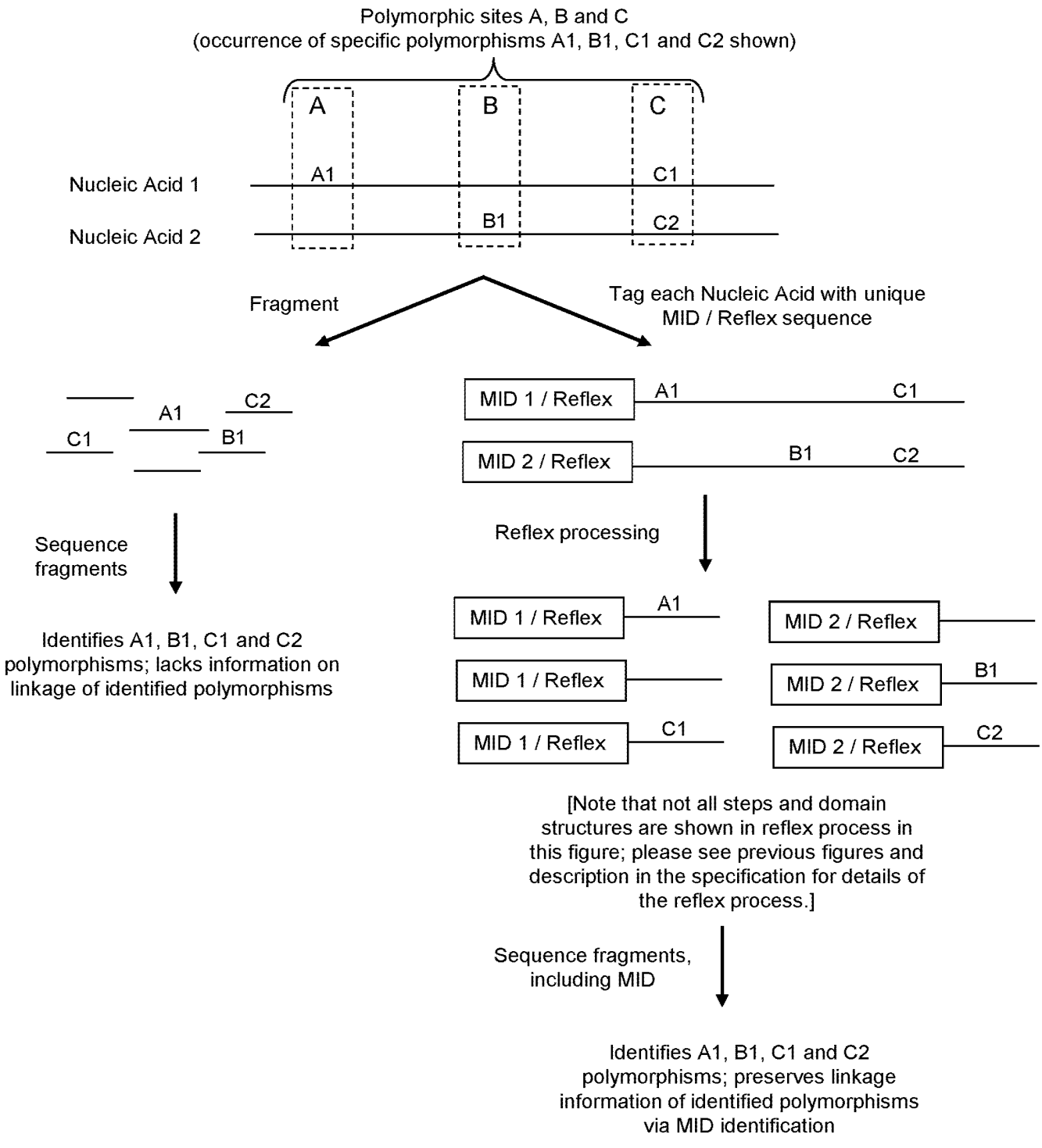
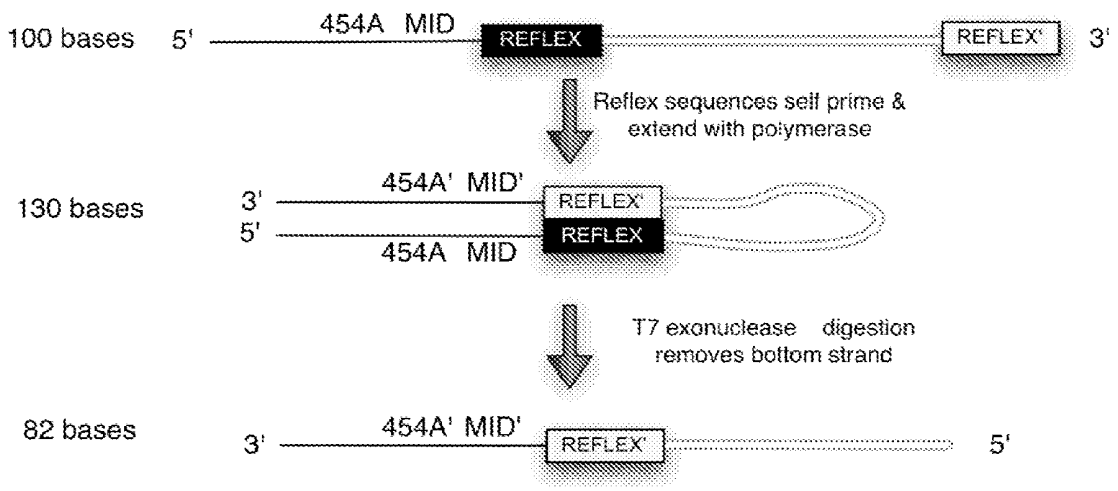
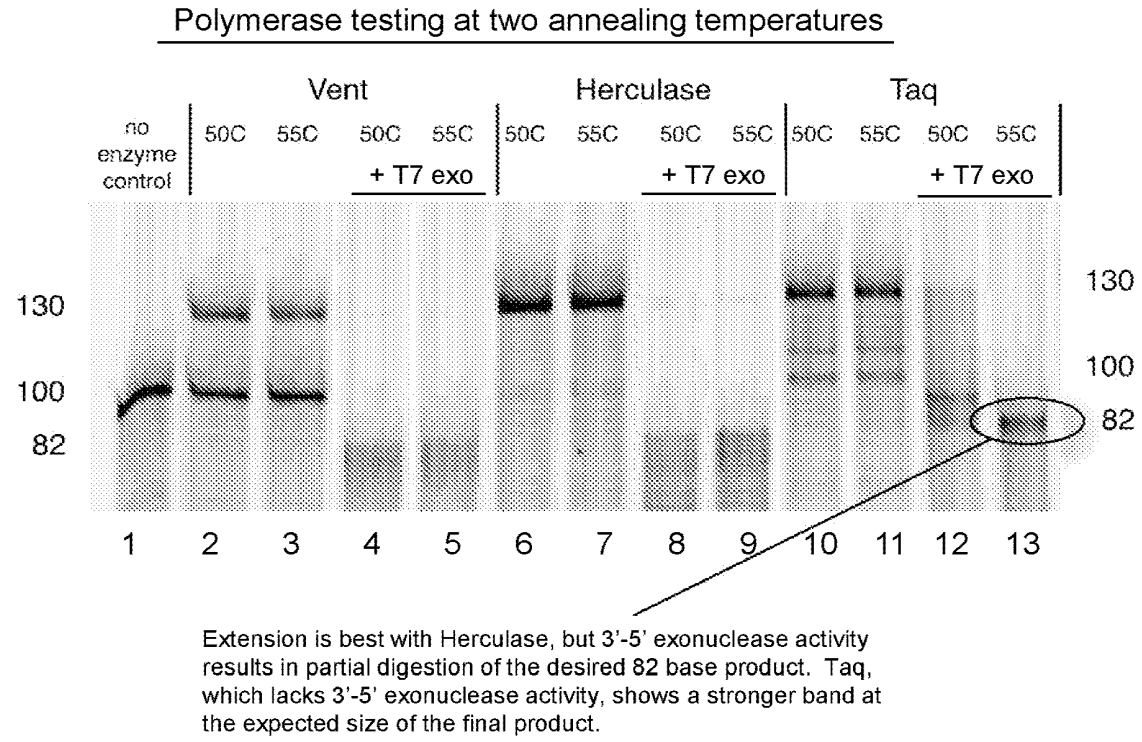

Polymorphic sites A, B and C
(occurrence of specific polymorphisms A1, B1, C1 and C2 shown)
A
B
C
Nucleic Acid 1
A1
C1
Nucleic Acid 2
B1
C2
Fragment
Tag each Nucleic Acid with unique MID / Reflex sequence
A1
C2
C1
B1
MID 1 / Reflex
A1
C1
MID 2 / Reflex
B1
C2
Sequence fragments
Identifies A1, B1, C1 and C2 polymorphisms; lacks information on linkage of identified polymorphisms
Reflex processing
MID 1 / Reflex
A1
MID 2 / Reflex
MID 1 / Reflex
MID 2 / Reflex
B1
MID 1 / Reflex
C1
MID 2 / Reflex
C2
[Note that not all steps and domain structures are shown in reflex process in this figure; please see previous figures and description in the specification for details of the reflex process.]
Sequence fragments, including MID
Identifies A1, B1, C1 and C2 polymorphisms; preserves linkage information of identified polymorphisms via MID identification

Fig. 5

A.



B.



Extension is best with Herculase, but 3'-5' exonuclease activity results in partial digestion of the desired 82 base product. Taq, which lacks 3'-5' exonuclease activity, shows a stronger band at the expected size of the final product.

Fig. 6

A.


5'
454A MID
REFLEX
REFLEX'
3'
+ Competitor
5'
REFLEX'
3'

B.

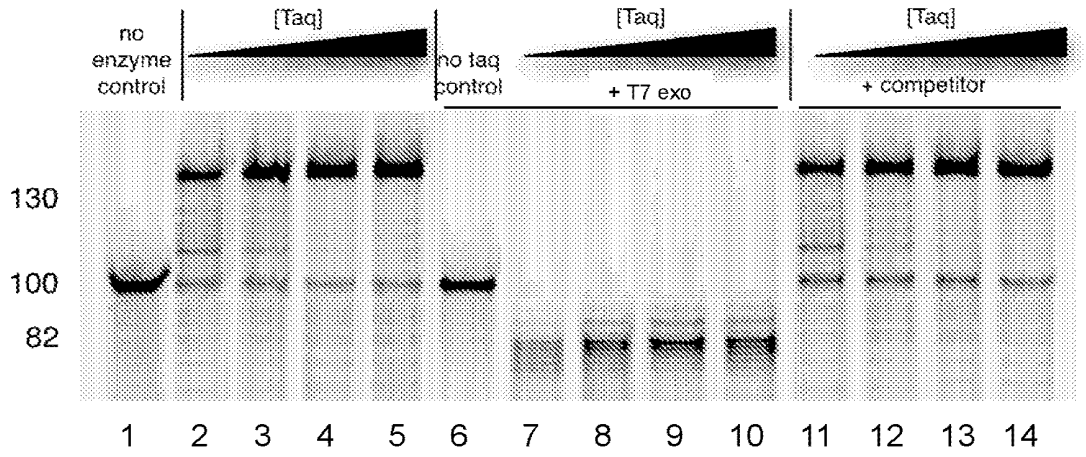
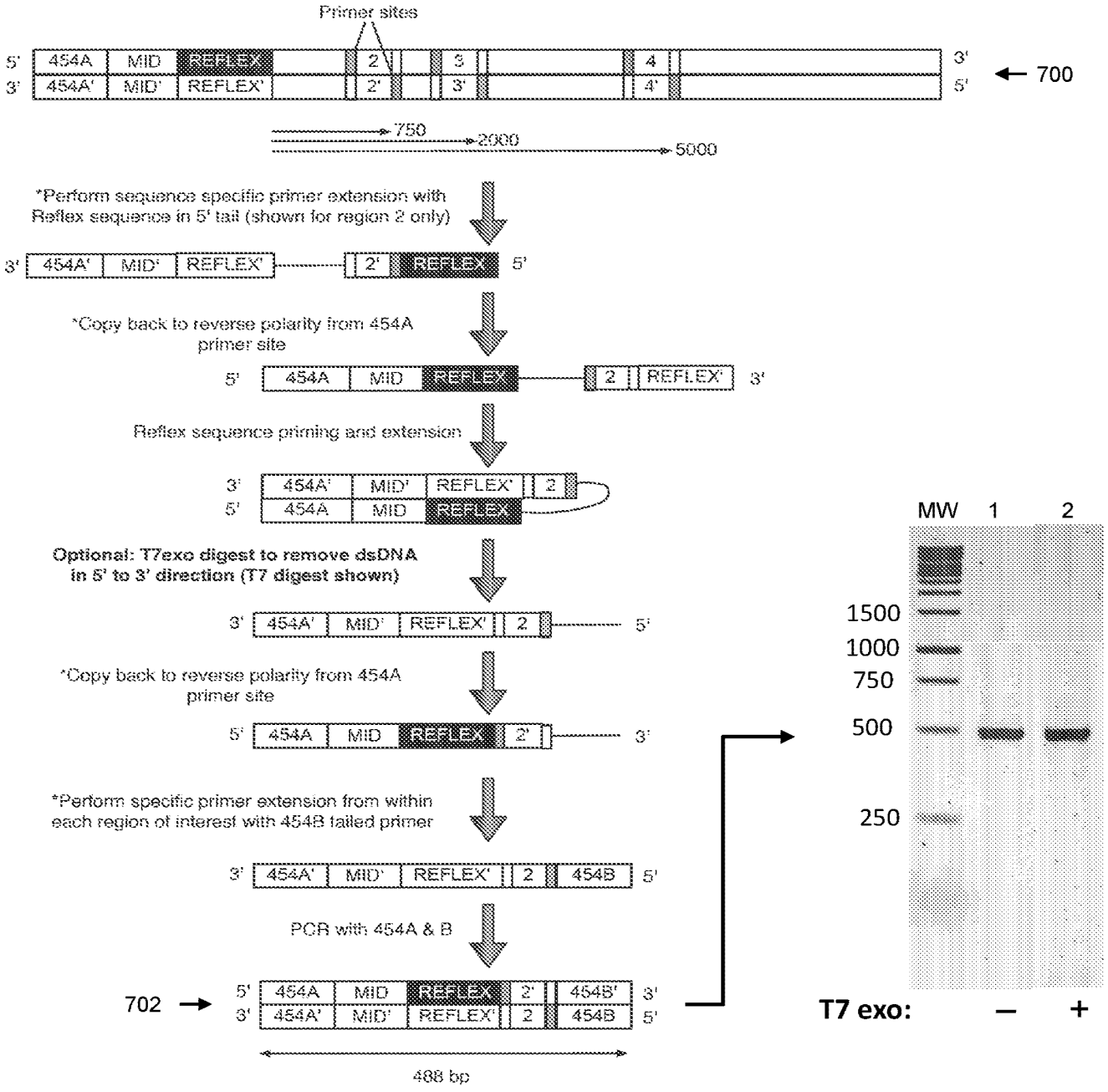

no enzyme control
[Taq]
no taq control
[Taq]
+ T7 exo
[Taq]
+ competitor
130
100
82
1 2 3 4 5 6 7 8 9 10 11 12 13 14

Fig. 7



Primer extension reactions with * may be performed such that isolation of single strand species is facilitated (e.g., using primers with binding moieties and/or multiple cycles of extension)

Fig. 8

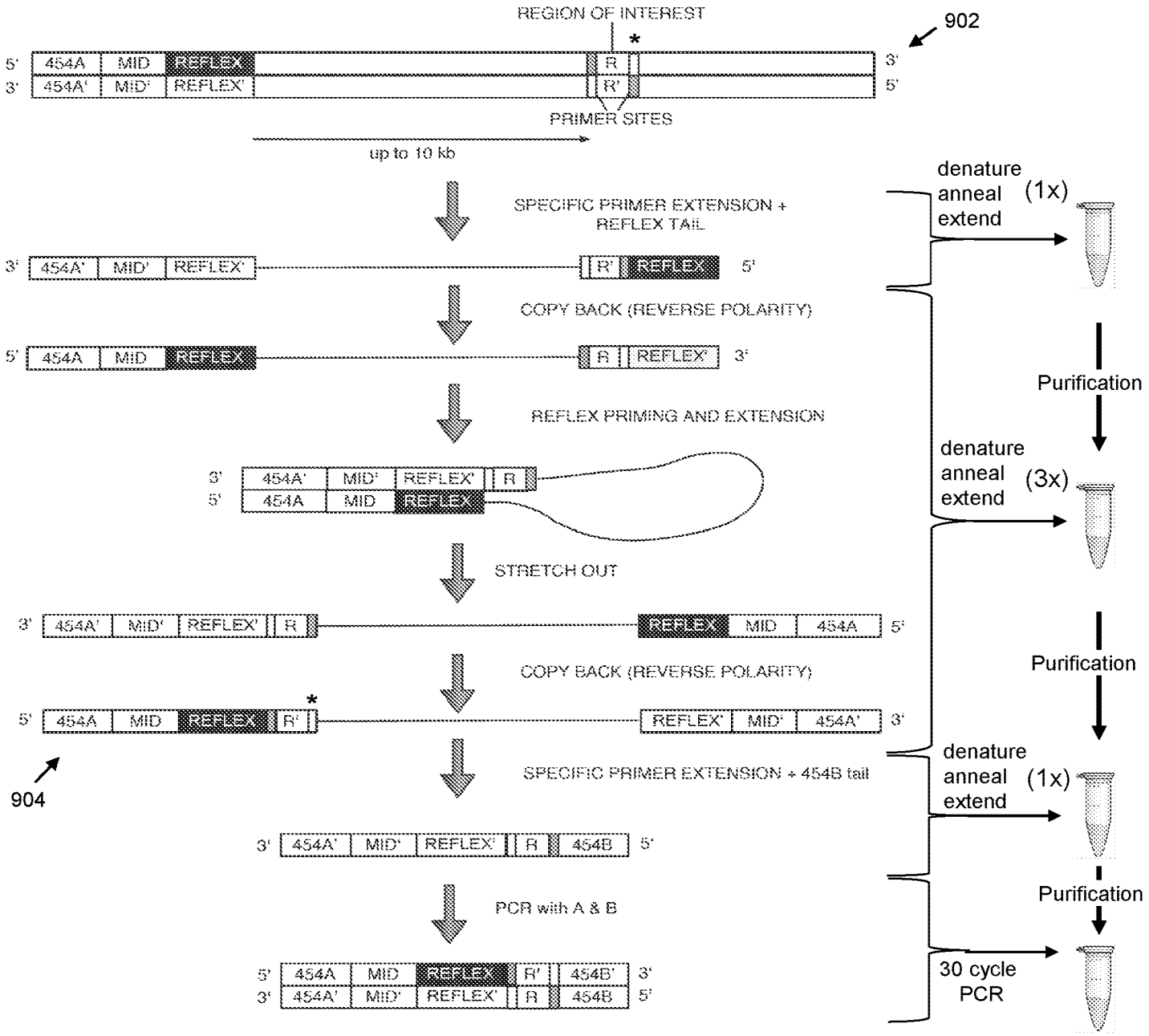

REGION OF INTEREST
902
5' 454A MID REFLEX R 3'
3' 454A' MID' REFLEX' R' 5'
PRIMER SITES
up to 10 kb
SPECIFIC PRIMER EXTENSION + REFLEX TAIL
3' 454A' MID' REFLEX' R' REFLEX 5'
COPY BACK (REVERSE POLARITY)
5' 454A MID REFLEX R REFLEX' 3'
REFLEX PRIMING AND EXTENSION
3' 454A' MID' REFLEX' R
5' 454A MID REFLEX
STRETCH OUT
3' 454A' MID' REFLEX' R REFLEX MID 454A 5'
COPY BACK (REVERSE POLARITY)
5' 454A MID REFLEX R' REFLEX' MID' 454A' 3'
SPECIFIC PRIMER EXTENSION + 454B tail
3' 454A' MID' REFLEX' R 454B 5'
PCR with A & B
5' 454A MID REFLEX R' 454B' 3'
3' 454A' MID' REFLEX' R 454B 5'
904
denature anneal extend (1x)
Purification
denature anneal extend (3x)
Purification
denature anneal extend (1x)
Purification
30 cycle PCR

Fig. 9

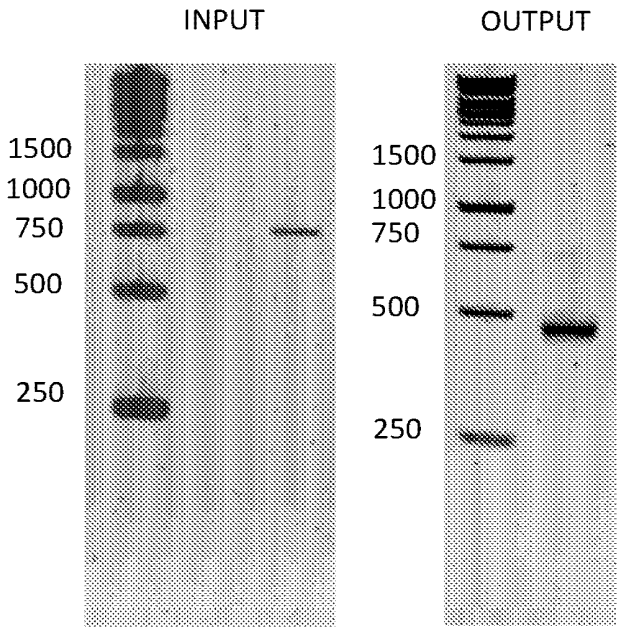
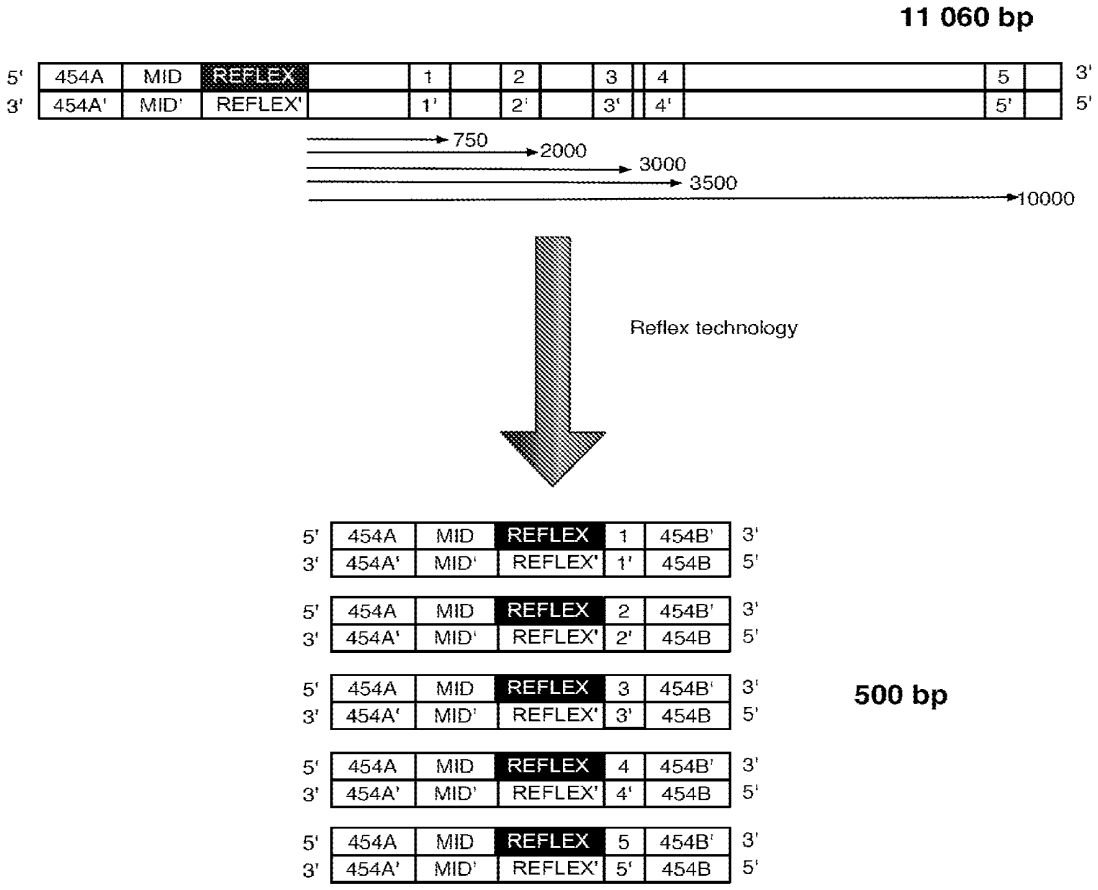


Fig. 10


11 060 bp
5' 454A MID REFLEX 1 2 3 4 5 3'
3' 454A' MID' REFLEX' 1' 2' 3' 4' 5' 5'
750
2000
3000
3500
10000
Reflex technology
5' 454A MID REFLEX 1 454B' 3'
3' 454A' MID' REFLEX' 1' 454B 5'
5' 454A MID REFLEX 2 454B' 3'
3' 454A' MID' REFLEX' 2' 454B 5'
5' 454A MID REFLEX 3 454B' 3'
3' 454A' MID' REFLEX' 3' 454B 5'
5' 454A MID REFLEX 4 454B' 3'
3' 454A' MID' REFLEX' 4' 454B 5'
5' 454A MID REFLEX 5 454B' 3'
3' 454A' MID' REFLEX' 5' 454B 5'
500 bp

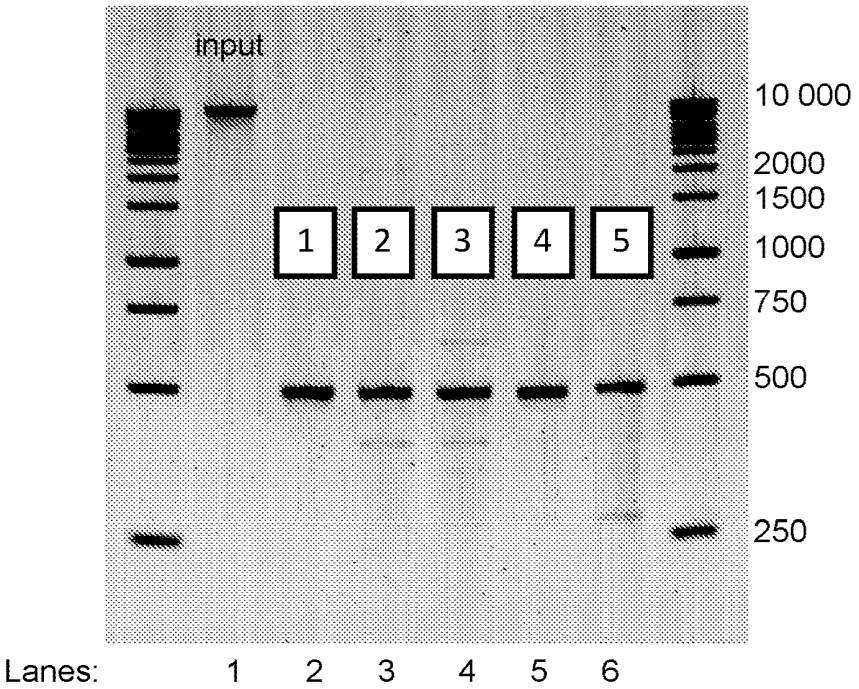
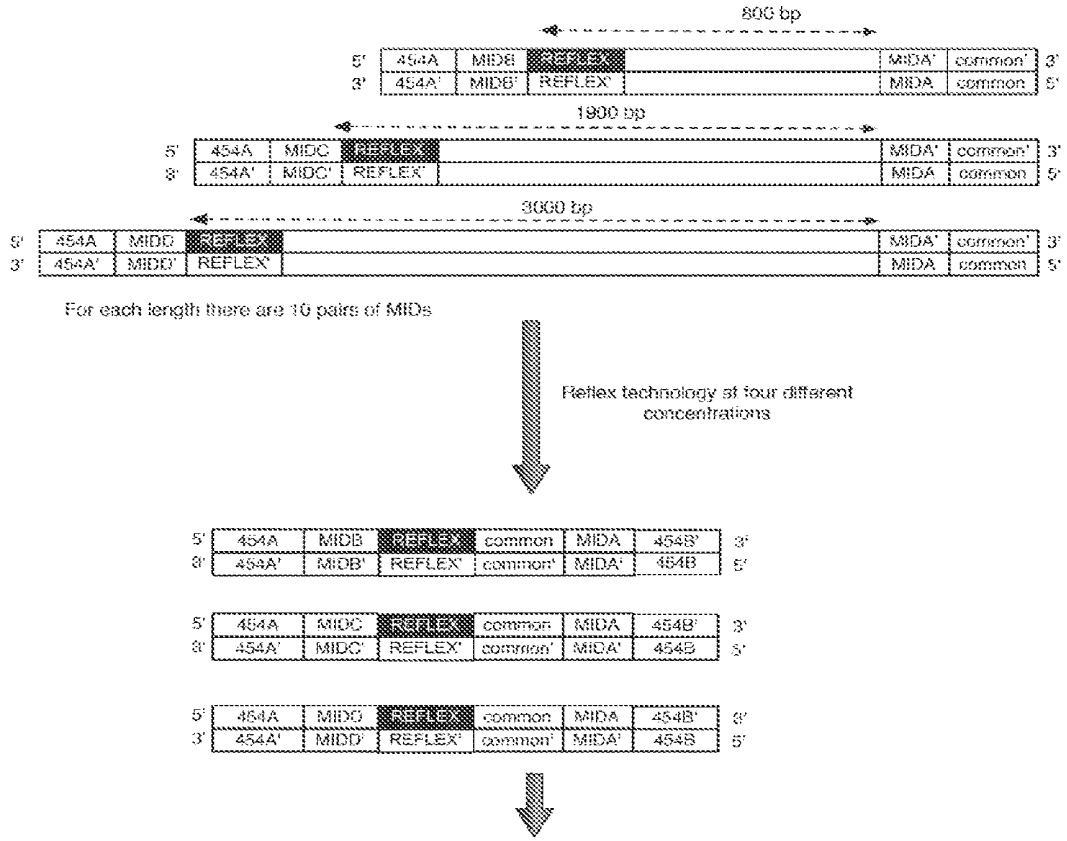
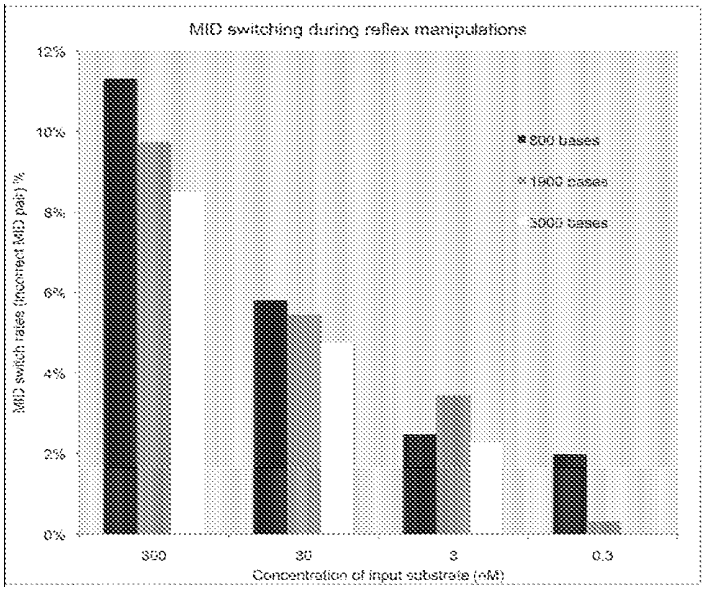

input
1
2
3
4
5
10 000
2000
1500
1000
750
500
250
Lanes: 1 2 3 4 5 6

Fig. 11


800 bp
5' 454A MIDB REFLEX' MIDA' common 3'
3' 454A' MIDB' REFLEX' MIDA common 5'
1900 bp
5' 454A MIDC REFLEX' MIDA' common' 3'
3' 454A' MIDC' REFLEX' MIDA common 5'
3000 bp
5' 454A MIDD REFLEX' MIDA' common' 3'
3' 454A' MIDD' REFLEX' MIDA common 5'
For each length there are 10 pairs of MIDs
Reflex technology at four different concentrations
5' 454A MIDB REFLEX' common MIDA 454B' 3'
3' 454A' MIDB' REFLEX' common' MIDA' 454B 5'
5' 454A MIDC REFLEX' common MIDA 454B' 3'
3' 454A' MIDC' REFLEX' common' MIDA' 454B 5'
5' 454A MIDD REFLEX' common MIDA 454B' 3'
3' 454A' MIDD' REFLEX' common' MIDA' 454B 5'
Roche 454 Sequencing


MID switching during reflex manipulations
MID switch rates (incorrect MID pair) %
12%
10%
8%
6%
4%
2%
0%
800 bases
1900 bases
3000 bases
300
30
3
0.3
Concentration of input substrate (nM)

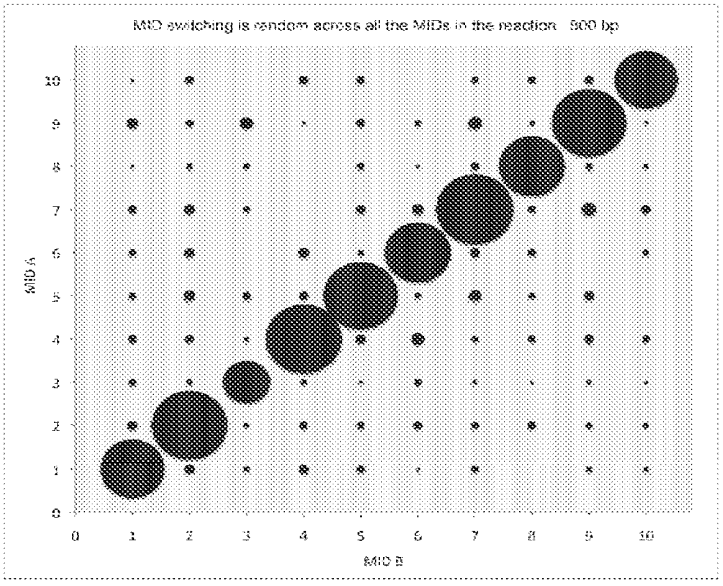

MID switching is random across all the MIDs in the reaction 900 bp
MID A
MID B

Fig. 12

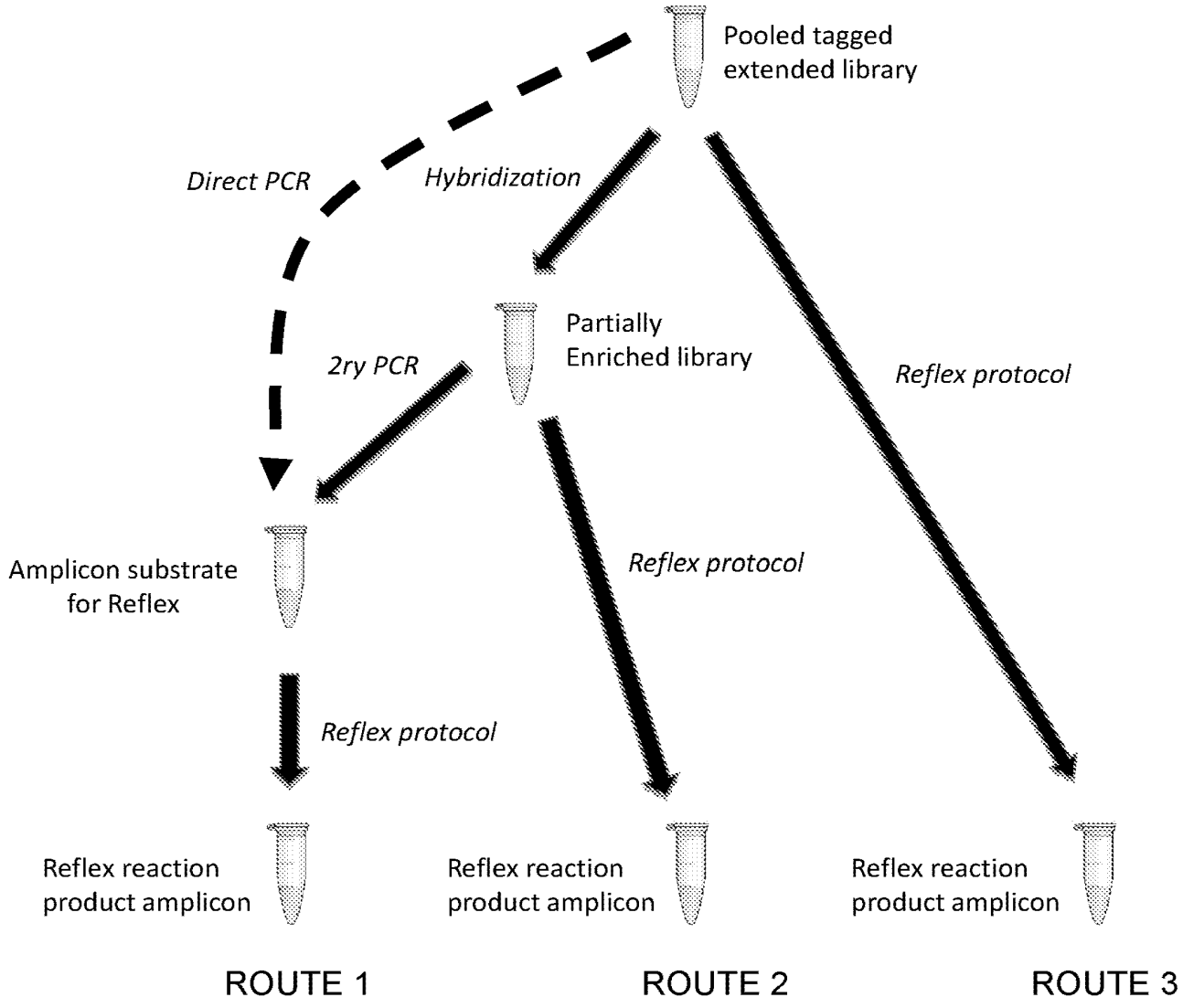

Pooled tagged
extended library
Direct PCR
Hybridization
Partially
Enriched library
2ry PCR
Reflex protocol
Amplicon substrate
for Reflex
Reflex protocol
Reflex protocol
Reflex reaction
product amplicon
Reflex reaction
product amplicon
Reflex reaction
product amplicon
ROUTE 1
ROUTE 2
ROUTE 3

Fig. 13

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

BACKGROUND OF THE INVENTION

[0001] We have previously described methods that enable tagging each of a population of fragmented genomes and then combining them together to create a 'population library' that can be processed and eventually sequenced as a mixture. The population tags enable analysis software to parse the sequence reads into files that can be attributed to a particular genome in the population. One limitation of the overall process stems from limitations of existing DNA sequencing technologies. In particular, if fragments in the regions of interest of the genome are longer than the lengths that can be sequenced by a particular technology, then such fragments will not be fully analyzed (since sequencing proceeds from an end of a fragment inward). Furthermore, a disadvantage of any sequencing technology dependent on fragmentation is that sequence changes in one part of a particular genomic region may not be able to be linked to sequence changes in other parts of the same genome (e.g., the same chromosome) because the sequence changes reside on different fragments. (See Figure 5 and its description below).

[0002] The present invention removes the limitations imposed by current sequencing technologies as well as being useful in a number of other nucleic acid analyses.

SUMMARY OF THE INVENTION

[0003] Aspects of the present invention are drawn to processes for moving a region of interest in a polynucleotide from a first position to a second position with regard to a domain within the polynucleotide, also referred to as a "reflex method" (or reflex process, reflex sequence process, reflex reaction, and the like). In certain embodiments, the reflex method results in moving a region of interest into functional proximity to specific domain elements present in the polynucleotide (e.g., primer sites and/or MID). Compositions, kits and systems that find use in carrying out the reflex processes described herein are also provided.

BRIEF DESCRIPTION OF THE DRAWINGS

[0004] The invention is best understood from the following detailed description when read in conjunction with the accompanying drawings. It is emphasized that, according to common practice, the various features of the drawings are not to scale. Indeed, the

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dimensions of the various features are arbitrarily expanded or reduced for clarity. Included in the drawings are the following figures:

[0005] Figure 1: Panel A is a schematic diagram illustrating moving a first domain from one site to another in a nucleic acid molecule using a reflex sequence. Panel B is a schematic diagram depicting the relative position of primer pairs (A_n-B_n primers) that find use in aspects of the reflex process described herein.

[0006] Figure 2 shows an exemplary embodiment of using binding partner pairs (biotin/streptavidin) to isolate single stranded polynucleotides of interest.

[0007] Figure 3 is a schematic diagram illustrating an exemplary embodiment for moving a primer site and a MID to a specific location in a nucleic acid of interest.

[0008] Figure 4 shows a schematic diagram illustrating an exemplary use of the reflex process for generating a sample enriched for fragments having a region of interest (e.g., from a population of randomly fragmented and asymmetrically tagged polynucleotides).

[0009] Figure 5 shows a comparison of methods for identifying nucleic acid polymorphisms in homologous nucleic acids in a sample (e.g., the same region derived from a chromosomal pair of a diploid cell or viral genomes/transcripts). The top schematic shows two nucleic acid molecules in a sample (1 and 2) having a different assortment of polymorphisms in polymorphic sites A, B and C (A1, B1, C1 and C2). Standard sequencing methods using fragmentation (left side) can identify the polymorphisms in these nucleic acids but do not retain linkage information. Employing the reflex process described herein to identify polymorphisms (right side) maintains linkage information.

[0010] Figure 6: Panel A is a schematic showing expected structures and sizes of nucleic acid species in the reflex process; Panel B is a polyacrylamide gel showing the nucleic acid species produced in the reflex process described in Example 1.

[0011] Figure 7: Panel A is a schematic showing the structure of the nucleic acid and competitor used in the reflex process; Panel B is a polyacrylamide gel showing the nucleic acid species produced in the reflex process described in Example 1.

[0012] Figure 8 shows a flow chart of a reflex process (left) in which the T7 exonuclease step is optional. The gel on the right shows the resultant product of the reflex process either without the T7 exonuclease step (lane 1) or with the T7 exonuclease step (lane 2).

[0013] Figure 9 shows an exemplary reflex process workflow with indications on the right as to where purification of reaction products is employed (e.g., using Agencourt beads to remove primer oligos).

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[0014] Figure 10 shows the starting material (left panel) and the resultant product generated (right panel) using a reflex process without using a T7 exonuclease step (as described in Example II). The reflex site in the starting material is a sequence normally present in the polynucleotide being processed (also called a "non-artificial" reflex site). This figure shows that the 755 base pair starting nucleic acid was processed to the expected 461 base pair product, thus confirming that a "non-artificial" reflex site is effective in transferring an adapter domain from one location to another in a polynucleotide of interest in a sequence specific manner.

[0015] Figure 11 shows a schematic and results of an experiment in which the reflex process is performed on a single large initial template (a "parent" fragment) to generate five different products ("daughter" products) each having a different region of interest (i.e., daughter products are produced having either region 1, 2, 3, 4 or 5).

[0016] Figure 12 shows a schematic and results of experiments performed to determine the prevalence of intramolecular rearrangement during the reflex process (as desired) vs. intermolecular rearrangement (MID switching).

[0017] Figure 13 shows a diagram of exemplary workflows for preparing material for and performing the reflex process.

DEFINITIONS

[0018] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Still, certain elements are defined for the sake of clarity and ease of reference.

[0019] Terms and symbols of nucleic acid chemistry, biochemistry, genetics, and molecular biology used herein follow those of standard treatises and texts in the field, e.g. Kornberg and Baker, DNA Replication, Second Edition (W.H. Freeman, New York, 1992); Lehninger, Biochemistry, Second Edition (Worth Publishers, New York, 1975); Strachan and Read, Human Molecular Genetics, Second Edition (Wiley-Liss, New York, 1999); Eckstein, editor, Oligonucleotides and Analogs: A Practical Approach (Oxford University Press, New York, 1991); Gait, editor, Oligonucleotide Synthesis: A Practical Approach (IRL Press, Oxford, 1984); and the like.

[0020] "Amplicon" means the product of a polynucleotide amplification reaction. That is, it is a population of polynucleotides, usually double stranded, that are replicated from one or more starting sequences. The one or more starting sequences may be one or more copies of

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the same sequence, or it may be a mixture of different sequences. Amplicons may be produced by a variety of amplification reactions whose products are multiple replicates of one or more target nucleic acids. Generally, amplification reactions producing amplicons are "template-driven" in that base pairing of reactants, either nucleotides or oligonucleotides, have complements in a template polynucleotide that are required for the creation of reaction products. In one aspect, template-driven reactions are primer extensions with a nucleic acid polymerase or oligonucleotide ligations with a nucleic acid ligase. Such reactions include, but are not limited to, polymerase chain reactions (PCRs), linear polymerase reactions, nucleic acid sequence-based amplification (NASBAs), rolling circle amplifications, and the like, disclosed in the following references that are incorporated herein by reference: Mullis et al, U.S. patents 4,683,195; 4,965,188; 4,683,202; 4,800,159 (PCR); Gelfand et al, U.S. patent 5,210,015 (real-time PCR with "TAQMAN™" probes); Wittwer et al, U.S. patent 6,174,670; Kacian et al, U.S. patent 5,399,491 ("NASBA"); Lizardi, U.S. patent 5,854,033; Aono et al, Japanese patent publ. JP 4-262799 (rolling circle amplification); and the like. In one aspect, amplicons of the invention are produced by PCRs. An amplification reaction may be a "real-time" amplification if a detection chemistry is available that permits a reaction product to be measured as the amplification reaction progresses, e.g. "real-time PCR" described below, or "real-time NASBA" as described in Leone et al, Nucleic Acids Research, 26: 2150-2155 (1998), and like references. As used herein, the term "amplifying" means performing an amplification reaction. A "reaction mixture" means a solution containing all the necessary reactants for performing a reaction, which may include, but not be limited to, buffering agents to maintain pH at a selected level during a reaction, salts, co-factors, scavengers, and the like.

[0021] The term "assessing" includes any form of measurement, and includes determining if an element is present or not. The terms "determining", "measuring", "evaluating", "assessing" and "assaying" are used interchangeably and includes quantitative and qualitative determinations. Assessing may be relative or absolute. "Assessing the presence of" includes determining the amount of something present, and/or determining whether it is present or absent. As used herein, the terms "determining," "measuring," and "assessing," and "assaying" are used interchangeably and include both quantitative and qualitative determinations.

[0022] Polynucleotides that are "asymmetrically tagged" have left and right adapter domains that are not identical. This process is referred to generically as attaching adapters asymmetrically or asymmetrically tagging a polynucleotide, e.g., a polynucleotide fragment.

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Production of polynucleotides having asymmetric adapter termini may be achieved in any convenient manner. Exemplary asymmetric adapters are described in: U.S. Patents 5,712,126 and 6,372,434; U.S. Patent Publications 2007/0128624 and 2007/0172839; and PCT publication WO/2009/032167; all of which are incorporated by reference herein in their entirety. In certain embodiments, the asymmetric adapters employed are those described in U.S. Patent Application Ser. No. 12/432,080, filed on April 29, 2009, incorporated herein by reference in its entirety.

[0023] As one example, a user of the subject invention may use an asymmetric adapter to tag polynucleotides. An "asymmetric adapter" is one that, when ligated to both ends of a double stranded nucleic acid fragment, will lead to the production of primer extension or amplification products that have non-identical sequences flanking the genomic insert of interest. The ligation is usually followed by subsequent processing steps so as to generate the non-identical terminal adapter sequences. For example, replication of an asymmetric adapter attached fragment(s) results in polynucleotide products in which there is at least one nucleic acid sequence difference, or nucleotide/nucleoside modification, between the terminal adapter sequences. Attaching adapters asymmetrically to polynucleotides (e.g., polynucleotide fragments) results in polynucleotides that have one or more adapter sequences on one end (e.g., one or more region or domain, e.g., a primer site) that are either not present or have a different nucleic acid sequence as compared to the adapter sequence on the other end. It is noted that an adapter that is termed an "asymmetric adapter" is not necessarily itself structurally asymmetric, nor does the mere act of attaching an asymmetric adapter to a polynucleotide fragment render it immediately asymmetric. Rather, an asymmetric adapter-attached polynucleotide, which has an identical asymmetric adapter at each end, produces replication products (or isolated single stranded polynucleotides) that are asymmetric with respect to the adapter sequences on opposite ends (e.g., after at least one round of amplification/primer extension).

[0024] Any convenient asymmetric adapter, or process for attaching adapters asymmetrically, may be employed in practicing the present invention. Exemplary asymmetric adapters are described in: U.S. Patents 5,712,126 and 6,372,434; U.S. Patent Publications 2007/0128624 and 2007/0172839; and PCT publication WO/2009/032167; all of which are incorporated by reference herein in their entirety. In certain embodiments, the asymmetric adapters employed are those described in U.S. Patent Application Ser. No. 12/432,080, filed on April 29, 2009, incorporated herein by reference in its entirety.

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[0025] "Complementary" or "substantially complementary" refers to the hybridization or base pairing or the formation of a duplex between nucleotides or nucleic acids, such as, for instance, between the two strands of a double stranded DNA molecule or between an oligonucleotide primer and a primer site on a single stranded nucleic acid. Complementary nucleotides are, generally, A and T (or A and U), or C and G. Two single stranded RNA or DNA molecules are said to be substantially complementary when the nucleotides of one strand, optimally aligned and compared and with appropriate nucleotide insertions or deletions, pair with at least about 80% of the nucleotides of the other strand, usually at least about 90% to 95%, and more preferably from about 98 to 100%. Alternatively, substantial complementarity exists when an RNA or DNA strand will hybridize under selective hybridization conditions to its complement. Typically, selective hybridization will occur when there is at least about 65% complementary over a stretch of at least 14 to 25 nucleotides, preferably at least about 75%, more preferably at least about 90% complementary. See, M. Kanehisa Nucleic Acids Res. 12:203 (1984), incorporated herein by reference.

[0026] "Duplex" means at least two oligonucleotides and/or polynucleotides that are fully or partially complementary undergo Watson-Crick type base pairing among all or most of their nucleotides so that a stable complex is formed. The terms "annealing" and "hybridization" are used interchangeably to mean the formation of a stable duplex. "Perfectly matched" in reference to a duplex means that the poly- or oligonucleotide strands making up the duplex form a double stranded structure with one another such that every nucleotide in each strand undergoes Watson-Crick base pairing with a nucleotide in the other strand. A stable duplex can include Watson-Crick base pairing and/or non-Watson-Crick base pairing between the strands of the duplex (where base pairing means the forming hydrogen bonds). In certain embodiments, a non-Watson-Crick base pair includes a nucleoside analog, such as deoxyinosine, 2, 6-diaminopurine, PNAs, LNA's and the like. In certain embodiments, a non-Watson-Crick base pair includes a "wobble base", such as deoxyinosine, 8-oxo-dA, 8-oxo-dG and the like, where by "wobble base" is meant a nucleic acid base that can base pair with a first nucleotide base in a complementary nucleic acid strand but that, when employed as a template strand for nucleic acid synthesis, leads to the incorporation of a second, different nucleotide base into the synthesizing strand (wobble bases are described in further detail below). A "mismatch" in a duplex between two oligonucleotides or polynucleotides means that a pair of nucleotides in the duplex fails to undergo Watson-Crick bonding.

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[0027] "Genetic locus," "locus," or "locus of interest" in reference to a genome or target polynucleotide, means a contiguous sub-region or segment of the genome or target polynucleotide. As used herein, genetic locus, locus, or locus of interest may refer to the position of a nucleotide, a gene or a portion of a gene in a genome, including mitochondrial DNA or other non-chromosomal DNA (e.g., bacterial plasmid), or it may refer to any contiguous portion of genomic sequence whether or not it is within, or associated with, a gene. A genetic locus, locus, or locus of interest can be from a single nucleotide to a segment of a few hundred or a few thousand nucleotides in length or more. In general, a locus of interest will have a reference sequence associated with it (see description of "reference sequence" below).

[0028] "Kit" refers to any delivery system for delivering materials or reagents for carrying out a method of the invention. In the context of reaction assays, such delivery systems include systems that allow for the storage, transport, or delivery of reaction reagents (e.g., probes, enzymes, etc. in the appropriate containers) and/or supporting materials (e.g., buffers, written instructions for performing the assay etc.) from one location to another. For example, kits include one or more enclosures (e.g., boxes) containing the relevant reaction reagents and/or supporting materials. Such contents may be delivered to the intended recipient together or separately. For example, a first container may contain an enzyme for use in an assay, while a second container contains probes.

[0029] "Ligation" means to form a covalent bond or linkage between the termini of two or more nucleic acids, e.g. oligonucleotides and/or polynucleotides, in a template-driven reaction. The nature of the bond or linkage may vary widely and the ligation may be carried out enzymatically or chemically. As used herein, ligations are usually carried out enzymatically to form a phosphodiester linkage between a 5' carbon of a terminal nucleotide of one oligonucleotide with 3' carbon of another oligonucleotide. A variety of template-driven ligation reactions are described in the following references, which are incorporated by reference: Whiteley et al, U.S. patent 4,883,750; Letsinger et al, U.S. patent 5,476,930; Fung et al, U.S. patent 5,593,826; Kool, U.S. patent 5,426,180; Landegren et al, U.S. patent 5,871,921; Xu and Kool, Nucleic Acids Research, 27: 875-881 (1999); Higgins et al, Methods in Enzymology, 68: 50-71 (1979); Engler et al, The Enzymes, 15: 3-29 (1982); and Namsaraev, U.S. patent publication 2004/0110213.

[0030] "Multiplex Identifier" (MID) as used herein refers to a tag or combination of tags associated with a polynucleotide whose identity (e.g., the tag DNA sequence) can be used to differentiate polynucleotides in a sample. In certain embodiments, the MID on a

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polynucleotide is used to identify the source from which the polynucleotide is derived. For example, a nucleic acid sample may be a pool of polynucleotides derived from different sources, (e.g., polynucleotides derived from different individuals, different tissues or cells, or polynucleotides isolated at different times points), where the polynucleotides from each different source are tagged with a unique MID. As such, a MID provides a correlation between a polynucleotide and its source. In certain embodiments, MIDs are employed to uniquely tag each individual polynucleotide in a sample. Identification of the number of unique MIDs in a sample can provide a readout of how many individual polynucleotides are present in the sample (or from how many original polynucleotides a manipulated polynucleotide sample was derived; see, e.g., U.S. Patent No. 7,537,897, issued on May 26, 2009, incorporated herein by reference in its entirety). MIDs can range in length from 2 to 100 nucleotide bases or more and may include multiple subunits, where each different MID has a distinct identity and/or order of subunits. Exemplary nucleic acid tags that find use as MIDs are described in U.S. Patent 7,544,473, issued on June 6, 2009, and titled "Nucleic Acid Analysis Using Sequence Tokens", as well as U.S. Patent 7,393,665, issued on July 1, 2008, and titled "Methods and Compositions for Tagging and Identifying Polynucleotides", both of which are incorporated herein by reference in their entirety for their description of nucleic acid tags and their use in identifying polynucleotides. In certain embodiments, a set of MIDs employed to tag a plurality of samples need not have any particular common property (e.g., Tm, length, base composition, etc.), as the methods described herein can accommodate a wide variety of unique MID sets. It is emphasized here that MIDs need only be unique within a given experiment. Thus, the same MID may be used to tag a different sample being processed in a different experiment. In addition, in certain experiments, a user may use the same MID to tag a subset of different samples within the same experiment. For example, all samples derived from individuals having a specific phenotype may be tagged with the same MID, e.g., all samples derived from control (or wildtype) subjects can be tagged with a first MID while subjects having a disease condition can be tagged with a second MID (different than the first MID). As another example, it may be desirable to tag different samples derived from the same source with different MIDs (e.g., samples derived over time or derived from different sites within a tissue). Further, MIDs can be generated in a variety of different ways, e.g., by a combinatorial tagging approach in which one MID is attached by ligation and a second MID is attached by primer extension. Thus, MIDs can be designed and implemented in a variety of different ways to track polynucleotide fragments during processing and analysis, and thus no limitation in this regard is intended.

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[0031] "Nucleoside" as used herein includes the natural nucleosides, including 2'-deoxy and 2'-hydroxyl forms, e.g. as described in Kornberg and Baker, DNA Replication, 2nd Ed. (Freeman, San Francisco, 1992). "Analogs" in reference to nucleosides includes synthetic nucleosides having modified base moieties and/or modified sugar moieties, e.g. described by Scheit, Nucleotide Analogs (John Wiley, New York, 1980); Uhlman and Peyman, Chemical Reviews, 90: 543-584 (1990), or the like, with the proviso that they are capable of specific hybridization. Such analogs include synthetic nucleosides designed to enhance binding properties, reduce complexity, increase specificity, and the like. Polynucleotides comprising analogs with enhanced hybridization or nuclease resistance properties are described in Uhlman and Peyman (cited above); Crooke et al, Exp. Opin. Ther. Patents, 6: 855-870 (1996); Mesmaeker et al, Current Opinion in Structual Biology, 5: 343-355 (1995); and the like. Exemplary types of polynucleotides that are capable of enhancing duplex stability include oligonucleotide N3'→P5' phosphoramidates (referred to herein as "amidates"), peptide nucleic acids (referred to herein as "PNAs"), oligo-2'-O-alkylribonucleotides, polynucleotides containing C-5 propynylpyrimidines, locked nucleic acids ("LNAs"), and like compounds. Such oligonucleotides are either available commercially or may be synthesized using methods described in the literature.

[0032] "Polymerase chain reaction," or "PCR," means a reaction for the in vitro amplification of specific DNA sequences by the simultaneous primer extension of complementary strands of DNA. In other words, PCR is a reaction for making multiple copies or replicates of a target nucleic acid flanked by primer sites, such reaction comprising one or more repetitions of the following steps: (i) denaturing the target nucleic acid, (ii) annealing primers to the primer sites, and (iii) extending the primers by a nucleic acid polymerase in the presence of nucleoside triphosphates. Usually, the reaction is cycled through different temperatures optimized for each step in a thermal cycler instrument. Particular temperatures, durations at each step, and rates of change between steps depend on many factors well-known to those of ordinary skill in the art, e.g. exemplified by the references: McPherson et al, editors, PCR: A Practical Approach and PCR2: A Practical Approach (IRL Press, Oxford, 1991 and 1995, respectively). For example, in a conventional PCR using Taq DNA polymerase, a double stranded target nucleic acid may be denatured at a temperature >90°C, primers annealed at a temperature in the range 50-75°C, and primers extended at a temperature in the range 72-78°C. The term "PCR" encompasses derivative forms of the reaction, including but not limited to, RT-PCR, real-time PCR, nested PCR, quantitative PCR, multiplexed PCR, and the like. Reaction volumes range from a few

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hundred nanoliters, e.g. 200 nL, to a few hundred μL, e.g. 200 μL. "Reverse transcription PCR," or "RT-PCR," means a PCR that is preceded by a reverse transcription reaction that converts a target RNA to a complementary single stranded DNA, which is then amplified, e.g. Tecott et al, U.S. patent 5,168,038, which patent is incorporated herein by reference. "Real-time PCR" means a PCR for which the amount of reaction product, i.e. amplicon, is monitored as the reaction proceeds. There are many forms of real-time PCR that differ mainly in the detection chemistries used for monitoring the reaction product, e.g. Gelfand et al, U.S. patent 5,210,015 ("TAQMAN™"); Wittwer et al, U.S. patents 6,174,670 and 6,569,627 (intercalating dyes); Tyagi et al, U.S. patent 5,925,517 (molecular beacons); which patents are incorporated herein by reference. Detection chemistries for real-time PCR are reviewed in Mackay et al, Nucleic Acids Research, 30: 1292-1305 (2002), which is also incorporated herein by reference. "Nested PCR" means a two-stage PCR wherein the amplicon of a first PCR becomes the sample for a second PCR using a new set of primers, at least one of which binds to an interior location of the first amplicon. As used herein, "initial primers" in reference to a nested amplification reaction mean the primers used to generate a first amplicon, and "secondary primers" mean the one or more primers used to generate a second, or nested, amplicon. "Multiplexed PCR" means a PCR wherein multiple target sequences (or a single target sequence and one or more reference sequences) are simultaneously carried out in the same reaction mixture, e.g. Bernard et al, Anal. Biochem., 273: 221-228 (1999)(two-color real-time PCR). Usually, distinct sets of primers are employed for each sequence being amplified.

[0033] "Quantitative PCR" means a PCR designed to measure the abundance of one or more specific target sequences in a sample or specimen. Quantitative PCR includes both absolute quantitation and relative quantitation of such target sequences. Quantitative measurements are made using one or more reference sequences that may be assayed separately or together with a target sequence. The reference sequence may be endogenous or exogenous to a sample or specimen, and in the latter case, may comprise one or more competitor templates. Typical endogenous reference sequences include segments of transcripts of the following genes: β-actin, GAPDH, β_2-microglobulin, ribosomal RNA, and the like. Techniques for quantitative PCR are well-known to those of ordinary skill in the art, as exemplified in the following references that are incorporated by reference: Freeman et al, Biotechniques, 26: 112-126 (1999); Becker-Andre et al, Nucleic Acids Research, 17: 9437-9447 (1989); Zimmerman et al, Biotechniques, 21: 268-279 (1996); Diviacco et al,

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Gene, 122: 3013-3020 (1992); Becker-Andre et al, Nucleic Acids Research, 17: 9437-9446 (1989); and the like.

[0034] "Polynucleotide" or "oligonucleotide" is used interchangeably and each means a linear polymer of nucleotide monomers. Monomers making up polynucleotides and oligonucleotides are capable of specifically binding to a natural polynucleotide by way of a regular pattern of monomer-to-monomer interactions, such as Watson-Crick type of base pairing, base stacking, Hoogsteen or reverse Hoogsteen types of base pairing, wobble base pairing, or the like. As described in detail below, by "wobble base" is meant a nucleic acid base that can base pair with a first nucleotide base in a complementary nucleic acid strand but that, when employed as a template strand for nucleic acid synthesis, leads to the incorporation of a second, different nucleotide base into the synthesizing strand. Such monomers and their internucleosidic linkages may be naturally occurring or may be analogs thereof, e.g. naturally occurring or non-naturally occurring analogs. Non-naturally occurring analogs may include peptide nucleic acids (PNAs, e.g., as described in U.S. Patent 5,539,082, incorporated herein by reference), locked nucleic acids (LNAs, e.g., as described in U.S. Patent 6,670,461, incorporated herein by reference), phosphorothioate internucleosidic linkages, bases containing linking groups permitting the attachment of labels, such as fluorophores, or haptens, and the like. Whenever the use of an oligonucleotide or polynucleotide requires enzymatic processing, such as extension by a polymerase, ligation by a ligase, or the like, one of ordinary skill would understand that oligonucleotides or polynucleotides in those instances would not contain certain analogs of internucleosidic linkages, sugar moieties, or bases at any or some positions. Polynucleotides typically range in size from a few monomeric units, e.g. 5-40, when they are usually referred to as "oligonucleotides," to several thousand monomeric units. Whenever a polynucleotide or oligonucleotide is represented by a sequence of letters (upper or lower case), such as "ATGCCTG," it will be understood that the nucleotides are in 5'→3' order from left to right and that "A" denotes deoxyadenosine, "C" denotes deoxycytidine, "G" denotes deoxyguanosine, and "T" denotes thymidine, "I" denotes deoxyinosine, "U" denotes uridine, unless otherwise indicated or obvious from context. Unless otherwise noted the terminology and atom numbering conventions will follow those disclosed in Strachan and Read, Human Molecular Genetics 2 (Wiley-Liss, New York, 1999). Usually polynucleotides comprise the four natural nucleosides (e.g. deoxyadenosine, deoxycytidine, deoxyguanosine, deoxythymidine for DNA or their ribose counterparts for RNA) linked by phosphodiester linkages; however, they may also comprise non-natural nucleotide analogs,

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e.g. including modified bases, sugars, or internucleosidic linkages. It is clear to those skilled in the art that where an enzyme has specific oligonucleotide or polynucleotide substrate requirements for activity, e.g. single stranded DNA, RNA/DNA duplex, or the like, then selection of appropriate composition for the oligonucleotide or polynucleotide substrates is well within the knowledge of one of ordinary skill, especially with guidance from treatises, such as Sambrook et al, Molecular Cloning, Second Edition (Cold Spring Harbor Laboratory, New York, 1989), and like references.

[0035] "Primer" means an oligonucleotide, either natural or synthetic, that is capable, upon forming a duplex with a polynucleotide template, of acting as a point of initiation of nucleic acid synthesis and being extended from its 3' end along the template so that an extended duplex is formed. The sequence of nucleotides added during the extension process is determined by the sequence of the template polynucleotide. Usually primers are extended by a DNA polymerase. Primers are generally of a length compatible with their use in synthesis of primer extension products, and are usually are in the range of between 8 to 100 nucleotides in length, such as 10 to 75, 15 to 60, 15 to 40, 18 to 30, 20 to 40, 21 to 50, 22 to 45, 25 to 40, and so on, more typically in the range of between 18-40, 20-35, 21-30 nucleotides long, and any length between the stated ranges. Typical primers can be in the range of between 10-50 nucleotides long, such as 15-45, 18-40, 20-30, 21-25 and so on, and any length between the stated ranges. In some embodiments, the primers are usually not more than about 10, 12, 15, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, or 70 nucleotides in length.

[0036] Primers are usually single-stranded for maximum efficiency in amplification, but may alternatively be double-stranded. If double-stranded, the primer is usually first treated to separate its strands before being used to prepare extension products. This denaturation step is typically affected by heat, but may alternatively be carried out using alkali, followed by neutralization. Thus, a "primer" is complementary to a template, and complexes by hydrogen bonding or hybridization with the template to give a primer/template complex for initiation of synthesis by a polymerase, which is extended by the addition of covalently bonded bases linked at its 3' end complementary to the template in the process of DNA synthesis.

[0037] A "primer pair" as used herein refers to first and second primers having nucleic acid sequence suitable for nucleic acid-based amplification of a target nucleic acid. Such primer pairs generally include a first primer having a sequence that is the same or similar to that of a first portion of a target nucleic acid, and a second primer having a sequence that is complementary to a second portion of a target nucleic acid to provide for amplification of

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the target nucleic acid or a fragment thereof. Reference to "first" and "second" primers herein is arbitrary, unless specifically indicated otherwise. For example, the first primer can be designed as a "forward primer" (which initiates nucleic acid synthesis from a 5' end of the target nucleic acid) or as a "reverse primer" (which initiates nucleic acid synthesis from a 5' end of the extension product produced from synthesis initiated from the forward primer). Likewise, the second primer can be designed as a forward primer or a reverse primer.

[0038] "Primer site" (e.g., a sequencing primer site, and amplification primer site, etc.) as used herein refers to a domain in a polynucleotide that includes the sequence of a primer (e.g., a sequencing primer) and/or the complementary sequence of a primer. When present in single stranded form (e.g., in a single stranded polynucleotide), a primer site can be either the identical sequence of a primer or the complementary sequence of a primer. When present in double stranded form, a primer site contains the sequence of a primer hybridized to the complementary sequence of the primer. Thus, a primer site is a region of a polynucleotide that is either identical to or complementary to the sequence of a primer (when in a single stranded form) or a double stranded region formed between a primer sequence and its complement. Primer sites may be present in an adapter attached to a polynucleotide. The specific orientation of a primer site can be inferred by those of ordinary skill in the art from the structural features of the relevant polynucleotide and/or context in which it is used.

[0039] "Readout" means a parameter, or parameters, which are measured and/or detected that can be converted to a number or value. In some contexts, readout may refer to an actual numerical representation of such collected or recorded data. For example, a readout of fluorescent intensity signals from a microarray is the address and fluorescence intensity of a signal being generated at each hybridization site of the microarray; thus, such a readout may be registered or stored in various ways, for example, as an image of the microarray, as a table of numbers, or the like.

[0040] "Reflex site", "reflex sequence" and equivalents are used to indicate sequences in a polynucleotide that are employed to move a domain intramolecularly from its initial location to a different location in the polynucleotide. The sequence of a reflex site can be added to a polynucleotide of interest (e.g., present in an adapter ligated to the polynucleotide), be based on a sequence naturally present within the polynucleotide of interest (e.g., a genomic sequence in the polynucleotide), or a combination of both. The reflex sequence is chosen so as to be distinct from other sequences in the polynucleotide (i.e., with little sequence homology to other sequences likely to be present in the polynucleotide, e.g., genomic or sub-genomic sequences to be processed). As such, a reflex sequence should be selected so as to

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not hybridize to any sequence except its complement under the conditions employed in the reflex processes herein described. As described later in this application, the complement to the reflex sequence is inserted on the same strand of the polynucleotide (e.g., the same strand of a double-stranded polynucleotide or on the same single stranded polynucleotide) in a particular location so as to facilitate an intramolecular binding event on such particular strand. Reflex sequences employed in the reflex process described herein can thus have a wide range of lengths and sequences. Reflex sequences may range from 5 to 200 nucleotide bases in length.

[0041] "Solid support", "support", and "solid phase support" are used interchangeably and refer to a material or group of materials having a rigid or semi-rigid surface or surfaces. In many embodiments, at least one surface of the solid support will be substantially flat, although in some embodiments it may be desirable to physically separate synthesis regions for different compounds with, for example, wells, raised regions, pins, etched trenches, or the like. According to other embodiments, the solid support(s) will take the form of beads, resins, gels, microspheres, or other geometric configurations. Microarrays usually comprise at least one planar solid phase support, such as a glass microscope slide.

[0042] "Specific" or "specificity" in reference to the binding of one molecule to another molecule, such as a labeled target sequence for a probe, means the recognition, contact, and formation of a stable complex between the two molecules, together with substantially less recognition, contact, or complex formation of that molecule with other molecules. In one aspect, "specific" in reference to the binding of a first molecule to a second molecule means that to the extent the first molecule recognizes and forms a complex with another molecule in a reaction or sample, it forms the largest number of the complexes with the second molecule. Preferably, this largest number is at least fifty percent. Generally, molecules involved in a specific binding event have areas on their surfaces or in cavities giving rise to specific recognition between the molecules binding to each other. Examples of specific binding include antibody-antigen interactions, enzyme-substrate interactions, formation of duplexes or triplexes among polynucleotides and/or oligonucleotides, biotin-avidin or biotin-streptavidin interactions, receptor-ligand interactions, and the like. As used herein, "contact" in reference to specificity or specific binding means two molecules are close enough that weak noncovalent chemical interactions, such as Van der Waal forces, hydrogen bonding, base-stacking interactions, ionic and hydrophobic interactions, and the like, dominate the interaction of the molecules.

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[0043] As used herein, the term "T_m" is used in reference to the "melting temperature." The melting temperature is the temperature (e.g., as measured in °C) at which a population of double-stranded nucleic acid molecules becomes half dissociated into single strands. Several equations for calculating the T_m of nucleic acids are known in the art (see e.g., Anderson and Young, Quantitative Filter Hybridization, in Nucleic Acid Hybridization (1985). Other references (e.g., Allawi, H.T. & SantaLucia, J., Jr., Biochemistry 36, 10581-94 (1997)) include alternative methods of computation which take structural and environmental, as well as sequence characteristics into account for the calculation of T_m.

[0044] "Sample" means a quantity of material from a biological, environmental, medical, or patient source in which detection, measurement, or labeling of target nucleic acids is sought. On the one hand it is meant to include a specimen or culture (e.g., microbiological cultures). On the other hand, it is meant to include both biological and environmental samples. A sample may include a specimen of synthetic origin. Biological samples may be animal, including human, fluid, solid (e.g., stool) or tissue, as well as liquid and solid food and feed products and ingredients such as dairy items, vegetables, meat and meat by-products, and waste. Biological samples may include materials taken from a patient including, but not limited to cultures, blood, saliva, cerebral spinal fluid, pleural fluid, milk, lymph, sputum, semen, needle aspirates, and the like. Biological samples may be obtained from all of the various families of domestic animals, as well as feral or wild animals, including, but not limited to, such animals as ungulates, bear, fish, rodents, etc. Environmental samples include environmental material such as surface matter, soil, water and industrial samples, as well as samples obtained from food and dairy processing instruments, apparatus, equipment, utensils, disposable and non-disposable items. These examples are not to be construed as limiting the sample types applicable to the present invention.

[0045] The terms "upstream" and "downstream" in describing nucleic acid molecule orientation and/or polymerization are used herein as understood by one of skill in the art. As such, "downstream" generally means proceeding in the 5' to 3' direction, i.e., the direction in which a nucleotide polymerase normally extends a sequence, and "upstream" generally means the converse. For example, a first primer that hybridizes "upstream" of a second primer on the same target nucleic acid molecule is located on the 5' side of the second primer (and thus nucleic acid polymerization from the first primer proceeds towards the second primer).

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[0046] It is further noted that the claims may be drafted to exclude any optional element. As such, this statement is intended to serve as antecedent basis for use of such exclusive terminology as "solely", "only" and the like in connection with the recitation of claim elements, or the use of a "negative" limitation.

DETAILED DESCRIPTION OF THE INVENTION

[0047] The invention is drawn to compositions and methods for intramolecular nucleic acid rearrangement that find use in various applications of genetic analysis, including sequencing, as well as general molecular biological manipulations of polynucleotide structures.

[0048] Before the present invention is described, it is to be understood that this invention is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0049] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limits of that range is also specifically disclosed. Each smaller range between any stated value or intervening value in a stated range and any other stated or intervening value in that stated range is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included or excluded in the range, and each range where either, neither or both limits are included in the smaller ranges is also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

[0050] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, some potential and preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited. It is understood that the present disclosure supersedes any disclosure of an incorporated publication to the extent there is a contradiction.

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[0051] It must be noted that as used herein and in the appended claims, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a nucleic acid" includes a plurality of such nucleic acids and reference to "the compound" includes reference to one or more compounds and equivalents thereof known to those skilled in the art, and so forth.

[0052] The practice of the present invention may employ, unless otherwise indicated, conventional techniques and descriptions of organic chemistry, polymer technology, molecular biology (including recombinant techniques), cell biology, biochemistry, and immunology, which are within the skill of the art. Such conventional techniques include polymer array synthesis, hybridization, ligation, and detection of hybridization using a label. Specific illustrations of suitable techniques can be had by reference to the example herein below. However, other equivalent conventional procedures can, of course, also be used. Such conventional techniques and descriptions can be found in standard laboratory manuals such as *Genome Analysis: A Laboratory Manual Series* (Vols. I-IV), *Using Antibodies: A Laboratory Manual, Cells: A Laboratory Manual, PCR Primer: A Laboratory Manual, and Molecular Cloning: A Laboratory Manual* (all from Cold Spring Harbor Laboratory Press), Stryer, L. (1995) *Biochemistry* (4th Ed.) Freeman, New York, Gait, "*Oligonucleotide Synthesis: A Practical Approach*" 1984, IRL Press, London, Nelson and Cox (2000), Lehninger, A., *Principles of Biochemistry* 3rd Ed., W. H. Freeman Pub., New York, N.Y. and Berg et al. (2002) *Biochemistry,* 5th Ed., W. H. Freeman Pub., New York, N.Y., all of which are herein incorporated in their entirety by reference for all purposes.

[0053] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates which may need to be independently confirmed.

[0054] As summarized above, aspects of the present invention are drawn to the use of a 'reflex' sequence present in a polynucleotide (e.g., in an adapter structure of the polynucleotide, in a genomic region of the polynucleotide, or a combination of both) to move a domain of the polynucleotide intra-molecularly from a first location to a second location. The reflex process described herein finds use in any number of applications, e.g., placing functional elements of a polynucleotide (e.g., sequencing primer sites and/or MID tags) into proximity to a desired sub-region of interest.

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Nucleic Acids

[0055] The reflex process (as described in detail below) can be employed for the manipulation and analysis of nucleic acid sequences of interest from virtually any nucleic acid source, including but not limited to genomic DNA, complementary DNA (cDNA), RNA (e.g., messenger RNA, ribosomal RNA, short interfering RNA, microRNA, etc.), plasmid DNA, mitochondrial DNA, synthetic DNA, etc. Furthermore, any organism, organic material or nucleic acid-containing substance can be used as a source of nucleic acids to be processed in accordance with the present invention including, but not limited to, plants, animals (e.g., reptiles, mammals, insects, worms, fish, etc.), tissue samples, bacteria, fungi (e.g., yeast), phage, viruses, cadaveric tissue, archaeological/ancient samples, etc. In certain embodiments, the nucleic acids in the nucleic acid sample are derived from a mammal, where in certain embodiments the mammal is a human.

[0056] In certain embodiments, the nucleic acid sequences are enriched prior to the reflex sequence process. By enriched is meant that the nucleic acid is subjected to a process that reduces the complexity of the nucleic acids, generally by increasing the relative concentration of particular nucleic acid species in the sample (e.g., having a specific locus of interest, including a specific nucleic acid sequence, lacking a locus or sequence, being within a specific size range, etc.). There are a wide variety of ways to enrich nucleic acids having a specific characteristic(s) or sequence, and as such any convenient method to accomplish this may be employed. The enrichment (or complexity reduction) can take place at any of a number of steps in the process, and will be determined by the desires of the user. For example, enrichment can take place in individual parental samples (e.g., untagged nucleic acids prior to adaptor ligation) or in multiplexed samples (e.g., nucleic acids tagged with primer sites, MID and/or reflex sequences and pooled; MID are described in further detail below).

[0057] In certain embodiments, nucleic acids in the nucleic acid sample are amplified prior to analysis. In certain of these embodiments, the amplification reaction also serves to enrich a starting nucleic acid sample for a sequence or locus of interest. For example, a starting nucleic acid sample can be subjected to a polymerase chain reaction (PCR) that amplifies one or more region of interest. In certain embodiments, the amplification reaction is an exponential amplification reaction, whereas in certain other embodiments, the amplification reaction is a linear amplification reaction. Any convenient method for performing amplification reactions on a starting nucleic acid sample can be used in practicing the subject invention. In certain embodiments, the nucleic acid polymerase employed in the

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amplification reaction is a polymerase that has proofreading capability (e.g., phi29 DNA Polymerase, Thermococcus litoralis DNA polymerase, Pyrococcus furiosus DNA polymerase, etc.).

[0058] In certain embodiments, the nucleic acid sample being analyzed is derived from a single source (e.g., a single organism, virus, tissue, cell, subject, etc.), whereas in other embodiments, the nucleic acid sample is a pool of nucleic acids extracted from a plurality of sources (e.g., a pool of nucleic acids from a plurality of organisms, tissues, cells, subjects, etc.), where by "plurality" is meant two or more. As such, in certain embodiments, a nucleic acid sample can contain nucleic acids from 2 or more sources, 3 or more sources, 5 or more sources, 10 or more sources, 50 or more sources, 100 or more sources, 500 or more sources, 1000 or more sources, 5000 or more sources, up to and including about 10,000 or more sources.

[0059] In certain embodiments, nucleic acid fragments that are to be pooled with nucleic acid fragments derived from a plurality of sources (e.g., a plurality of organisms, tissues, cells, subjects, etc.), where by "plurality" is meant two or more. In such embodiments, the nucleic acids derived from each source includes a multiplex identifier (MID) such that the source from which the each tagged nucleic acid fragment was derived can be determined. In such embodiments, each nucleic acid sample source is correlated with a unique MID, where by unique MID is meant that each different MID employed can be differentiated from every other MID employed by virtue of at least one characteristic, e.g., the nucleic acid sequence of the MID. Any type of MID can be used, including but not limited to those described in co-pending U.S. Patent Application Serial Number 11/656,746, filed on January 22, 2007, and titled "Nucleic Acid Analysis Using Sequence Tokens", as well as U.S. Patent 7,393,665, issued on July 1, 2008, and titled "Methods and Compositions for Tagging and Identifying Polynucleotides", both of which are incorporated herein by reference in their entirety for their description of nucleic acid tags and their use in identifying polynucleotides. In certain embodiments, a set of MIDs employed to tag a plurality of samples need not have any particular common property (e.g., T_m, length, base composition, etc.), as the asymmetric tagging methods (and many tag readout methods, including but not limited to sequencing of the tag or measuring the length of the tag) can accommodate a wide variety of unique MID sets.

[0060] In certain embodiments, each individual polynucleotide (e.g., double-stranded or single-stranded, as appropriate to the methodological details employed) in a sample to be analyzed is tagged with a unique MID so that the fate of each polynucleotide can be tracked

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in subsequent processes (where, as noted above, unique MID is meant to indicate that each different MID employed can be differentiated from every other MID employed by virtue of at least one characteristic, e.g., the nucleic acid sequence of the MID). For example (and as described below), having each nucleic acid tagged with a unique MID allows analysis of the sequence of each individual nucleic acid using the reflex sequence methods described herein. This allows the linkage of sequence information for large nucleic acid fragments that cannot be sequenced in a single sequencing run.

Reflex Sequence Process

[0061] As summarized above, aspects of the present invention include methods and compositions for moving a domain in a polynucleotide from a first location to a second location in the polynucleotide. An exemplary embodiment is shown in Figure 1A.

[0062] Figure 1A shows a single stranded polynucleotide 100 comprising, in a 5' to 3' orientation, a first domain (102; the domain to be moved); a reflex sequence 104; a nucleic acid sequence 106 having a site distal to the first domain (Site A), and a complement of the reflex sequence 108 (positioned at the 3' terminus of the polynucleotide). The steps of the reflex method described below will move the first domain into closer proximity to Site A. It is noted here that the prime designation in Figure 1A denotes a complementary sequence of a domain. For example, First Domain' is the complement of the First Domain.

[0063] In Step 1, the reflex sequence and its complement in the polynucleotide are annealed intramolecularly to form polynucleotide structure 112, with the polynucleotide folding back on itself and hybridizing to form a region of complementarity (i.e., double stranded reflex/reflex' region). In this configuration, the 3' end of the complement of the reflex sequence can serve as a nucleic acid synthesis priming site. Nucleic acid synthesis from this site is then performed in extension Step 2 producing a complement of the first domain at the 3' end of the nucleic acid extension (shown in polynucleotide 114; extension is indicated with dotted arrow labeled "extend").

[0064] Denaturation of polynucleotide 114 (e.g., by heat) generates linear single stranded polynucleotide 116. As shown in Figure 1, resultant polynucleotide 116 contains a complement of the first domain at a position proximal to Site A (i.e., separated by only the complement of the reflex sequence). This resultant polynucleotide may be used for any subsequent analysis or processing steps as desired by the user (e.g., sequencing, as a template for amplification (linear, PCR, etc.), sequence specific extraction, etc.).

[0065] In alternative embodiments, the first domain and reflex sequence are removed from the 5' end of the double-stranded region of polynucleotide 114 (shown in polynucleotide

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118; removal is shown in the dotted arrow labeled "remove"). Removal of this region may be accomplished by any convenient method, including, but not limited to, treatment (under appropriate incubation conditions) of polynucleotide structure 114 with T7 exonuclease or by treatment with Lambda exonuclease; the Lambda exonuclease can be employed so long as the 5' end of the polynucleotide is phosphorylated. If the region is removed enzymatically, resultant polynucleotide 118 is used in place of polynucleotide 116 in subsequent steps (e.g., copying to reverse polarity).

[0066] In certain embodiments, polynucleotide 116 or 118 is used as a template to produce a double stranded polynucleotide, for example by performing a nucleic acid synthesis reaction with a primer that primes in the complement of the first domain. This step is sometimes referred to as copying to reverse polarity of a single stranded polynucleotide, and in some instances, the double-stranded intermediate product of this copying is not shown (see, e.g., Figure 3). For example, copying to reverse the polarity of polynucleotide 116 results in single-stranded polynucleotide 120 having, in a 5' to 3' orientation, the first domain (122); the reflex sequence (124); the complement of polynucleotide 106 (oriented with the complement of Site A (Site A'; 126) proximal to the reflex sequence); the complement of the reflex sequence (128); and the complement of the first domain (130).

[0067] In certain embodiments, the first domain in the polynucleotide comprises one or more elements that find use in one or more subsequent processing or analysis steps. Such sequences include, but are not limited to, restriction enzyme sites, PCR primer sites, linear amplification primer sites, reverse transcription primer sites, RNA polymerase promoter sites (such as for T7, T3 or SP6 RNA polymerase), MID tags, sequencing primer sites, etc. Any convenient element can be included in the first domain and, in certain embodiments, is determined by the desires of the user of the methods described herein.

[0068] As an exemplary embodiment, suppose we want to sequence a specific polynucleotide region from multiple genomes in a pooled sample where the polynucleotide region is too long to sequence in a single reaction. For example, sequencing a polynucleotide region that is 2 kilobases or more in length using Roche 454 (Branford, CT) technology, in which the length of a single sequencing run is about 400 bases. In this scenario, we can design a set of left hand primers (A_n) and right hand primers (B_n) specific for the polynucleotide region that are positioned in such a way that we can obtain direct sequences of all parts of the insert, as shown in Figure 1B. Note that the polynucleotide shown in Figure 1B (140) has a domain (142) containing a primer site and an MID denoting from which original sample(s) the polynucleotide is derived. Site 142 thus represents an

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example of a First Domain site such identified as 122 in the Figure 1A. The polynucleotide also includes a reflex site (144), which can be part of the polynucleotide region itself (e.g., a genomic sequence), added in a ligated adapter domain along with the primer site and the MID (an artificial sequence), or a combination of both (a sequence spanning the adapter/polynucleotide junction).

[0069] It is noted here that polynucleotide 140 can be categorized as a precursor to polynucleotide 100 in Figure 1A, as it does not include a 3' reflex sequence complementary to the reflex site (domain 108 in Figure 1A). As detailed below, polynucleotide 140 can be converted to a polynucleotide having the structural configuration of polynucleotide 100, a polynucleotide suitable as a substrate for the reflex process described herein (e.g., by primer extension using a B_n primer and reversal of polarity).

[0070] In an exemplary embodiment, each A_n-B_n primer pair defines a nucleic acid region that is approximately 400 bases in length or less. This size range is within the single-sequencing run read length of the current Roche 454 sequencing platform; a different size range for the defined nucleic acid region may be utilized for a different sequencing platform. Thus, each product from each reflex process can be sequenced in a single run. It is noted here that primer pairs as shown in Figure 1B can be used to define regions 1 to 5 shown in Figure 3 (described in further detail below).

[0071] In certain embodiments, to obtain the first part of the sequence of the polynucleotide region (i.e., in the original structure, that part of the polynucleotide closest to the first domain), we only need a right hand primer (e.g., B_0) and we do not need to transfer the MID as it is within reach of this sequencing primer (i.e., the MID is within 400 bases of sequencing primer B_0). All other B_n primers have the reflex sequence added to their 5' ends ("R" element shown on B primers) so that they read 5' reflex-B_n. However, in certain embodiments, the B_0 primer does include the reflex sequence and is used in the reflex process (along with a corresponding A_0 primer) as detailed below.

[0072] As described above, we obtain a single stranded polynucleotide having, in the 5' to 3' orientation, a primer site (e.g., for Roche 454 sequencing), an MID, a reflex sequence and the polynucleotide to be sequenced. Numerous methods for obtaining single-stranded polynucleotides of interest have been described and are known in the art, including in U.S. Patent 7,217,522, issued on May 15, 2007; U.S. Patent Application 11/377,462, filed on March 16, 2006; and U.S. Patent Application 12/432,080, filed on April 29, 2009; each of which is incorporated by reference herein in their entirety. For example, a single stranded product can be produced using linear amplification with a primer specific for the primer site

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of the template. In certain embodiments, the primer includes a binding moiety to facilitate isolation of the single stranded nucleic acid of interest, e.g., to immobilize the top strand on a binding partner of the binding moiety immobilized on a solid support. Removal of a hybridized, non-biotinylated strand by denaturation using heat or high pH (or any other convenient method) serves to isolate the biotinylated strand. Binding moieties and their corresponding binding partners are sometimes referred to herein as binding partner pairs. Any convenient binding partner pairs may be used, including but not limited to biotin/avidin (or streptavidin), antigen/antibody pairs, etc.

[0073] It is noted here that while the figures and description of the reflex process provided herein depict manipulations with regard to a single stranded polynucleotide, it is not necessarily required that the single stranded polynucleotide described or depicted in the figures be present in the sample in an isolated form (i.e., isolated from its complementary strand). In other words, double stranded polynucleotides may be used where only one strand is described/depicted, which will generally be determined by the user.

[0074] The implementation of a single strand isolation step using the methods described above or variations thereof (or any other convenient single strand isolation step) will generally be based on the desires of the user. One example of isolating single stranded polynucleotides is shown in Figure 2. In this Figure, a starting double stranded template (with 5' to 3' orientation shown as an arrow) is denatured and primed with a biotinylated synthesis primer specific for the primer site. After extension of the primer (i.e., nucleic acid synthesis), the sample is contacted with a solid support having streptavidin bound to it. The biotin moiety (i.e., the binding partner of streptavidin) on the extended strands will bind to the solid-phase streptavidin. Denaturation and washing is then performed to remove all non-biotinylated polynucleotide strands. If desired, the bound polynucleotide, which can be used in subsequent reflex process steps (e.g., as a template for B_n primer extension reactions), may be eluted from the streptavidin support. Alternatively, the bound polynucleotide may be employed in subsequent steps of the desired process while still bound to the solid support (e.g., in solid phase extension reactions using B_n primers). This process, with minor variations depending on the template being used and the identity of the desired single stranded polynucleotide, may be employed at any of a number of steps in which a single stranded product is to be isolated. It is noted that in certain embodiments, substrate bound biotinylated polynucleotide can be used to produce and isolate non-biotinylated single stranded products (i.e., by eluting the non-biotinylated products while leaving the biotinylated templates bound to the streptavidin on the solid support). Thus, the specifics of

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how binding partners are used to isolate single stranded polynucleotides of interest will vary depending on experimental design parameters.

Additional single-stranded isolation/production methods include asymmetric PCR, strand-specific enzymatic degradation, and the use of in-vitro transcription followed by reverse transcriptase (IVT-RT) with subsequent destruction of the RNA strand. As noted above, any convenient single stranded production/isolation method may be employed.

[0075] To the single stranded polynucleotide shown in Figure 1B we anneal one of the B_n primers having the appended reflex sequence, denoted with a capital "R" (e.g., B_1) and extend the primer under nucleic acid synthesis conditions to produce a copy of the polynucleotide that has a reflex sequence at its 5' end. A single stranded copy of this polynucleotide is then produced to reverse polarity using a primer specific for the primer site in the first domain' (complement of the first domain 102). The resulting nucleic acid has structure 100 shown in Figure 1A, where the first domain 102 includes the primer site and the MID. Site A (110) in Figure 1 is determined by the specificity of the 5' reflex-B_n primer used.

[0076] The reflex process (e.g., as shown in Figure 1) is then performed to produce a product in which the primer site and the MID are now in close proximity to the desired site (or region of interest (ROI)) within the original polynucleotide (i.e., the site defined by the primer used, e.g., B_1). The resulting polynucleotide can be used in subsequent analyses as desired by the user (e.g., Roche 454 sequencing technology).

[0077] It is noted here that, while not shown in Figure 1A and 1B, any convenient method for adding adapters to a polynucleotide to be processed as described herein may be used in the practice of the reflex process (adapters containing, e.g., primer sites, polymerase sites, MIDs, restriction enzyme sites, and reflex sequences). For example, adapters can be added at a particular position by ligation. For double stranded polynucleotides, an adapter can be configured to be ligated to a particular restriction enzyme cut site. Where a single stranded polynucleotide is employed, a double stranded adapter construct that possesses an overhang configured to bind to the end of the single-stranded polynucleotide can be used. For example, in the latter case, the end of a single stranded polynucleotide can be modified to include specific nucleotide bases that are complementary to the overhang in the double stranded adaptor using terminal transferase and specific nucleotides. In other embodiments, PCR or linear amplification methods using adapter-conjugated primers is employed to add an adapter at a site of interest. Again, any convenient method for producing a starting polynucleotide may be employed in practicing the methods of the subject invention.

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[0078] In certain embodiments, the nucleic acid may be sequenced directly using a sequencing primer specific for the primer site. This sequencing reaction will read through the MID and desired site in the insert.

[0079] In certain embodiments, the polynucleotide may be isolated (or fractionated) using an appropriate A_n primer (e.g., when using B_1 as the first primer, primer A_1 can be used). In certain embodiments, the A_n primed polynucleotide is subjected to nucleic acid synthesis conditions to produce a copy of the fragment produced in the reflex process. In certain of these embodiments, the A_n primer has appended on its 5' end a primer site that can be used in subsequent steps, including sequencing reactions. Providing a primer site in the A_n primer allows amplifying and/or sequencing from both ends of the resultant fragment: from the primer site in the first domain 102 and the primer site in the A_n primer (not shown in Figure 1B). Because of the position of the primer sites and their distance apart (i.e., less than one sequencing run apart), sequencing from both ends will usually capture the sequence of the desired site (or ROI) and the sequence of the MID, which can be used for subsequent bioinformatic analyses, e.g., to positively identify the sample of origin. It is noted here that while sequencing in both directions is possible, it is not necessary, as sequencing from either primer site alone will capture the sequence of the ROI as well as its corresponding MID sequence.

[0080] Note that in certain embodiments, the first fragment obtained by amplification/extension from primer B_0 directly, the polarity of the ROI in the resulting fragment is reversed as compared to the ROI in fragments obtained by primers B_1-B_n. This is because the B_0-generated fragment, unlike the B_1-B_n generated fragments, has not been subjected to a reflex process which reverses the orientation of the ROI sequence with respect to the first domain/reflex sequence (as described above). Therefore, the B_0 primer may have appended to it a primer site (e.g., at its 5' end) that can be used for subsequent amplification and/or sequencing reactions (e.g., in Roche 454 sequencing system) rather than a reflex sequence as with primers B_1-B_n. However, in certain embodiments, as noted above, the reflex process may be used with a corresponding B_0-A_0 primer pair as described above, i.e., using a B_0 primer having a 5' reflex sequence and a corresponding A_0 primer with its corresponding 5' adapter domain (e.g., a primer site).

[0081] It is noted here that because the particular sections of sequence to be analyzed are defined by the A_n-B_n primer pairs (as shown and described above), a much higher sequence specificity is achieved as compared to using previous extraction methods that employ only a single oligo binding event (e.g., using probes on a microarray).

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[0082] Figure 3 provides a detailed flow chart for an exemplary embodiment that employs reflex sequences for use in sequencing multiple specific regions in a polynucleotide (i.e., regions 1, 2, 3, 4 and 5 in an 11kb region of lambda DNA).

[0083] A single parent DNA fragment 202 is generated that includes adapter domains (i.e., a Roche 454 sequencing primer site, a single MID, and a reflex sequence) and the sequence of interest. In the example shown, the sequence of interest is from lambda DNA and the reflex sequence is present on the top strand (with its complement shown in the bottom strand). Any convenient method for producing this parent DNA fragment may be used, including amplification with a primer that includes the adapter domains (e.g., using PCR), cloning the fragment into a vector that includes the adapter domains (e.g., a vector with the adapter domains adjacent to a cloning site), or by attaching adapters to polynucleotide fragments (e.g., fragment made by random fragmentation, by sequence-specific restriction enzyme digestion, or combinations thereof). While only a single fragment with a single MID is shown, the steps in Figure 3 are applicable to samples having multiple different fragments each with a different MID, e.g., a sample having a population of homologous fragments from any number of different sources (e.g., different individuals). Figure 3 describes the subsequent enzymatic steps involved in creating the five daughter fragments in which regions 1, 2, 3, 4 and 5 (shown in polynucleotide 204) are rearranged to be placed within a functional distance of the adapter domains (i.e., close enough to the adapter domains to be sequenced in a single Roche 454 sequencing reaction). Note that certain steps are shown for region 4 only (206).

[0084] In step 1, the five regions of interest are defined within the parent fragment (labeled 1 to 5 in polynucleotide 204) and corresponding primer pairs are designed for each. The distance of each region of interest from the reflex sequence is shown below polynucleotide 204. The primer pairs are designed as described and shown in Figure 1B (i.e., the A_n-B_n primer pairs). For clarity, only primer sites for region 4 are shown in Figure 3 ("primer sites" surrounding region 4). In step 2, sequence specific primer extensions are performed (only region 4 is shown) with corresponding B_n primers to produce single stranded polynucleotides having structure 208 (i.e., having the reflex sequence on the 5' terminus). As shown, the B_n primer for region 4 will include a sequence specific primer site that primes at the 3'-most primer site noted for region 4 (where "3'-most" refers to the template strand, which in Figure 3 is the top strand). This polynucleotide is copied back to produce polynucleotide 210 having reversed polarity (e.g., copied using a primer that hybridizes to the 454A' domain). Polynucleotide 210 has structure similar to polynucleotide 100 shown at

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the top of Figure 1. Step 4 depicts the result of the intramolecular priming between the reflex sequence and its complement followed by extension to produce the MID' and 454A' structures at the 3' end (polynucleotide 212). In the embodiments shown in Figure 3, polynucleotide 212 is treated with T7 exonuclease to remove double stranded DNA from the 5' end (as indicated above, this step is optional). The polynucleotide formed for region 4 is shown as 216 with polynucleotides for the other regions also shown (214).

[0085] It is noted here that the formation of each of the polynucleotides 214 may be accomplished either in separate reactions (i.e., structure with region 1 in proximity to the adapter domains is in a first sample, the structure with region 2 in proximity to the adapter region is in a second sample, etc.) or in one or more combined sample.

[0086] In step 6 the polynucleotides 214 are copied to reverse polarity to form polynucleotides 218. In step 7, each of these products are then primed with the second primer of the specific primer pair (see A_n primers as shown in Figure 1B) each having a second Roche 454 primer site (454B) attached at the 5' end, and extended to form products 220. Steps 6 and 7 may be combined (e.g., in a single PCR or other amplification reaction).

[0087] In summary, Figure 3 shows how the reflex process can be employed to produce five daughter fragments 220 of similar length (e.g., ~500 bp) each of which contain DNA sequences that differ in their distance from the reflex sequence in the starting structure 202 while maintaining the original MID.

[0088] Figure 4 shows another exemplary use of the reflex process as described herein. In the embodiment shown in Figure 4, a target sequence (i.e., containing region of interest "E") is enriched from a pool of adapter-attached fragments. In certain embodiments, the fragments are randomly sheared, selected for a certain size range (e.g., DNA having a length from 100 to 5000 base pairs), and tagged with adapters (e.g., asymmetric adapters, e.g., as described in US Patent Application Ser. No. 12/432,080, filed on April 29, 2009). The asymmetric adaptor employed in Figure 4 contains a sequencing primer site (454A, as used in the Roche 454 sequencing platform), an MID, an X sequence, and an internal stem region (ISR), which denotes the region of complementarity for the asymmetric adapter that is adjacent to the adapter attachment site (see, e.g., the description in US Application Ser. No. 12/432,080, filed on April 29, 2009, incorporated herein by reference in its entirety). The X sequence can be any sequence that can serve as a binding site for a polynucleotide containing the complement of the X sequence (similar to a primer site). As described below, the X sequence allows for the annealing of an oligonucleotide having a 5' overhang that can serve as a template for extension of the 3' end of the adaptor oligonucleotide. The

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sequencing direction of the sequencing primer site (454A primer site in structure 401 of Figure 4) is oriented such that amplification of the adapter ligated fragment using the sequencing primer site proceeds away from the ligated genomic insert. This has the effect of making the initial asymmetric adapter ligated library 'inert' to amplification using this primer, e.g., in a PCR reaction.

[0089] To extract a region of interest (the "E" region), the library is mixed with an oligonucleotide (403) containing a 3' X' sequence and a target specific priming sequence (the 1' sequence) under hybridization/annealing conditions. The target specific sequence 1' is designed to flank one side of the region of interest (the 1' sequence adjacent to E in the genomic insert; note that only the E-containing polynucleotide fragment is shown in Figure 4), much like a PCR primer. After annealing primer 403, the hybridized complex is extended, whereby all of the adaptor tagged fragments will obtain the complement of the target specific sequence (i.e., the 1 sequence) on the 3' end (see structure 405; arrows denote the direction of extension).

[0090] Extended products 405 are then denatured and the 1/1' regions allowed to hybridize intramolecularly in a reflex process priming event, after which nucleic acid extension is performed to form structure 407 (extension is from the 1 priming site; shown with an arrow). This reflex reaction creates a product (407) that, unlike its parent structure (405), has a sequencing primer site (454A) that is oriented such the extension using this primer sequence proceeds towards the region of interest. Thus, in the absence of a priming and extension reflex reaction, extension with a sequencing primer will not generate a product containing the region of interest (the E region). In other words, only E-region containing target polynucleotides will have a 454A sequence that can amplify genomic material (structure 407).

[0091] After completing the reflex process (using 1/1' as the reflex sequences), a PCR amplification reaction is performed to amplify the region of interest (with associated adapter domains). However, before performing the PCR reaction, the fragment sample is "inactivated" from further extension using terminal transferase and ddNTPs. This inactivation prevents non-target adaptor tagged molecules from performing primer extension from the 3' primer 1 site. Once inactivated, a PCR reaction is performed using a sequencing primer (i.e., 454A primer 409) and a second primer that primes and extends from the opposite side of the region of interest (i.e., primer 411, which includes a 5' 454B sequencing primer site and a 3' "2" region that primes on the opposite end of E from the 1 region). Only

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fragments that have undergone the reflex process and contain the E region will be suitable templates for the PCR reaction and produce the desired product (413).

[0092] Thus, the process exemplified in Figure 4 allows for the movement of an adapter domain (e.g., containing functional elements and/or MID) into proximity to a desired region of interest.

[0093] The reflex process described herein can be used to perform powerful linkage analysis by combining it with nucleic acid counting methods. Any convenient method for tagging and /or counting individual nucleic acid molecules with unique tags may be employed (see, e.g., U.S. Patent 7,537,897, issued on May 26, 2009; U.S. Patent 7,217,522, issued on May 15, 2007; U.S. Patent Application 11/377,462, filed on March 16, 2006; and U.S. Patent Application 12/432,080, filed on April 29, 2009; each of which is incorporated by reference herein in their). All of this can be conducted in parallel thus saving on the cost of labor, time and materials.

[0094] In one exemplary embodiment, a large collection of sequences is tagged with MID such that each polynucleotide molecule in the sample has a unique MID. In other words, each polynucleotide in the sample (e.g., each individual double stranded or single stranded polynucleotide) is tagged with a MID that is different from every other MID on every other polynucleotide in the sample. In general, to accomplish such molecular tagging the number of distinct MID tags to be used should be many times greater than the actual number of molecules to be analyzed. This will result in the majority of individual nucleic acid molecules being labeled with a unique ID tag (see, e.g., Brenner et al., Proc. Natl. Acad. Sci. USA. 2000 97(4):1665-70). Any sequences that then result from the reflex process on that particular molecule (e.g., as described above) will thus be labeled with the same unique MID tag and thus inherently linked. Note that once all molecules in a sample are individually tagged, they can be manipulated and amplified as much as needed for processing so long as the MID tag is maintained in the products generated.

[0095] For example, we might want to sequence one thousand viral genomes (or a specific genomic region) or one thousand copies of a gene present in somatic cells. After tagging each polynucleotide in the sample with a sequencing primer site, MID and reflex sequence (as shown in the figures and described above), we use the reflex process to break each polynucleotide into lengths appropriate to the sequencing procedure being used, transferring the sequencing primer site and MID to each fragment (as described above). Obtaining sequence information from all of the reflex-processed samples can be used to determine the sequence of each individual polynucleotide in the starting sample, using the MID sequence

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to defining linkage relationships between sequences from different regions in the polynucleotide being sequenced. Using a sequencing platform with longer read lengths can minimize the number of primers to be used (and reflex fragments generated).

[0096] The advantages noted above are shown in Figure 5. This figure shows a comparison of methods for identifying nucleic acid polymorphisms in homologous nucleic acids in a sample (e.g., the same region derived from a chromosomal pair of a diploid cell or viral genomes/transcripts). The top schematic shows two nucleic acid molecules in a sample (1 and 2) having a different assortment of polymorphisms in polymorphic sites A, B and C (A1, B1, C1 and C2). Standard sequencing methods using fragmentation (left side) can identify the polymorphisms in these nucleic acids but do not retain linkage information. Employing the reflex process described herein to identify polymorphisms (right side) maintains linkage information. It is noted that not all domain structures and steps are shown in the reflex process for simplicity.

Kits and Systems

[0097] Also provided by the subject invention are kits and systems for practicing the subject methods, as described above, such vectors configured to add reflex sequences to nucleic acid inserts of interest and regents for performing any steps in the cloning or reflex process described herein (e.g., restriction enzymes, nucleotides, polymerases, primers, exonucleases, etc.). The various components of the kits may be present in separate containers or certain compatible components may be precombined into a single container, as desired.

[0098] The subject systems and kits may also include one or more other reagents for preparing or processing a nucleic acid sample according to the subject methods. The reagents may include one or more matrices, solvents, sample preparation reagents, buffers, desalting reagents, enzymatic reagents, denaturing reagents, where calibration standards such as positive and negative controls may be provided as well. As such, the kits may include one or more containers such as vials or bottles, with each container containing a separate component for carrying out a sample processing or preparing step and/or for carrying out one or more steps of a nucleic acid variant isolation assay according to the present invention.

[0099] In addition to above-mentioned components, the subject kits typically further include instructions for using the components of the kit to practice the subject methods, e.g., to prepare nucleic acid samples for perform the reflex process according to aspects of the subject methods. The instructions for practicing the subject methods are generally recorded on a suitable recording medium. For example, the instructions may be printed on a substrate,

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such as paper or plastic, etc. As such, the instructions may be present in the kits as a package insert, in the labeling of the container of the kit or components thereof (i.e., associated with the packaging or sub-packaging) etc. In other embodiments, the instructions are present as an electronic storage data file present on a suitable computer readable storage medium, e.g. CD-ROM, diskette, etc. In yet other embodiments, the actual instructions are not present in the kit, but means for obtaining the instructions from a remote source, e.g. via the internet, are provided. An example of this embodiment is a kit that includes a web address where the instructions can be viewed and/or from which the instructions can be downloaded. As with the instructions, this means for obtaining the instructions is recorded on a suitable substrate.

[0100] In addition to the subject database, programming and instructions, the kits may also include one or more control samples and reagents, e.g., two or more control samples for use in testing the kit.

Utility

[0101] The reflex process described herein provides significant advantages in numerous applications, a few of which are noted below (as well as described above).

[0102] For example, as described above, certain aspects of the reflex process define the particular sections of sequence to be analyzed by a primer pair, as in PCR (e.g., the two oligos shown as A_n-B_n in Figure 1B). This results in higher sequence specificity as compared to other extraction methods (e.g., using probes on a microarray) that only use a single oligo sequence. The separation of the probes defines a length that can be relatively uniform (hence making subsequent handling including amplification more uniform) and can also be tailored to the particular sequencing platform being employed.

[0103] Further, as described above, aspects of the present invention can be used to analyze homologous genomic locations in a multiplexed sample (i.e., a sample having polynucleotides from different genomic samples) in which the polynucleotides are tagged with the MID. This is possible because the reflex process, which operates intramolecularly, maintains the MID thus linking any particular fragment to the sample from which it originates.

[0104] Finally, as the reflex processes described herein function intramolecularly, one can determine the genetic linkage between different regions on the same large fragment that are too far apart to be sequenced in one sequence read. Such a determination of linkage may be of great value in plant or animal genetics (e.g., to decide if a particular set of variations are linked together on the same stretch of chromosome) or in viral studies (e.g., to determine if

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particular variations are linked together on the same stretch of a viral genome/transcripts, e.g., HIV, hepatitis virus, etc.).

EXAMPLES

Example I

[0105] Figures 6 and 7 provide experimental data and validation of the reflex process described herein using synthetic polynucleotide substrates.

METHODS

Substrate:

[0106] The 100 base oligonucleotide substrate (as shown diagrammatically in Figure 6A) was synthesized with internal fluorescein-dT positioned between the REFLEX and REFLEX' sequences. This label provides convenient and sensitive method of detection of oligonucleotide species using polyacrylamide gel electrophoresis.

Extension reactions:

[0107] Reactions were prepared which contained 1 μM of the 100 base oligonucleotide substrate, 200 μM dNTPs, presence or absence of 1 μM competitor oligonucleotide, 0.5 μl of each DNA polymerase ("DNAP"): Vent (NEB, 2 units/μl), Taq (Qiagen HotStarTaq 5 units/μl) and Herculase (Stratagene), and made up to 50 μl with the appropriate commercial buffers for each polymerase and dH_20. For Taq titrations 0.5 μl, 1 μl, 2 μl, and 3 μl enzyme was used in the same 50 μl volume. Reactions were heated in a Biometra thermocycler to 95 °C for 15 minutes (Taq) or 5 minutes (Herculase, Vent), followed by 55 °C or 50 °C for 30 seconds, and a final incubation at 72 °C for 10 minutes.

T7 exonuclease digestions:

[0108] Reactions were prepared with 10 μl extension reactions above, 0.5 μl T7 exonuclease (NEB, 10 units/μl), and made up to 50 μl using NEB Buffer 4 and dH_20. Reactions were incubated at 25 °C for 30 minutes.

Gel Electrophoresis analysis:

[0109] An 8% denaturing polyacrylamide gel was used to analyze reaction species. 0.4 μl of extension reactions, and 2 μl of digestion reactions were loaded and ran at 800V for ~1.5 hours. Gels were analyzed for fluorescein using an Amersham/General Electric Typhoon imager.

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RESULTS

[0110] Figure 6A shows the structure of each stage of reflex sequence processing with the expected nucleic acid size shown on the left. The initial single stranded nucleic acid having a sequencing primer site (the Roche 454 sequencing primer A site; listed as 454A); an MID; a reflex sequence; the insert; and a complement of the reflex sequence is 100 nucleotides in length. After self-annealing and extension, the product is expected to be 130 nucleotides in length. After removal of the double stranded region from the 5' end, the nucleic acid is expected to be 82 bases in length.

[0111] Figure 6B shows the results of three experiments using three different nucleic acid polymerases (Vent, Herculase and Taq, indicated at the top of the lanes). The temperature at which the annealing was carried out is shown at the top of each lane (either 50°C or 55°C). The sizes of the three nucleic acids as noted above are indicated on the left and right side of the gel.

[0112] As shown in figure 6B, extension appears to be most efficient under the conditions used with Herculase (Herculase is a mixture of two enzymes: modified Pfu DNAP and Archaemax (dUTPase)). Most (or all) of the initial 100 base pair nucleic acid are converted to the 130 base pair product (see lanes 6 and 7). However, after T7 exonuclease digestion the 3'-5' exonuclease activity of Herculase results in partial digestion of the desired 82 base product (note bands at and below the 82 base pairs in lanes 8 and 9).

[0113] Taq, which lacks 3'-5' exonuclease activity, shows a stronger band at the expected size of the final product after T7 exonuclease digestion (see lane 13).

[0114] Figure 7 shows the effect on the reflex process of increasing amounts of Taq polymerase as well as the use of a reflex sequence competitor (schematically shown in Figure 7A).

[0115] As shown in lanes 2 to 5, increased Taq concentration improves extension to ~90% conversion of the starting nucleic acid (see lane 5). Lanes 7 to 8 show that T7 exonuclease digestion does not leave a perfect 82 base product. This may be due to collapse of dsDNA when T7 exonuclease has nearly completed its digestion from the 5' end in the double stranded region of the fold-back structure. It is noted that in many embodiments, the removal of a few additional bases from the 5' end of the polynucleotide will not interfere with subsequent analyses, as nucleotide bases at the 5' end are often removed during subsequent steps.

[0116] As shown in Lanes 11-14, addition of a competitor (which can interfere with annealing of the reflex sequences to form the fold-back structure) results in only a small

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decrease (~5-10%) of fully extended product. Thus, as expected, the intramolecular reaction is heavily favored. Although not shown, we have observed that the competitor oligonucleotide also gets extended by the same amount (~5-10%).

[0117] The concentration of the competitor, the concentration of the reflex substrate, and the overall genetic complexity, will all likely affect specific results. The experiments shown in Figures 6 and 7 demonstrate that the core parts of the reflex processes as described herein is functional and can be implemented.

Example II

[0118] Figure 8 shows the reflex workflow (diagram at left) and exemplary results of the workflow (gel at right) for a specific region of interest (ROI). The starting material is a double stranded nucleic acid molecule (700) that contains a 454A primer site, an MID, a reflex site, and a polynucleotide of interest having three ROIs (2, 3 and 4) at different locations therein. This starting material was subjected to reflex processes (as described in above) specific for ROI 2 as shown in the diagram at the left of the figure, both with and without the use of a T7 exonuclease step (the T7 exonuclease step is shown in the diagram is indicated as "Optional").

[0119] Completion of all steps shown in the reflex process should result in a double stranded polynucleotide of 488 base pairs (702) with or without the T7 exonuclease step.

[0120] As shown in the gel on the right of Figure 8, the 488 base pair product was produced in reflex processes with and without the T7 exonuclease step.

[0121] Figure 9 shows an exemplary protocol for a reflex process based on the results discussed above. The diagram shows specific reflex process steps with indications on the right as to where purification of reaction products is employed (e.g., using Agencourt SPRI beads to remove primer oligos). One reason for performing such purification steps is to reduce the potential for generating side products in a reaction (e.g., undesirable amplicons). While Figure 9 indicates three purification steps, fewer or additional purification steps may be employed depending on the desires of the user. It is noted that the steps of reversing polarity, reflex priming and extension, and "stretch out" (or denaturation) / second reversing polarity step can be performed without intervening purification steps.

[0122] The protocol shown in Figure 9 includes the following steps:

annealing a first primer containing a 5' reflex sequence (or reflex tail, as noted in the figure) specific for the 3' primer site for the R' region to the starting polynucleotide and extending (the primer anneals to the top strand at the primer site at the right of R in

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polynucleotide 902, indicated with a *; this step represents the first denature, anneal and extend process indicated on the right);

after purification, adding a 454A primer and performing three cycles of denaturing, annealing and extending: the first cycle results in the copy-back from the 454A primer to reverse the polarity of the strand just synthesized; the second cycle breaks apart the double stranded structure produced, allows the reflex structure to form and then extend; the third cycle results in another copy-back using the same 454A primer originally added;

after purification, adding a second primer specific for the second primer site for the R' region having a 5' 454B tail (this primer anneals to the primer site 3' of the R' region in polynucleotide 904, indicated with a *) and denaturing, annealing and extending resulting in a polynucleotide product having 454A and 454B sites surrounding the MID, the reflex sequence, and R'. Note that the first primer specific for the R' region and the second primer specific for the R' region define its boundaries, as described above and depicted in Figure 1B);

after another purification, adding 454A and 454B primers and performing a PCR amplification reaction.

Example III

[0123] As described above, a reflex sequence can be an "artificial" sequence added to a polynucleotide as part of an adapter or can be based on a sequence present in the polynucleotide of interest being analyzed, e.g., a genomic sequence (or "non-artificial").

[0124] The data shown in prior Examples used "artificial" reflex sites. In this Example, the reflex site is a genomic sequence present in the polynucleotide being analyzed.

[0125] The starting material is a double stranded DNA containing a 454A site, an MID and a polynucleotide to be analyzed. The 454A and MID were added by adapter ligation to parent polynucleotide fragments followed by enrichment of the polynucleotide to be analyzed by a hybridization-based pull-out reaction and subsequent secondary PCR amplification (see Route 1 in Figure 13). Thus, the reflex site employed in this example is a sequence normally present at the 5' end of the subject polynucleotide (a genomic sequence). The polynucleotide being analyzed includes a region of interest distal to the 454A and MID sequences that is 354 base pairs in length.

[0126] This starting double stranded nucleic acid is 755 base pairs in length. Based on the length of each of the relevant domains in this starting nucleic acid, the reflex process should result in a product of 461 base pairs.

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[0127] Figure 10 shows the starting material for the reflex process (left panel) and the resultant product generated using the reflex process (right panel; reflex process was performed as described in Example II, without using a T7 exonuclease step). A size ladder is included in the left hand lane of each gel to allow estimation of the size of the test material. This figure shows that the 755 base pair starting nucleic acid was processed to the expected 461 base pair product, thus confirming that a "non-artificial" reflex site is effective in moving an adapter domain from one location to another in a polynucleotide of interest in a sequence specific manner.

Example IV

[0128] Figure 11 shows a schematic of an experiment in which the reflex process is performed on a single large initial template (a "parent" fragment) to generate 5 different products ("daughter" products) each having a different region of interest (i.e., daughter products are produced having either region 1, 2, 3, 4 or 5). The schematic in Figure 11 shows the starting fragment (11,060 base pairs) and resulting products (each 488 base pairs) generated from each of the different region of interest-specific reflex reactions (reflex reactions are performed as described above). The panel (gel) on the bottom of Figure 11 shows the larger starting fragment (Lane 1) and the resulting daughter products for each region-specific reflex reaction (lanes 2 to 6, with the region of interest noted in each in the box), where the starting and daughter fragments have the expected lengths. Sequencing of the products confirmed the identity of the region of interest in each of the reflex products shown in the gel. These results demonstrate that multiple different reflex products can be generated from a single, asymmetrically tagged parent fragment while maintaining the adapter domains (e.g., the primer sites and MID).

Example V

[0129] Figure 12 details experiments performed to determine the prevalence of intramolecular rearrangement (as desired in the reflex process) vs. intermolecular rearrangement. Intermolecular rearrangement is undesirable because it can lead to the transfer of an MID from one fragment to another (also called MID switching). MID switching can occur if a reflex sequence in a first fragment hybridizes to its complement in a second fragment during the reflex process, leading to appending the MID from the second fragment to the first fragment. Thus, intermolecular rearrangement, or MID switching, should be minimized to prevent the transfer of an MID from one fragment in the sample to another, which could lead to a misrepresentation of the source of a fragment.

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[0130] To measure the prevalence of MID switching under different reflex conditions, fragments having different sizes were generated that included two different MIDs, as shown in the top panel of Figure 12. The common sequence on these fragments serves as the priming site for the first extension reaction to add the second reflex sequence (see, e.g., step 2 of Figure 3). Three exemplary fragments are shown in Figure 12 for each different fragment size (i.e., 800 base pairs with an MIDB and MIDA combination; 1900 base pairs with MIDC and MIDA combination; and 3000 base pairs with MIDD and MIDA combination). For each MID family (A, B, C and D), there are 10 different members (i.e., MIDA had 10 different members, MIDB has 10 different members, etc.). A set of 10 dual MID fragments for each different size fragment (i.e., 800, 1900 and 3000 base pairs) were generated, where the MID pairs (i.e., MIDA/MIDB, MIDA/MIDC, and MIDA/MIDD) were designated as 1/1, 2/2, 3/3, 4/4, 5/5, 6/6, 7/7, 8/8, 9/9, and 10/10. All 10 fragments of the same size were then mixed together and a reflex protocol was performed.

[0131] Due to the domain structure of the fragments, a successful reflex process results in the two MIDs for each fragment being moved to within close enough proximity to be sequenced in a single read using the Roche 454 sequencing platform (see the reflex products shown in the schematic of Figure 12). The reflex reactions for each fragment size were performed at four different fragment concentrations to determine the effect of this parameter, as well as fragment length, in the prevalence of MID switching. The reflex products from each reaction performed were subjected to 454 sequencing to determine the identity of both MIDs on each fragment, and thereby the proportion of MID switching that occurred.

[0132] The panel on the bottom left of Figure 12 shows the rate of MID switching (Y axis, shown in % incorrect (or switched) MID pair) for each different length fragment at each different concentration (X axis; 300, 30, 3 and 0.3 nM). As shown in this panel, the MID switch rate decreases with lower concentrations, as would be expected, because intermolecular, as opposed to intramolecular, binding events are concentration dependent (i.e., lower concentrations lead to reduced intermolecular hybridization/binding). In addition, the MID switch rate decreases slightly with length. This is somewhat unexpected as the ends of longer DNA fragments are effectively at a lower concentration with respect to one another. The reasons for why we do not see this is probably because the production of reflex priming intermediates continues during the final PCR, which means that reflex priming reactions are happening continuously which contributes to MID switching. It is probably the case that the shorter reflex products are able to undergo a higher rate of 'background' reflexing, and therefore increase the overall MID switch rate a little.

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[0133] These results demonstrate that MID switching can be minimized (e.g., to below 2%, below 1% or even to nearly undetectable levels) by altering certain parameters of the reaction, e.g., by reducing fragment concentration and/or fragment length.

[0134] The panel on the bottom right of Figure 12 shows the frequency of MID switching in the reflex process for the 800 base pair fragments (i.e., MIDA/MIDB containing fragments). In this figure, the area of each circle is proportional to the number of reads containing the corresponding MIDA and MIDB species (e.g., MIDA1/MIDB1; MIDA1/MIDB2; etc.). Thus, a circle representing 200 reads will be 40 times larger in terms of area than a circle representing 5 reads.

[0135] As noted above, the MIDA/MIDB combinations having the same number (shown on the X and Y axis, respectively) represent the MIDA/MIDB combinations present in the sample prior to the reflex process being performed (i.e., MIDA/MIDB combinations 1/1, 2/2, 3/3, 4/4, 5/5, 6/6, 7/7, 8/8, 9/9, and 10/10 were present in the starting sample). All other MIDA/MIDB combinations identified by Roche 454 sequencing were the result of MID switching.

[0136] This figure shows that the MID switching that occurs during the reflex process is random, i.e., that MID switching is not skewed based on the identity of the MIDs in the reaction).

Exemplary Reflex Protocols

[0137] Figure 13 shows a diagram of exemplary protocols for performing the reflex process on pools of nucleic acids, for example, pools of nucleic acids from different individuals, each of which are labeled with a unique MID. In Route 3, a pooled and tagged extended library is subjected directly to a reflex process. In Route 2, the pooled library is enriched by target-specific hybridization followed by performing the reflex process. In Route 1 employs enrichment by PCR amplification. As shown in Figure 13, PCR enrichment can be performed directly on the pooled tagged extended library or in a secondary PCR reaction after a hybridization-based enrichment step has been performed (as in Route 2) to generate an amplicon substrate that is suitable for the reflex process. Additional routes for preparing a polynucleotide sample for performing a reflex process can be implemented (e.g., having additional amplification, purification, and/or enrichment steps), which will generally be dependent on the desires of the user.

[0138] Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it is readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes

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and modifications may be made thereto without departing from the spirit or scope of the appended claims.

[0139] Accordingly, the preceding merely illustrates the principles of the invention. It will be appreciated that those skilled in the art will be able to devise various arrangements which, although not explicitly described or shown herein, embody the principles of the invention and are included within its spirit and scope. Furthermore, all examples and conditional language recited herein are principally intended to aid the reader in understanding the principles of the invention and the concepts contributed by the inventors to furthering the art, and are to be construed as being without limitation to such specifically recited examples and conditions. Moreover, all statements herein reciting principles, aspects, and embodiments of the invention as well as specific examples thereof, are intended to encompass both structural and functional equivalents thereof. Additionally, it is intended that such equivalents include both currently known equivalents and equivalents developed in the future, i.e., any elements developed that perform the same function, regardless of structure. The scope of the present invention, therefore, is not intended to be limited to the exemplary embodiments shown and described herein. Rather, the scope and spirit of present invention is embodied by the appended claims.

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CLAIMS

What is claimed:

1. A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
   (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
   (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
      (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
      (ii) a multiplex identifier (MID) sequence comprising:
         I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived; and
         II. a second tag sequence distinguishing the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell;
   (c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;
   (d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the polynucleotide sequence is derived; and
   (e) using the second tag sequence to correlate the identified polynucleotide sequence with the plurality of sample polynucleotides from which the polynucleotide sequence is derived.

2. The method of claim 1, wherein the method further comprises amplifying the tagged polynucleotides prior to the sequencing step (c).

3. The method of claim 1, wherein the sample polynucleotides are selected from DNA and RNA.

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4. The method of claim 3, wherein the sample polynucleotides comprise mRNA.

5. The method of claim 1, wherein the tagged polynucleotides are generated through at least one ligation reaction.

6. The method of claim 1, wherein the tagged polynucleotides are generated through PCR or linear amplification of the plurality of sample polynucleotides using an adapter sequence comprising the MID sequence and an amplification primer.

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ABSTRACT OF THE DISCLOSURE

Aspects of the present invention include analyzing nucleic acids from single cells using methods that include using tagged polynucleotides containing multiplex identifier sequences.

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Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Filer:	Gargi Talukder/Sheila Gloss
Attorney Docket Number:	104371-5016-US08

Filed as Small Entity

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

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY FILING FEE (ELECTRONIC FILING)	4011	1	70	70
UTILITY SEARCH FEE	2111	1	300	300
UTILITY EXAMINATION FEE	2311	1	360	360
REQUEST FOR PRIORITIZED EXAMINATION	2817	1	2000	2000
Pages:				
Claims:				
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
PUBL. FEE- EARLY, VOLUNTARY, OR NORMAL	1504	1	0	0
PROCESSING FEE, EXCEPT PROV. APPLS.	2830	1	70	70
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**2800**

Electronic Acknowledgement Receipt	
EFS ID:	30083470
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Gargi Talukder/Sheila Gloss
Filer Authorized By:	Gargi Talukder
Attorney Docket Number:	104371-5016-US08
Receipt Date:	15-AUG-2017
Filing Date:	
Time Stamp:	19:06:43
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$2800
RAM confirmation Number	081617INTEFSW00005704500310
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	TrackOne Request	104371-5016-US08_TRK1.pdf	92727 61bf8a58acb01e22b058960ec3df592ab59b16f3	no	1
Warnings:					
Information:					
2		104371-5016-US08_TRANS.pdf	169701 deebe80159b0139fb253cbd66a8068f452c81451	yes	2
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Transmittal of New Application		1	1	
	Fee Worksheet (SB06)		2	2	
Warnings:					
Information:					
3	Application Data Sheet	104731-5016-US08_ADS.pdf	183024 cd1ef64db8998bcedceed1b558a5db619ceca4a6	no	9
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
4	Drawings-only black and white line drawings	104371-5016-US08_DRW.pdf	2471077 f35e8812fdc5d89f3b245218a95f1cb3e8d8def3	no	13
Warnings:					
Information:					
5		104371-5016-US08_APPL.pdf	387498 03d2ae612c52c67bbc8243b992d831d722681a4e	yes	42

	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Specification		1	39	
	Claims		40	41	
	Abstract		42	42	
Warnings:					
Information:					
6	Fee Worksheet (SB06)	fee-info.pdf	40189 d5d698ce4e177b6cbc1260c785f0cfa0a2cd9bb3	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	3344216		

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.

Doc Code: TRACK1.REQ
Document Description: TrackOne Request

PTO/AIA/424 (04-14)

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

First Named Inventor:	Sydney Brenner	Nonprovisional Application Number (if known):	
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS		

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

1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently $0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.
2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.
3. The applicable box is checked below:

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

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

---OR---

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

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

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

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

Signature Garg Talukder	Date Aug. 15, 2017
Name (Print/Typed) Gargi Talukder	Practitioner Registration Number 61,368

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

☐ *Total of _____ forms are submitted.

SCORE Placeholder Sheet for IFW Content

Application Number: 15677957 Document Date: 08/15/2017

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

- Drawings – Other than Black and White Line Drawings

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

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

At the time of document entry (noted above):

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

Form Revision Date: September 30. 2013

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/677,957	08/15/2017	1637	730	104371-5016-US08	6	1

CONFIRMATION NO. 1051

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

FILING RECEIPT

OC000000093827682

Date Mailed: 08/24/2017

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

Inventor(s)

Sydney Brenner, Ely, UNITED KINGDOM;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, Lindon, UNITED KINGDOM;

Applicant(s)

10X Genomics, Inc., Pleasanton, CA;

Power of Attorney: None

Domestic Applications for which benefit is claimed - None.
A proper domestic benefit claim must be provided in an Application Data Sheet in order to constitute a claim for domestic benefit. See 37 CFR 1.76 and 1.78.

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.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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If Required, Foreign Filing License Granted: 08/22/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/677,957**

Projected Publication Date: To Be Determined - pending completion of Corrected Papers

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

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).

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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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).

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

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 15/677,957

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	70		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	300		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	360		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	6 minus 20 =	*	x 40 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*	x 210 =	0.00			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	730		TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT A

	(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($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
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	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)		RATE($)	ADDITIONAL FEE($)
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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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08

CONFIRMATION NO. 1051

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

FORMALITIES LETTER

OC000000093627663

Date Mailed: 08/24/2017

NOTICE TO FILE CORRECTED APPLICATION PAPERS

Filing Date Granted

An application number and filing date have been accorded to this application. The application is informal since it does not comply with the regulations for the reason(s) indicated below. Applicant is given TWO MONTHS from the date of this Notice within which to correct the informalities indicated below. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

The required item(s) identified below must be timely submitted to avoid abandonment:

- Replacement drawings in compliance with 37 CFR 1.84 and 37 CFR 1.121(d) are required. The drawings submitted are not acceptable because:
  - The drawing sheets do not have the appropriate margin(s) (see 37 CFR 1.84(g)). Each sheet must include a top margin of at least 2.5 cm. (1 inch), a left side margin of at least 2.5 cm. (1 inch), a right side margin of at least 1.5 cm. (5/8 inch), and a bottom margin of at least 1.0 cm. (3/8 inch).See Figures(s) 9,12.

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.

- Surcharge as set forth in 37 CFR 1.16(f) must be submitted.
  The surcharge is due for any one of:
  - late submission of the basic filing fee, search fee, or examination fee,
  - late submission of inventor's oath or declaration,
  - filing an application that does not contain at least one claim on filing, or
  - submission of an application filed by reference to a previously filed application.

SUMMARY OF FEES DUE:

The fee(s) required within **TWO MONTHS** from the date of this Notice to avoid abandonment is/are itemized below. Small entity discount is in effect. If applicant is qualified for micro entity status, an acceptable Certification of Micro Entity Status must be submitted to establish micro entity status. (See 37 CFR 1.29 and forms PTO/SB/15A and 15B.)

- $ **70** surcharge.
- $(**0**) previous unapplied payment amount.
- $ **70** TOTAL FEE BALANCE DUE.

Items Required To Avoid Processing Delays:

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00078

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

- A properly executed inventor's oath or declaration has not been received for the following inventor(s):
  Sydney Brenner
  Gi Mikawa
  Robert Osborne
  Andrew Slatter

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**.

/dnguyen/

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Conf. No.: **1051**
Sydney BRENNER	Art Unit: **1637**
Application No.: **15/677,957**	Examiner: **To be determined**
Filed: **August 15, 2017**	Docket No.: **104371-5016-US08**
For: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	*Certificate of Transmission (37 C.F.R. § 1.8)* *I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office electronic filing system in accordance with § 1.6(a)(4) on September 8, 2017.* / Sheila R. Gloss / *Sheila R. Gloss*

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

RESPONSE TO NOTICE TO FILE CORRECTED APPLICATION PAPERS AND PRELIMINARY AMENDMENT

Sir:

Responsive to the *Notice to File Corrected Application Papers* mailed August 24, 2017, and prior to the first Office Action in the above-identified application, Applicants submit the following amendments and remarks.

AMENDMENTS

Amendments to the Drawings begin on page **2** of this paper, and include attached replacement sheets. Remarks begin on page **3** of this paper.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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In the Drawings:

The attached Replacement Sheets of drawings replace the originally filed FIGS. 9 and 12.

Attachment: Two (2) Replacement Sheets including FIGS. 9 and 12.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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REMARKS

Responsive to the *Notice to File Corrected Application Papers* mailed August 24, 2017, Applicants submit the above Amendments and the following Remarks.

Drawings

Replacement Sheets are submitted in compliance with 37 C.F.R. §§ 1.84 and 1.121(d). Applicants respectfully submit that the drawings are now acceptable because Figures 9 and 12 have the appropriate margin(s), in accordance with 37 C.F.R. 1.84(g). Because the foregoing replacement sheets introduce no new matter, their entry is respectfully requested.

Fees

Applicant submits herewith $70 surcharge for late filing of oath or declaration.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided below.

Although Applicants do not believe any additional fees are required, the Commissioner is hereby authorized to charge any underpayment of the following fees associated with this communication, including any necessary fees for extension of time, or credit any overpayment to Deposit Account No. 50-0310 (Order No. 104371-5016-US08).

Respectfully submitted,

Date: Sept 8, 2017

By: Gargi Talukder

Gargi Talukder, Reg. No. 61,386
Filed Under 37 CFR § 1.34

Customer No. 43850
MORGAN LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
San Francisco, California 94105
Tel: 415.442.1000, Fax: 415.442.1001

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00082

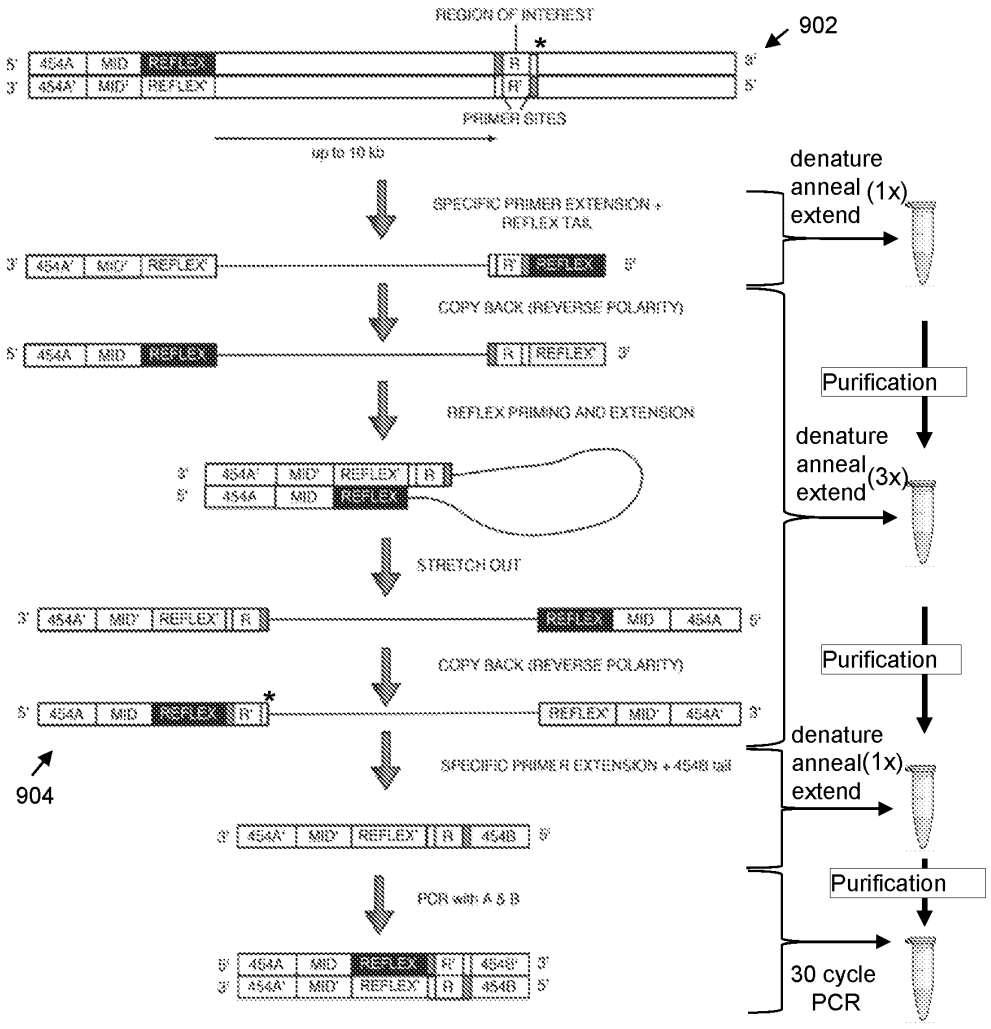
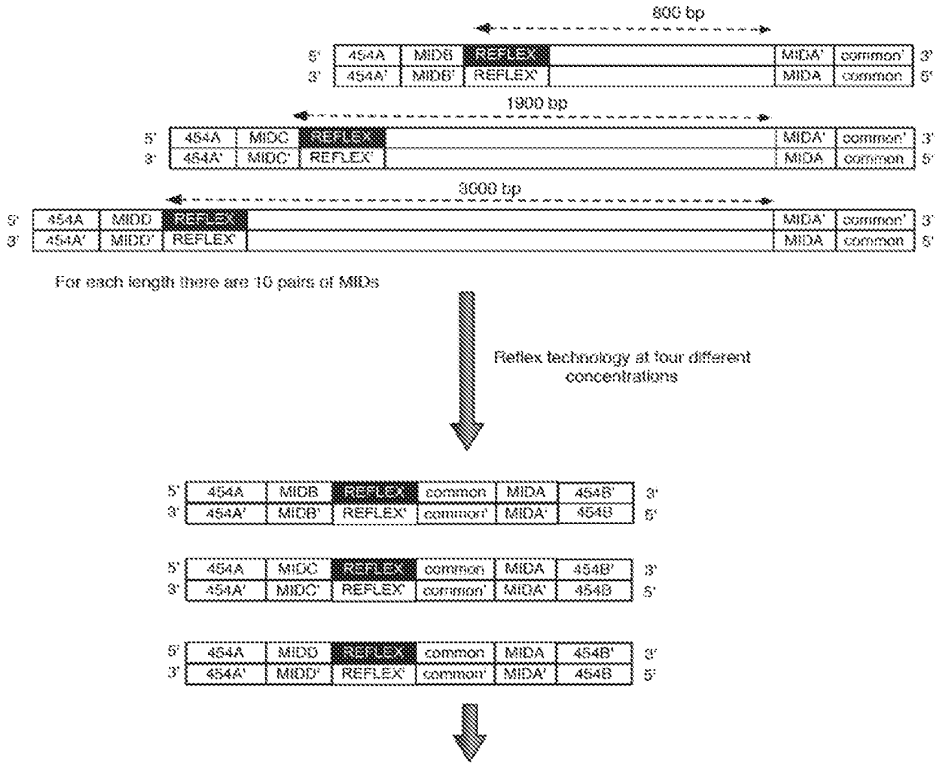

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COPY BACK (REVERSE POLARITY)
REFLEX PRIMING AND EXTENSION
STRETCH OUT
COPY BACK (REVERSE POLARITY)
SPECIFIC PRIMER EXTENSION + 454B tail
904
PCR with A & B
denature
anneal (1x)
extend
Purification
denature
anneal (3x)
extend
Purification
denature
anneal(1x)
extend
Purification
30 cycle
PCR

Fig. 9


800 bp
1900 bp
3000 bp
454A
MIDB
MIDC
MIDD
REFLEX
MIDA
common
454B
For each length there are 10 pairs of MIDs
Reflex technology at four different concentrations
Roche 454 Sequencing

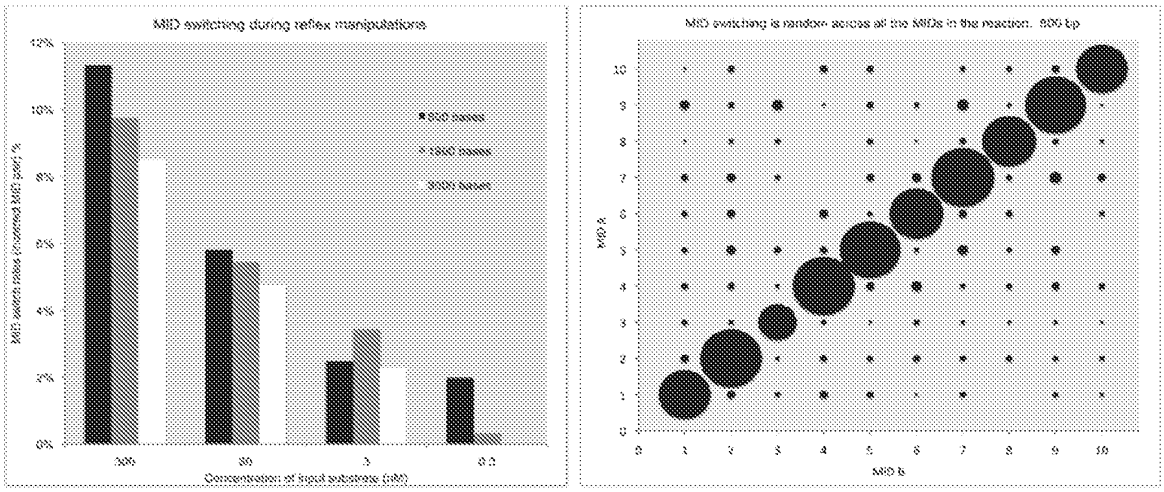

MID switching during reflex manipulations
MID switching is random across all the MIDs in the reaction. 800 bp

Fig. 12

Electronic Patent Application Fee Transmittal

Application Number:	15677957
Filing Date:	15-Aug-2017
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Filer:	Gargi Talukder/Sheila Gloss
Attorney Docket Number:	104371-5016-US08

Filed as Small 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:				
LATE FILING FEE FOR OATH OR DECLARATION	2051	1	70	70
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**70**

Electronic Acknowledgement Receipt	
EFS ID:	30315454
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Gargi Talukder/Sheila Gloss
Filer Authorized By:	Gargi Talukder
Attorney Docket Number:	104371-5016-US08
Receipt Date:	08-SEP-2017
Filing Date:	15-AUG-2017
Time Stamp:	19:07:38
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$70
RAM confirmation Number	091117INTEFSW00005728500310
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	Applicant Response to Pre-Exam Formalities Notice	104731-5016-US08_RESP.pdf	656399 a336df14f2b5f24c3e43bab7f2947836f0d149e3	no	3
Warnings:					
Information:					
2	Drawings-only black and white line drawings	104371-5016-US08_REVISEDFIG9_12.pdf	323244 803b64635d390001695f42f559717ee202e40c5d	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30357 26fdb1863e5ff3c5ecf4e244c58dc6e668f66cfe	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1010000		

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.

SCORE Placeholder Sheet for IFW Content

Application Number: 15677957 Document Date: 09/08/2017

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

- Drawings – Other than Black and White Line Drawings

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

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

At the time of document entry (noted above):

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

Form Revision Date: September 30, 2013

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08

CONFIRMATION NO. 1051

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

INFORMAL NOTICE

OC000000093996390

Date Mailed: 09/13/2017

INFORMATIONAL NOTICE TO APPLICANT

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

The item(s) indicated below are also required and should be submitted with any reply to this notice to avoid further processing delays.

- A properly executed inventor's oath or declaration has not been received for the following inventor(s):
  Sydney Brenner
  Gi Mikawa
  Robert Osborne
  Andrew Slatter

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**.

/dnguyen/

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00090

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 15/677,957

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	70		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	300		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	360		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	6 minus 20 =	*	x 40 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*	x 210 =	0.00			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	730		TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT A

	(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($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
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	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
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
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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
15/677,957	08/15/2017	1637	800	104371-5016-US08	6	1

CONFIRMATION NO. 1051

UPDATED FILING RECEIPT

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

OC000000093998389

Date Mailed: 09/13/2017

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

Inventor(s)

Sydney Brenner, Ely, UNITED KINGDOM;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, Lindon, UNITED KINGDOM;

Applicant(s)

10X Genomics, Inc., Pleasanton, CA;

Power of Attorney: None

Domestic Applications for which benefit is claimed - None.
A proper domestic benefit claim must be provided in an Application Data Sheet in order to constitute a claim for domestic benefit. See 37 CFR 1.76 and 1.78.

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.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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If Required, Foreign Filing License Granted: 08/22/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/677,957**

Projected Publication Date: 02/21/2019

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

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).

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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.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
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MAILED
SEP 14 2017
OFFICE OF PETITIONS

MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco CA 94105

Doc Code: TRACK1.GRANT

Decision Granting Request for Prioritized Examination (Track I or After RCE)	Application No.: 15/677,957

1. THE REQUEST FILED August 15, 2017 IS **GRANTED.**

The above-identified application has met the requirements for prioritized examination

A. ☒ for an original nonprovisional application (Track I).
B. ☐ for an application undergoing continued examination (RCE).

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

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

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

/Brian W. Brown/
[*Signature*]

Petitions Examiner, Office of Petitions
(Title)

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: **1051**
Sydney Brenner et al.	Examiner: **Karla A. Dines**
Application No.: **15/677,957**	Art Unit: **1639**
Filed: **August 15, 2017**	
For: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	**PRELIMINARY AMENDMENT**

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

Commissioner:

Prior to examination of the above-referenced application, please enter the following amendments and remarks:

Amendments to the Specification being on page 2 of this paper.

Remarks begin on page **3** of this paper.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00096

Amendments to the Specification:

Please insert the following header and paragraph immediately after the title on Page 1:

CROSS REFERENCE TO RELATED APPLICATION

This application is continuation of U.S. Application No. 14/792,094, filed July 6, 2015, which is a continuation of U.S. Application No. 14/172,694, filed February 4, 2014, now Patent No. 9,102,980, which is a continuation of U.S. Application No. 14/021,790, filed September 9, 2013, now Patent No. 8,679,756, which is a continuation of U.S. Application No. 13/859,450, filed April 9, 2013, now Patent No. 8,563,274, which is a continuation of U.S. Application No. 13/622,872, filed September 19, 2012, which is a continuation of U.S. Application No. 13/387,343, filed February 15, 2012, now Patent No. 8,298,767, which is a §371 National Phase Application of PCT/IB2010/002243, filed August 13, 2010, which claims priority to U.S. Provisional Application No. 61/235,595, filed August 20, 2009 and U.S. Provisional Application No. 61/288,792, filed December 21, 2009; all of which are herein incorporated by reference.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Remarks

The specification has been amended to include priority information, in accordance with 37 C.F.R. 1.78(d)(3)(ii). This Amendment is timely filed on or before **December 15, 2017**, within four-months of the application filing date of **August 15, 2017**.

A Request for Corrected Filing Receipt and Supplemental Application Data Sheet is submitted herewith to update the priority information.

Inventor's oath or declaration for each of the inventors is also submitted herewith.

CONCLUSION

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Order No.: 104371-5016-US08).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: December 13, 2017 By: /Gargi Talukder/
Gargi Talukder, Reg. No. 61,368

Customer No.: 43850
Morgan, Lewis & Bockius LLP
One Market, Spear Street Tower
San Francisco, CA 94105
Telephone: (415) 442-1000
Facsimile: (415) 442-1001

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Remarks

The specification has been amended to include priority information, in accordance with 37 C.F.R. 1.78(d)(3)(ii). This Amendment is timely filed on or before **December 15, 2017**, within four-months of the application filing date of **August 15, 2017**.

A Request for Corrected Filing Receipt and Supplemental Application Data Sheet is submitted herewith to update the priority information.

Inventor's oath or declaration for each of the inventors is also submitted herewith.

CONCLUSION

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Order No.: 104371-5016-US08).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: December 13, 2017 By: /Gargi Talukder/
Gargi Talukder, Reg. No. 61,368

Customer No.: 43850
Morgan, Lewis & Bockius LLP
One Market, Spear Street Tower
San Francisco, CA 94105
Telephone: (415) 442-1000
Facsimile: (415) 442-1001

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: **Karla A. Dines**
Sydney Brenner et al.	Art Unit: **1639**
Application No. **15/677,957**	Confirmation No. **1051**
Filed: **August 15, 2017**	Attorney Docket No. **104371-5016-US08**
Title: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	

REQUEST FOR CORRECTED FILING RECEIPT

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

Commissioner:

Applicants request correction of the official Filing Receipt for the above-captioned application. Attached hereto is a copy of the Filing Receipt indicating the following requested corrections:

After the **Power of Attorney** information, please insert the following:

Domestic Priority data as claimed by the applicant:

This application is a CON of 14/792,094 07/06/2015
which is a CON of 14/172,694 02/04/2014 PAT 9102980
which is a CON of 14/021,790 09/09/2013 PAT 8679756
which is a CON of 13/859,450 04/09/2013 PAT 8563274
which is a CON of 13/622,872 09/19/2012 ABN
which is a CON of 13/387,343 02/15/2012 PAT 8298767
which is a 371 of PCT/IB2010/002243 08/13/2010
which claims benefit of 61/288,792 12/21/2009
and claims benefit of 61/235,595 08/20/2009

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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A supplemental Application Data Sheet to add the domestic priority chain, as set forth above, is submitted herewith.

This Request is timely filed on or before **December 15, 2017**, within four-months of the application filing date of **August 15, 2017**.

A Preliminary Amendment, to add priority information to the Specification, is being filed concurrently.

CONCLUSION

Although Applicant does not believe any additional fees are required, the Commissioner is authorized to charge any additional required fees or to credit any overpayment to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 (File No. 104371-5016-US08).

Please direct any calls in connection with this application to the undersigned at (415) 442-1000.

Respectfully submitted,

Dated: December 13, 2017

/Gargi Talukder/

Gargi Talukder, Reg. No. 61,368
MORGAN, LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
San Francisco, CA 94105
Telephone: 415.442.1000
Facsimile: 415.442.1001

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00101

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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
15/677,957	08/15/2017	1637	800	104371-5016-US08	6	1

CONFIRMATION NO. 1051

UPDATED FILING RECEIPT

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

OC000000093998389

Date Mailed: 09/13/2017

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

Inventor(s)

Sydney Brenner, Ely, UNITED KINGDOM;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, Lindon, UNITED KINGDOM;

Applicant(s)

10X Genomics, Inc., Pleasanton, CA;

Domestic Priority Data as claimed by the applicant:
This application is a CON of 14/792,094 07/06/2015
which is a CON of 14/172,694 02/04/2014 PAT 9102980
which is a CON of 14/021,790 09/09/2013 PAT 8679756
which is a CON of 13/859,450 04/09/2013 PAT 8563274
which is a CON of 13/622,872 09/19/2012 ABN
which is a CON of 13/387,343 02/15/2012 PAT 8298767
which is a 371 of PCT/IB2010/002243 08/13/2010
which claims benefit of 61/288,792 12/21/2009
and claims benefit of 61/235,595 08/20/2009

Power of Attorney: None

Domestic Applications for which benefit is claimed - None.
A proper domestic benefit claim must be provided in an Application Data Sheet in order to constitute a claim for domestic benefit. See 37 CFR 1.76 and 1.78.

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.

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Parse Biosciences, Inc. v. 10x Genomics, Inc.
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If Required, Foreign Filing License Granted: 08/22/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/677,957**

Projected Publication Date: 02/21/2019

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

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).

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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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SUPPLEMENTAL **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/667,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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
	Sydney		Brenner	

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

City	Ely	Country of Residence	GB

Mailing Address of Inventor:

Address 1	3 Barton Square		
Address 2			
City	Ely	**State/Province**	
Postal Code	CB7 4PJ	**Country**	GB

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gi		Mikawa	

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

City	Great Shelford	Country of Residence	GB

Mailing Address of Inventor:

Address 1	104 High Street		
Address 2			
City	Great Shelford	**State/Province**	
Postal Code	CB1 6A3	**Country**	GB

Inventor 3 Remove

Legal Name

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SUPPLEMENTAL **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		Osborne	

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

City	Great Chesterford	Country of Residence	GB

Mailing Address of Inventor:

Address 1	38 Pilgrim Close		
Address 2			
City	Great Chesterford	**State/Province**	
Postal Code	CB10 1QB	**Country**	GB

Inventor 4 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Andrew		Slatter	

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

City	Lindon	Country of Residence	GB

Mailing Address of Inventor:

Address 1	65a Huddleston Road		
Address 2			
City	London	**State/Province**	
Postal Code	N7 0AE	**Country**	GB

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	43850		
Email Address	sfipdocketing@morganlewis.com	Add Email	Remove Email

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SUPPLEMENTAL **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/667,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Application Information:

Title of the Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS		
Attorney Docket Number	104371-5016-US08	**Small Entity Status Claimed** ☒	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	13	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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

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

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

Publication Information:

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

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

Representative Information:

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

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	43850		

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SUPPLEMENTAL **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/667,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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	14/792094	2015-07-06

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14/792094	Continuation of	14/172694	2014-02-04	9102980	2015-08-11

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14/172694	Continuation of	14/021790	2013-09-09	8679756	2014-03-25

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14/021790	Continuation of	13/859450	2013-04-09	8563274	2013-10-22

Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13/859450	Continuation of	13/622872	2012-09-19

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13/622872	Continuation of	13/387343	2012-02-15	8298767	2012-10-30

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13/387343	a 371 of international	PCTIB2010002243	2010-08-13

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
PCTIB2010002243	Claims benefit of provisional	61/288792	2009-12-21

10x Genomics, Inc. Exhibit 2001
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SUPPLEMENTAL **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
PCTIB2010002243	Claims benefit of provisional	61/235595	2009-08-20
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	104371-5016-US08
	Application Number	15/667,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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	104371-5016-US08
	Application Number	15/667,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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	10X Genomics, Inc.		
Mailing Address Information For Applicant:			
Address 1	7068 Koll Center Parkway, Suite 401		
Address 2			
City	Pleasanton	**State/Province**	CA
Country	US	Postal Code	94566
Phone Number		Fax Number	
Email Address			

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	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

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

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

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	/Gargi Talukder/			Date (YYYY-MM-DD)	2017-12-13
First Name	Gargi	Last Name	Talukder	Registration Number	61368

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	104371-5016-US08
	Application Number	15/667,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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.**

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00113

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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Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00114

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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	Compositions and Methods for Intramolecular Nucleic Acid Rearrangement

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 13622872 filed on September 19, 2012.

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: Sydney Brenner Date (Optional) :

Signature: Sydney Brenner

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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LEGAL NAME OF INVENTOR

Inventor: Gi Mikawa Date (Optional): 5-Nov-2012

Signature: Gi Mikawa

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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LEGAL NAME OF INVENTOR

Inventor: Robert Osborne Date (Optional): 5/11/12

Signature: Robert Osborne

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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LEGAL NAME OF INVENTOR

Inventor: Andrew Slatter Date (Optional): 5th November 2012

Signature: Andrew Slatter

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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Electronic Acknowledgement Receipt

EFS ID:	31221640
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Gargi Talukder/Sheila Gloss
Filer Authorized By:	Gargi Talukder
Attorney Docket Number:	104371-5016-US08
Receipt Date:	13-DEC-2017
Filing Date:	15-AUG-2017
Time Stamp:	19:11:33
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		104371-5016-US08_AMEND.pdf	132821 71becb9b817de17b65474b93d3444011cd1a4e74	yes	3

	Multipart Description/PDF files in .zip description				
	Document Description	**Start**	**End**		
	Preliminary Amendment	1	1		
	Specification	2	2		
	Applicant Arguments/Remarks Made in an Amendment	3	3		
Warnings:					
Information:					
2	Request for Corrected Filing Receipt	104731-5016-US08_REQ.pdf	367497 7f47fb0fbf694bf4fbfc1af257f85b7e45e17c01	no	5
Warnings:					
Information:					
3	Application Data Sheet	104371-5016-US08_SuppADS.pdf	198965 57564976bf41658f1ae9a7115f217d37a9d63541	no	10
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
4	Oath or Declaration filed	104731-5016-US08_DECL.pdf	299084 b234c4947ef90721f5f8127e660b8240edc26f57	no	4
Warnings:					
Information:					
		Total Files Size (in bytes):	998367		

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Conf. No.: **1051**
Sidney BRENNER	Art Unit: **1639**
Application No.: **15/677,957**	Examiner: **Karla A. Dines**
Filed: **August 15, 2017**	Docket No.: **104371-5016-US08**
For: **Methods for Analyzing Nucleic Acids from Single Cells**	*Certificate of Transmission (37 C.F.R. § 1.8)* *I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office electronic filing system (EFS-Web) to the USPTO on December 19, 2017.* / Sheila R. Gloss / *Sheila R. Gloss*

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

INFORMATION DISCLOSURE STATEMENT

Commissioner:

This Information Disclosure Statement is hereby submitted in accordance with 37 C.F.R. 1.98 and pursuant to Applicant's continuing duty under 37 C.F.R. 1.56 to bring any information which may be material to patentability of this application to the Examiner's attention.

Applicant makes no representation that a search has been conducted by the Applicant, or that there is not possibly more relevant art. 37 C.F.R. § 1.97(g). Applicant also makes no representation that the information submitted herewith is in fact material to patentability. The filing of this Information Disclosure Statement shall not be construed as an admission against interest in any manner. 37 C.F.R. § 1.97(h).

The Examiner's attention is directed to the reference(s) cited on the accompanying substitute for forms 1449A/PTO and PTO/SB/08. Except for U.S. Patents and U.S. Patent Application Publications, *see* 37 C.F.R. § 1.98(a)(2)(i), copies of the cited references are enclosed, unless otherwise noted below.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00122

This Information Disclosure Statement is being filed within three months of the filing date of a national application other than a continued prosecution application, within three months of the date of entry of a national stage, before the mailing of a first Office action on the merits, or before the mailing of a first Office action after the filing of a request for continued examination. 37 C.F.R. § 1.97(b). No fee is required.

This Application relies on the earlier filing date of prior Application No. 14/792,094, filed July 6, 2015; Application No. 14/021,790, filed September 9, 2013; Application No. 13/859,450, filed April 9, 2013; Application No. 13/622,872, filed September 19, 2012; and Application No. 13/387,343, filed February 12, 2012, under 35 U.S.C. § 120. It is understood that the Examiner will consider information that was submitted to or cited by the Office in such prior applications. M.P.E.P. § 609.02(A)(2). Copies of documents previously submitted to or cited by the Office in the prior application are not required to be provided in this application and thus are not attached. 37 C.F.R. § 1.98(d).

The Commissioner is hereby authorized to charge any underpayment of the following fees associated with this communication, including any necessary fees for the submission of an information disclosure statement under 37 CFR § 1.17(p) or for the extension of time, or credit any overpayment to Deposit Account No. 50-0310.

Respectfully submitted,

Date: December 19, 2017

By: /Gargi Talukder/
Gargi Talukder, Reg. No. 61,368
Filed Under 37 C.F.R. § 1.34

MORGAN LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
San Francisco, California 94105
Tel: 415.442.1000
Fax: 415.442.1001

10x Genomics, Inc. Exhibit 2001
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IPR2023-00958
Page 00123

Substitute for form 1449A/PTO (Substitute PTO/SB/8A)				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	**15/677,957**
				Filing Date	**August 15, 2017**
(use as many sheets as necessary)				First Named Inventor	**Sidney BRENNER**
				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**1**	of	**4**	Attorney Docket Number	**104371-5016-US08**

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	US-2003/0022231-A1	01-30-2003	WANGH	
	A2	US-2004/0224331	11-11-2004	CANTOR et al.	
	A3	US-2006/0008799	01-12-2006	CAI et al.	
	A4	US 2006/0177832 A1	08-10-2006	BRENNER	
	A5	US 2006/0177833 A1	08-10-2006	BRENNER	
	A6	US-2007/0020640	01-25-2007	MCCLOSKEY et al.	
	A7	US-2007/0072208-A1	03-29-2007	DRMANAC	
	A8	US-2007/0238113-A1	11-10-2007	KANDA et al.	
	A9	US-2007/0259357-A1	11-08-2007	BRENNER	
	A10	US-2009/0105959-A1	04-23-2009	BRAVERMAN	
	A11	US-2009/0155780	06-18-2009	XIAO et al.	
	A12	US-2010/0086914	04-08-2010	BENTLEY et al.	
	A13	US-2010/0113296	05-06-2010	MYERSON	
	A14	US-2010/0120098	05-13-2010	GRUNENWALD et al.	
	A15	US-2011/0287435	11-24-2011	GRUNENWALD et al.	
	A16	US-2012/0208724	08-16-2012	STEEMERS	
	A17	US-2012/0316074-A1	12-13-2012	SAXONOV	
	A18	US-2013/0059310	03-07-2013	BRENNER et al.	
	A19	US-6723513	04-20-2004	LEXOW	
	A20	US 7,329,493 B2	02-12-2008	CHOU et al.	
	A21	US-7544473	06-09-2009	BRENNER	
	A22	US-7700325	04-20-2010	CANTOR et al.	
	A23	US-8101346	01-24-2012	TAKAHAMA	
	A24	US-8168385-B2	05-01-2012	BRENNER	
	A25	US-8298767-B2	10-30-2012	BRENNER et al.	
	A26	US-8318433-B2	11-27-2012	BRENNER	
	A27	US-8318460-B2	11-27-2012	CANTOR et al.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.[1] Applicant's unique citation designation number (optional).[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).[4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.[6] Applicant is to place a check mark here if English language Translation is attached.

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

DB2/ 32412136.1

Substitute for form 1449A/PTO (Substitute PTO/SB/8A)				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	**15/677,957**
				Filing Date	**August 15, 2017**
				First Named Inventor	**Sidney BRENNER**
(use as many sheets as necessary)				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**2**	of	**4**	Attorney Docket Number	**104371-5016-US08**

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A28	US-8563274-B2	10-22-2013	BRENNER	
	A29	US-8679756-B1	03-25-2014	BRENNER et al.	
	A30	US-9102980-B2	08-11-2015	BRENNER	
	A31	US-9290808-B2	03-22-2016	FODOR	

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Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[2] Number[4] Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	A32	EP-1672064-A1	06-21-2006	Riken		
	A33	EP-1841879-A2	10-10-2007	Compass Genetics, LLC		
	A34	WO-2001090418-A1	11-29-2001	The Regents of the University of California		
	A35	WO-2003062462-A2	07-31-2003	Bosnes		
	A36	WO-2004061083-A2	07-22-2004	Amgen Inc.		
	A37	WO-2004065617-A2	08-05-2004	The Trustees of Boston University		
	A38	WO-2007018601-A1	02-15-2007	Rubicon Genomics, Inc.		
	A39	WO 2007147079 A2	12-21-2007	Living Microsystems, Inc. et al.		
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	A41	WO-2008150432-A1	12-11-2008	454 Life Sciences Corp		
	A42	WO 2010117620 A3	10-14-2010	Illumina, Inc.		
	A43	WO-2012148497-A2	11-01-2012	Robinson et al.		
	A44	WO-2013036929-A1	03-14-2013	The Board of Trustees of the Leland Stanford Jr University		

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	A45	"Using Multiplex Identifier (MID) Adaptors for the GS FLX Titanium Chemistry Basic MID Set" Genome Sequencer FLX System, Technnical Bulletin 004-2009, (Apr 1 2009) pp 1-7. URL:http://454.com/downloads/my454/documentation/technical-bulletins/TCB-09004 Using MultiplexIdentifierAdaptorsForTheGSFLXTitaniumSeriesChemistry-BasicMIDSet.pdf	

Examiner Signature		Date Considered	

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DB2/ 32412136.1

Substitute for form 1449A/PTO (Substitute PTO/SB/8A)				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	**15/677,957**
				Filing Date	**August 15, 2017**
				First Named Inventor	**Sidney BRENNER**
(use as many sheets as necessary)				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**3**	of	**4**	Attorney Docket Number	**104371-5016-US08**

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	A46	"Using Multiplex Identifier (MID) Adaptors for the GS FLX Titanium Chemistry Extended MID Set" Genome Sequencer FLX System, Technnical Bulletin 005-2009, (Apr 1 2009) pp 1-7. URL:http://454.com/downloads/my454/documentation/technical-bulletins/TCB-09005 UsingMultiplexIdentifierAdaptorsForTheGSFLXTitaniumChemistry-ExtendedMIDSet.pdf	
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	A48	BOULANGER, et al, "Massively parallel haplotyping on microscopic beads for the high-throughput phase analysis of single molecules", PLoS One, vol. 7:1-10, 2012.	
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	A52	IMBURGIO, et al, "Studies of promoter recognition and start site selection by T7 RNA polymerase using a comprehensive collection of promoter variants", Biochemistry., 39:10419-30, 2000.	
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	A60	LUNDIN, et al, "Hierarchical molecular tagging to resolve long continuous sequences by massively parallel sequencing", Sci Rep., 3:1186, 2003.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.[1] Applicant's unique citation designation number (optional).[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).[4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.[6] Applicant is to place a check mark here if English language Translation is attached.

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				Filing Date	**August 15, 2017**
(use as many sheets as necessary)				First Named Inventor	**Sidney BRENNER**
				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**4**	of	**4**	Attorney Docket Number	**104371-5016-US08**

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Examiner Initials*	Cite No.[1]	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[6]
	A61	OYOLA, et al, "Optimizing Illumina next-generation sequencing library preparation for extremely AT-biased genomes", BMC Genomics.,13:1, 2012. cited by applicant .	
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	A63	REISNER, et al, "Single-molecule denaturation mapping of DNA in nanofluidic channels", Proc Natl Acad Sci U.S.A., 107: 13294-9, 2010.	
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	A70	WANG; et al., "Self-Formed Adaptor PCR: a Simple and Efficient Method for Chromosome Walking", Applied and Environmental Microbiology (Aug. 2007), 73(15):5048-5051.	
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Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.[1] Applicant's unique citation designation number (optional).[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).[4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.[6] Applicant is to place a check mark here if English language Translation is attached.

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Electronic Acknowledgement Receipt

EFS ID:	31274078
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Gargi Talukder/Sheila Gloss
Filer Authorized By:	Gargi Talukder
Attorney Docket Number:	104371-5016-US08
Receipt Date:	19-DEC-2017
Filing Date:	15-AUG-2017
Time Stamp:	19:00:54
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	104371-5016-US08_IDS.pdf	352852 d0d9ed20d7fdba68a52e2457017c5eb2b4a1c578	no	6

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New International Application Filed with the USPTO as a Receiving Office
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08

CONFIRMATION NO. 1051

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

NEW OR REVISED PPD NOTICE

OC000000096246021

NOTICE OF NEW OR REVISED PROJECTED PUBLICATION DATE

The above-identified application has a new or revised projected publication date. The current projected publication date for this application is 03/22/2018. If this is a new projected publication date (there was no previous projected publication date), the application has been cleared by Licensing & Review or a secrecy order has been rescinded and the application is now in the publication queue.

If this is a revised projected publication date (one that is different from a previously communicated projected publication date), the publication date has been revised due to processing delays in the USPTO or the abandonment and subsequent revival of an application. The application is anticipated to be published on a date that is more than six weeks different from the originally-projected publication date.

More detailed publication information is available through the private side of Patent Application Information Retrieval (PAIR) System. The direct link to access PAIR is currently http://pair.uspto.gov. Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Questions relating to this Notice 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.

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Page 00130

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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
15/677,957	08/15/2017	1639	800	104371-5016-US08	6	1

CONFIRMATION NO. 1051

CORRECTED FILING RECEIPT

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

OC000000098118838

Date Mailed: 12/22/2017

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

Inventor(s)

Sydney Brenner, Ely, UNITED KINGDOM;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, Lindon, UNITED KINGDOM;

Applicant(s)

10X Genomics, Inc., Pleasanton, CA;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/792,094 07/06/2015
which is a CON of 14/172,694 02/04/2014 PAT 9102980
which is a CON of 14/021,790 09/09/2013 PAT 8679756
which is a CON of 13/859,450 04/09/2013 PAT 8563274
which is a CON of 13/622,872 09/19/2012 ABN
which is a CON of 13/387,343 02/15/2012 PAT 8298767
which is a 371 of PCT/IB2010/002243 08/13/2010
which claims benefit of 61/288,792 12/21/2009
and claims benefit of 61/235,595 08/20/2009

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.

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Page 00131

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

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If Required, Foreign Filing License Granted: 08/22/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/677,957**

Projected Publication Date: 03/22/2018

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

Preliminary Class

506

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

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Page 00134

PATENT

Application No. 15/677,957
Attorney Docket No. 104371-5016-US08

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Conf. No.: **1051**
Sidney BRENNER	Art Unit: **1639**
Application No.: **15/677,957**	Examiner: **Karla A. Dines**
Filed: **August 15, 2017**	Docket No.: **104371-5016-US08**
For: **Methods for Analyzing Nucleic Acids from Single Cells**	*Certificate of Transmission (37 C.F.R. § 1.8)* *I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office electronic filing system (EFS-Web) to the USPTO on December 19, 2017.* / Sheila R. Gloss / *Sheila R. Gloss*

Mail Stop AMENDMENT
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INFORMATION DISCLOSURE STATEMENT

Commissioner:

This Information Disclosure Statement is hereby submitted in accordance with 37 C.F.R. 1.98 and pursuant to Applicant's continuing duty under 37 C.F.R. 1.56 to bring any information which may be material to patentability of this application to the Examiner's attention.

Applicant makes no representation that a search has been conducted by the Applicant, or that there is not possibly more relevant art. 37 C.F.R. § 1.97(g). Applicant also makes no representation that the information submitted herewith is in fact material to patentability. The filing of this Information Disclosure Statement shall not be construed as an admission against interest in any manner. 37 C.F.R. § 1.97(h).

The Examiner's attention is directed to the reference(s) cited on the accompanying substitute for forms 1449A/PTO and PTO/SB/08. Except for U.S. Patents and U.S. Patent Application Publications, *see* 37 C.F.R. § 1.98(a)(2)(i), copies of the cited references are enclosed, unless otherwise noted below.

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This Information Disclosure Statement is being filed within three months of the filing date of a national application other than a continued prosecution application, within three months of the date of entry of a national stage, before the mailing of a first Office action on the merits, or before the mailing of a first Office action after the filing of a request for continued examination. 37 C.F.R. § 1.97(b). No fee is required.

This Application relies on the earlier filing date of prior Application No. 14/792,094, filed July 6, 2015; Application No. 14/021,790, filed September 9, 2013; Application No. 13/859,450, filed April 9, 2013; Application No. 13/622,872, filed September 19, 2012; and Application No. 13/387,343, filed February 12, 2012, under 35 U.S.C. § 120. It is understood that the Examiner will consider information that was submitted to or cited by the Office in such prior applications. M.P.E.P. § 609.02(A)(2). Copies of documents previously submitted to or cited by the Office in the prior application are not required to be provided in this application and thus are not attached. 37 C.F.R. § 1.98(d).

The Commissioner is hereby authorized to charge any underpayment of the following fees associated with this communication, including any necessary fees for the submission of an information disclosure statement under 37 CFR § 1.17(p) or for the extension of time, or credit any overpayment to Deposit Account No. 50-0310.

Respectfully submitted,

Date: December 19, 2017
By: /Gargi Talukder/
Gargi Talukder, Reg. No. 61,368
Filed Under 37 C.F.R. § 1.34

MORGAN LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
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Substitute for form 1449A/PTO (Substitute PTO/SB/8A)				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	15/677,957
				Filing Date	August 15, 2017
(use as many sheets as necessary)				First Named Inventor	Sidney BRENNER
				Art Unit	1639
				Examiner Name	Karla A. Dines
Sheet	1	of	4	Attorney Docket Number	104371-5016-US08

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	US-2003/0022231-A1	01-30-2003	WANGH	
	A2	US-2004/0224331	11-11-2004	CANTOR et al.	
	A3	US-2006/0008799	01-12-2006	CAI et al.	
	A4	US 2006/0177832 A1	08-10-2006	BRENNER	
	A5	US 2006/0177833 A1	08-10-2006	BRENNER	
	A6	US-2007/0020640	01-25-2007	MCCLOSKEY et al.	
	A7	US-2007/0072208-A1	03-29-2007	DRMANAC	
	A8	US-2007/0238113-A1	11-10-2007	KANDA et al.	
	A9	US-2007/0259357-A1	11-08-2007	BRENNER	
	A10	US-2009/0105959-A1	04-23-2009	BRAVERMAN	
	A11	US-2009/0155780	06-18-2009	XIAO et al.	
	A12	US-2010/0086914	04-08-2010	BENTLEY et al.	
	A13	US-2010/0113296	05-06-2010	MYERSON	
	A14	US-2010/0120098	05-13-2010	GRUNENWALD et al.	
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	A16	US-2012/0208724	08-16-2012	STEEMERS	
	A17	US-2012/0316074-A1	12-13-2012	SAXONOV	
	A18	US-2013/0059310	03-07-2013	BRENNER et al.	
	A19	US-6723513	04-20-2004	LEXOW	
	A20	US 7,329,493 B2	02-12-2008	CHOU et al.	
	A21	US-7544473	06-09-2009	BRENNER	
	A22	US-7700325	04-20-2010	CANTOR et al.	
	A23	US-8101346	01-24-2012	TAKAHAMA	
	A24	US-8168385-B2	05-01-2012	BRENNER	
	A25	US-8298767-B2	10-30-2012	BRENNER et al.	
	A26	US-8318433-B2	11-27-2012	BRENNER	
	A27	US-8318460-B2	11-27-2012	CANTOR et al.	

Examiner Signature		Date Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	15/677,957
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(use as many sheets as necessary)				First Named Inventor	Sidney BRENNER
				Art Unit	1639
				Examiner Name	Karla A. Dines
Sheet	2	of	4	Attorney Docket Number	104371-5016-US08

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A28	US-8563274-B2	10-22-2013	BRENNER	
	A29	US-8679756-B1	03-25-2014	BRENNER et al.	
	A30	US-9102980-B2	08-11-2015	BRENNER	
	A31	US-9290808-B2	03-22-2016	FODOR	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] Number[4] Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	A32	EP-1672064-A1	06-21-2006	Riken		
	A33	EP-1841879-A2	10-10-2007	Compass Genetics, LLC		
	A34	WO-2001090418-A1	11-29-2001	The Regents of the University of California		
	A35	WO-2003062462-A2	07-31-2003	Bosnes		
	A36	WO-2004061083-A2	07-22-2004	Amgen Inc.		
	A37	WO-2004065617-A2	08-05-2004	The Trustees of Boston University		
	A38	WO-2007018601-A1	02-15-2007	Rubicon Genomics, Inc.		
	A39	WO 2007147079 A2	12-21-2007	Living Microsystems, Inc. et al.		
	A40	WO-2008061193-A3	11-13-2008	Biospherex LLC et al.		
	A41	WO-2008150432-A1	12-11-2008	454 Life Sciences Corp		
	A42	WO 2010117620 A3	10-14-2010	Illumina, Inc.		
	A43	WO-2012148497-A2	11-01-2012	Robinson et al.		
	A44	WO-2013036929-A1	03-14-2013	The Board of Trustees of the Leland Stanford Jr University		

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	A45	"Using Multiplex Identifier (MID) Adaptors for the GS FLX Titanium Chemistry Basic MID Set" Genome Sequencer FLX System, Technnical Bulletin 004-2009, (Apr 1 2009) pp 1-7. URL:http://454.com/downloads/my454/documentation/technical-bulletins/TCB-09004 Using MultiplexIdentifierAdaptorsForTheGSFLXTitaniumSeriesChemistry-BasicMIDSet.pdf	

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				First Named Inventor	**Sidney BRENNER**
(use as many sheets as necessary)				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**3**	of	**4**	Attorney Docket Number	**104371-5016-US08**

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	A46	"Using Multiplex Identifier (MID) Adaptors for the GS FLX Titanium Chemistry Extended MID Set" Genome Sequencer FLX System, Technnical Bulletin 005-2009, (Apr 1 2009) pp 1-7. URL:http://454.com/downloads/my454/documentation/technical-bulletins/TCB-09005 UsingMultiplexIdentifierAdaptorsForTheGSFLXTitaniumChemistry-ExtendedMIDSet.pdf	
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	A48	BOULANGER, et al, "Massively parallel haplotyping on microscopic beads for the high-throughput phase analysis of single molecules", PLoS One, vol. 7:1-10, 2012.	
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	A57	KOZAREWA, et al. "Amplification-free Illumina sequencing-library preparation facilitates improved mapping and assembly of GC-biased genomes", Nat Methods., 6: 291-5, 2009.	
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	A59	LAIRD et al, Hairpin-bisulfite PCR: Assessing epigenetic methylation patterns on complementary strands of individual DNA molecules, 2004, PNAS, 101, 204-209.	
	A60	LUNDIN, et al, "Hierarchical molecular tagging to resolve long continuous sequences by massively parallel sequencing", Sci Rep., 3:1186, 2003.	

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(use as many sheets as necessary)				First Named Inventor	**Sidney BRENNER**
				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**4**	of	**4**	Attorney Docket Number	**104371-5016-US08**

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	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[6]
	A61	OYOLA, et al, "Optimizing Illumina next-generation sequencing library preparation for extremely AT-biased genomes", BMC Genomics.,13:1, 2012. cited by applicant .	
	A62	PCT/IB2010/002243, International Search Report and Written Opinion, mailed Feb. 9, 2011, 13pgs.	
	A63	REISNER, et al, "Single-molecule denaturation mapping of DNA in nanofluidic channels", Proc Natl Acad Sci U.S.A., 107: 13294-9, 2010.	
	A64	REPP et al. "Genotyping by Multiplex Polymerase Chain Reaction for Detection of Endemic Hepatitis B Virus Transmission" J Clinical Microbiology (1993) 31:1095-1102	
	A65	SCHWARTZ; et al., "Capturing native long-range contiguity by in situ library construction and optical sequencing", PNAS (Nov. 2012), 109(46)18749-18754. cited by applicant .	
	A66	TURNER, et al, "Assaying chromosomal inversions by single molecule haplotyping", Nat Methods., 3:439-445, 2006.	
	A67	TURNER, et al, "High-throughput haplotype determination over long distances by haplotype fusion PCR and ligation haplotyping", Nat Protoc., 4:1771-83, 2009.	
	A68	USHIJIMA et al, Detection and interpretation of altered methylation patterns in cancer cells, 2005, Nature reviews, 5, 223-231.	
	A69	Van Nieuwerburgh, et al, "Illumina mate-paired DNA sequencing-library preparation using Cre-Lox recombination", Nucleic Acids Res., 40:1-8, 2012.	
	A70	WANG; et al., "Self-Formed Adaptor PCR: a Simple and Efficient Method for Chromosome Walking", Applied and Environmental Microbiology (Aug. 2007), 73(15):5048-5051.	
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	A72	XIAO, et al, "Determination of haplotypes from single DNA molecules: a method for single-molecule barcoding", Hum Mutat., 28:913-21, 2007.	
	A73	YAN, PU et al. "Rapid on-step construction of hairpin RNA" Biochem and Biophys Res Comm (Jun 12 2009) 383(4):464-468	

Examiner Signature	/KARLA A DINES/	Date Considered	12/21/2017

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	58	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 11:59
L2	27	mikawa-gi.in. and tags	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:05
L3	22	mikawa-gi.in. and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:06
L4	184	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
L5	14	l4 and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
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L7	44	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
L8	14	l7 and ((tags or barcodes) with "linear	US-PGPUB;	OR	OFF	2017/12/20

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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		amplification")	USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			12:11
L9	19	l7 and (tags or barcodes)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:22
L10	0	l7 and (tags or barcodes)with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:23
L11	38	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:24
L12	2655	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:26
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L14	54	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with amplification with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
L15	54	l14 not l11	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
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S2	73	S1 and "single cell"	USPAT	OR	OFF	2017/12/18

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						09:27
S3	9	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))and "single cell sequencing"	USPAT	OR	OFF	2017/12/18 09:31
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S6	97	barcode same "nucleic acid" same "single cell" same sequenc$4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 12:30
S7	172	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:42
S8	49	S7 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:43
S9	48	S7 and "single cell" and sequenc$3	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S10	1	S7 and "single cell" and sequenc$3 and ("multiplex identifier" or "MID")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S11	5	S7 and ("single cell" and sequenc$3).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 14:22

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S12	442	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:13
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Search	Add to builder	
#7	Add	Search **Slater, Andrew[Author]**
#6	Add	Search **(#5) AND #2**
#5	Add	Search **Osborne, Robert[Author]**
#4	Add	Search **mikawa, gi[Author]**
#3	Add	Search **(#1) AND #2**
#2	Add	Search **(barcode) OR tag**
#1	Add	Search **Brenner, Sydney[Author]**

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	Art Unit
	KARLA A DINES	1639

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
EAST and PALM searches	12/18/2017	kd
EAST and PubMed Searches	12/18/2017	kd
EAST inventor search	12/20/2017	kd

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

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

43850 7590 12/27/2017

MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CALIFORNIA 94105

EXAMINER	
DINES, KARLA A	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
12/27/2017	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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donald.mixon@morganlewis.com
sfipdocketing@morganlewis.com

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Office Action Summary	**Application No.** 15/677,957	**Applicant(s)** Brenner et al.	
	Examiner KARLA A DINES	**Art Unit** 1639	**AIA Status** No

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

Period for Reply

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

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

Status

1)☑ Responsive to communication(s) filed on 15 August 2017 .

☐ 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) 1-6 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) 1-6 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 08 September 2017 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

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

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

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

Attachment(s)

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

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date 12/19/2017.

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

4) ☐ Other: _____.

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Notice of Pre-AIA or AIA Status

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

DETAILED ACTION

Track1 Request

The track1 request filed by the applicant on August 15, 2017 has been granted by the office on September 14, 2017. Therefore instant application has been examined on a priority basis. To maintain its status applicant is required to follow the requirements listed in the Track 1 grant document.

Status of the Claims

Claims 1-6 are currently pending and examined on the merits.

Information Disclosure Statement

The information disclosure statement filed 12/19/2017 is acknowledged. A signed copy of the corresponding 1449 form has been included with this Office action.

Drawings

The drawings filed on 9/8/2017 are received and accepted.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a judicial exception (i.e. a law of nature, a natural phenomenon, or an abstract idea) without significantly more. Claims 1-6 are directed to an abstract idea of mathematical relationships and a law of nature. The rationale for this determination is explained below and is based on the analysis presented in the "2014 Interim Guidance on Patent Subject Matter Eligibility" of December 16, 2014. This information can be found at: http://www.uspto.gov/patent/laws-and-regulations/examination-policy/2014-interim-guidance-subject-matter-eligibility-0

According to the 2014 interim Eligibility Guidance an initial two step analysis is required for determining statutory eligibility. Step 1 requires a determination of whether the claims are directed to a process, machine, manufacture, or a composition of matter. In the instant case the Step 1 requirement is satisfied as the claims are directed towards a process. The Step 2 analysis is a two-part analysis, Step 2A and Step 2B, with the first part Step 2A requiring a determination of whether the claims are directed towards a judicial exception, i.e. a law of nature, natural phenomenon, or an abstract idea.

In the instant case, the claims as stated are drawn to a method of analyzing nucleic acids from a plurality of cells, with the last 2 steps in the method, steps (d) and (e), reciting using a first tag to correlate an identified polynucleotide sequence with the single cell from which the polynucleotide sequence is derived and a second tag sequence is used to correlate an identified to correlate an identified polynucleotide sequence with the plurality of sample polynucleotides from which the polynucleotide sequence is derived. These steps involve the mental step of performing a correlation.

This judicial exception is of the type identified by the Courts as an abstract idea akin to the following cases: “the collection, analysis, and display of available information in a particular field” (*Electric Power Group* (Fed. Cir. 2016)); “the broad concept of monitoring audit log data” (*FairWarning IP LLC* (Fed Cir 2016)). As summarized in *FairWarning*, the courts have explained that the "realm of abstract ideas" includes "collecting information, including when limited to particular content." (*Electric Power* (Fed. Cir. 2016) (collecting cases)). The courts have also "treated analyzing information by steps people go through in their minds, or by mathematical algorithms, without more, as essentially mental processes within the abstract-idea category." And the courts have found that "merely presenting the results of abstract processes of collecting and analyzing information, without more (such as identifying a particular tool for presentation), is abstract as an ancillary part of such collection and analysis." *Id.* Therefore, as in *Electric Power,* "the focus of the claims is not on . . . an improvement in computers as tools, but on certain independently abstract ideas that use computers as tools." The remaining steps in claim 1 were well-understood, routine steps before the filing of the instant invention and the claim, and when viewed as a whole, fail to result in something significantly more than the judicial exception of an abstract idea.

The dependent claims add elements in addition to the judicial exception(s) that fail to rise to the level of significantly more than the judicial exception(s) as they are routine, well-understood and conventional in molecular biology.

As such, the instant claims are drawn to an abstract idea of analyzing nucleic acids by correlating tag sequences with sequencing data. Therefore the result of Step 2A analysis is that the claims are directed towards a judicial exceptions, i.e. an abstract

idea. The second part, Step 2B of the two step analysis is to determine whether any element or combination of elements, in the claim is sufficient to ensure that the claim as a whole amounts to significantly more than the judicial exception. Generating a plurality of tagged polynucleotides from a plurality of single cells comprising a first tag sequence associated with a single cell and a second tag sequence distinguishing the sample polynucleotides from the plurality of other sample polynucleotides and sequencing the plurality of tagged polynucleotides are well-known, routine and conventional in genetics technology. No additional steps are recited in the instantly claimed invention that would amount to significantly more than the judicial exception. Without additional limitations, a process that employs mental steps to manipulate existing information to generate additional information is not patent eligible. Furthermore, if a claim is directed essentially to a method of employing mental steps, even if the solution is for a specific purpose, the claimed method is non-statutory. In summation, the limitations of the claims, individually, *and in ordered combination as a whole*, do not rise to the level of significantly more than the judicial exception(s) identified above, and the claims are not patent eligible subject matter.

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 1-6 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps (See MPEP § 2172.01). The omitted steps are:

(i) the details of the steps of tagging first and second MID sequences to the plurality of segments of the nucleic acid molecules from the plurality of nucleic acid samples from plurality of single isolated cells,

(ii) not specifying the step of tagging nucleic acid molecules from, for example, single isolated cell 1 with first MID sequences separately from the step of tagging nucleic acid molecules from single isolated cells with first MID sequences and

(iii) not specifying the step of how plurality of tagged segments of nucleic acid molecules with first MID sequences from plurality of nucleic acid samples uniquely identifies the nucleic acid molecules from single isolated cell because claim 1 does not specify if first MID sequences from isolated single cells are different from first MID sequences from isolated single cell 2. Similarly, the steps of tagging different second MID sequences to the type of nucleic acid molecules from plurality of nucleic acid samples are omitted.

Claims 2-6 are rejected due to their dependency on claim 1.

Claim Rejections - 35 USC § 102

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

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

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 1-6 are rejected under pre-AIA 35 U.S.C. 102(A)(1)/(A)(2) as being anticipated by Linnarsson (WO2010117620, cited in the IDS filed 12/19/2017).

Instant Claim 1 is drawn to a method of analyzing nucleic acids from a plurality of single cells.

Regarding claims 1 and 6, Linnarsson teaches a method of preparing nucleic acid libraries from a plurality of single cells, the method comprising the steps of: releasing mRNA from each single cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell, synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell, pooling the

tagged cDNA samples, and amplifying the pooled cDNA samples to generate a cDNA library, wherein the method further comprises processing the cDNA library to obtain a library suitable for sequencing and sequencing the cDNA library to identify genes originated from the cell source; e.g. Figs. 1-4 and claims 1-5 and 9-11. The cell specific tag (e.g., see figure 3) in the nucleic acid sample from each of the single cell is the first Multiplex Identifier (first MID) sequences associated with a segment of a nucleic acid molecule of (a) uniquely identifies the single isolated cell from which the nucleic acid molecule is provided.

Linnarsson also teaches that the synthesis of the first strand of cDNA is directed by a cDNA synthesis primer (CDS) that includes an RNA complementary sequence (RCS) that is at least partially complementary to one or more mRNA in an individual mRNA sample (Linnarsson claim 3), wherein a template-switching oligonucleotide (TSO) is added to each individual mRNA sample, wherein said TSO comprises a portion which is at least partially complementary to a portion at the 3' end of the first strand of cDNA (Linnarsson claim 5), wherein the CDS and the TSO each include a different tag (Linnarsson claims 10 and 11). Different tags associated with cDNA segment of Linnarsson meets the limitation of second MID sequences are different from each other.

Regarding the limitations in claim 1, steps (d) and (e), these limitations are reasonably interpreted as at best either a characteristic or an intended use limitation.

It is further noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited

or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Regarding claim 2, Linnarsson teach amplifying the tagged polynucleotide prior to sequencing; e.g. claim 1.

Regarding claims 3 and 4, Linnarsson teach mRNA sample polynucleotides; e.g. claim 1.

Regarding claim 5, Linnarsson teaches ligating the adaptor to the nucleic acid segments; e.g. pg. 29, lines 3-11.

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 claims at issue 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); and *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 a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l) (1) - 706.02(l) (3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/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 http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 9,410,149 in view of Linnarsson (WO 2010/117620 published Oct. 14, 2010, priority date Mar. 30, 2009) for the following reasons.

Regarding instant claim 1 and 3 and claims 1, 10, 12 and 13 of '149 patent disclose a method of analyzing DNA. One having ordinary skill in the art would

recognize that nucleic acid from a bacterium meets the limitation of an isolated single cell.

Claims of '149 patent do not disclose step of generating a tag sequence that distinguishes sample polynucleotides from the other pluralities of sample polynucleotides derived from the same single cell. However, this limitation is taught by Linnarsson, who teaches a method of preparing a nucleic acid libraries from a plurality of single cells, the method comprising the steps of: releasing mRNA from each single cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell; synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell; pooling the tagged cDNA samples; and amplifying the pooled cDNA samples to generate a cDNA library comprising double-stranded cDNA, wherein the method further comprises processing the cDNA library to obtain a library suitable for sequencing and sequencing the cDNA library to identify genes originated from the cell source; e.g. Fig. 1 and its legend, and Linnarsson, claims 1-5 and 9-11. Linnarsson also teaches pooling the samples simplifies handling of the samples from each single cell and reduces the time required to analyze gene expression in the single cells, which allows high throughput analysis of gene expression. Pooling the samples prior to amplification also provides the advantage that technical variation between samples is virtually eliminated (pg. 11, paragraph 1), thus providing motivation to include the step of including the tagging the nucleic acid

sample for each of the isolated single cell and pooling the plurality of isolated single cell nucleic acids in the claims of '149 patent.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include the step of including the tagging the nucleic acid sample for each of the isolated single cells and pooling the plurality of isolated single cell nucleic acids in the claims of '149 patent with a reasonable expectation of success with the expected benefit of allowing high throughput analysis of gene expression and eliminating the technical variation between samples as taught by Linnarsson (pg. 11, paragraph 1). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves including additional step of tagging nucleic acid sample with identifier sequence which is routinely practiced in the art as exemplified Linnarsson.

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12, 13 and 19 of U.S. Patent No. 9,410,150 in view of Linnarsson (WO 2010/117620) for the following reasons.

Regarding instant claims 1 and 3 and claims 1, 10, 12, 13 and 19 of '150 patent, although the conflicting claims are not identical, they are not patentably distinct from each other because the difference between the instant claims and claims 1, 10, 12, 13 and 19 of '150 patent is that instant claim 1 recites a step of generating a tag sequence that distinguishes sample polynucleotides from the other pluralities of sample polynucleotides derived from the same single cell, a step not recited by the '150 patent. However, this limitation is taught by Linnarsson, who teaches a method of preparing a

nucleic acid libraries from a plurality of single cells, the method comprising the steps of: releasing mRNA from each single cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell; synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell; pooling the tagged cDNA samples; and amplifying the pooled cDNA samples to generate a cDNA library comprising double-stranded cDNA, wherein the method further comprises processing the cDNA library to obtain a library suitable for sequencing and sequencing the cDNA library to identify genes originated from the cell source; e.g. Fig. 1 and its legend, and Linnarsson, claims 1-5 and 9-11. Linnarsson also teaches pooling the samples simplifies handling of the samples from each single cell and reduces the time required to analyze gene expression in the single cells, which allows high throughput analysis of gene expression. Pooling the samples prior to amplification also provides the advantage that technical variation between samples is virtually eliminated (pg. 11, paragraph 1), thus providing motivation to include the step of including the tagging the nucleic acid sample for each of the isolated single cell and pooling the plurality of isolated single cell nucleic acids in the claims of '150 patent.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include the step of providing a plurality of nucleic acid samples each made from single isolated cells and analyzing the nucleic acid samples of Linnarsson in the claims of '150 patent with a reasonable expectation of success with the expected benefit of allowing high throughput analysis of gene

expression and eliminating the technical variation between samples as taught by Linnarsson (pg. 11, paragraph 1). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves including additional step of tagging nucleic acid sample with identifier sequence which is routinely practiced in the art as exemplified Linnarsson.

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 11 and 12 of U.S. Patent No. 8,679,756 in view of Linnarsson (WO 2010/117620 as cited above) for the following reasons.

It is noted that the subject matter of claims 1-12 of '756 patent are similar to claims 1-13 and 12of '149 patent. Therefore analysis is very similar. Thus it is maintained that steps of instant claims 1 and 3 are not significantly different from claims 1, 11 and 12 of '756 patent in view of Linnarsson.

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 8,563,274 in view of Linnarsson (WO 2010/117620 as cited above) for the following reasons.

It is noted that the subject matter of claims 1-11 of '274 patent is similar to claims 1-13 of '149 patent. Therefore analysis is very similar. Thus it is maintained that steps of instant claims 1 and 3 are not significantly different from claims 1-11 of '274 patent in view of Linnarsson.

Claims 1-6 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 56-60 of copending Application No. 14/792,094 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims differ only in that they recite using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the polynucleotide sequence is derived and using the second tag sequence to correlate the identified polynucleotide sequence with the plurality of sample polynucleotides from which the polynucleotide sequence is derived. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph). Likewise, these limitations are reasonably interpreted as at best either a characteristic or an intended use limitation.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLA A DINES whose telephone number is (571)272-6837. The examiner can normally be reached on Monday-Friday 7am-4pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

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

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

/KARLA A DINES/
Primary Examiner, Art Unit 1639

UNITED STATES PATENT AND TRADEMARK OFFICE

USPTO Automated Interview Request (AIR)

Mar 8 2018

This paper requesting to schedule and/or conduct an interview is appropriate because:

This submission is requested to be accepted as an authorization for this interview to communicate via the internet. Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with the undersigned concerning scheduling of the interview via video conference, instant messaging, or electronic mail, and to conduct the interview in accordance with office practice including video conferencing.

Name(s):
Gargi Talukder

S-signature:
/Gargi Talukder/

Registration Number:
61368

U.S. Application Number:
15677957

Confirmation Number:
1051

E-mail Address:
gargi.talukder@morganlewis.com

Phone Number:
4154421266

Proposed Time of Interview:
3-19-2018 4:00 PM ET

Prefered Interview Type:
Telephonic

I am the applicant or applicant's representative for this application.

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PALM-SILVER

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08

CONFIRMATION NO. 1051

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

PUBLICATION NOTICE

OC000000098225058

Title:METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

Publication No.US-2018-0080075-A1
Publication Date:03/22/2018

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.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

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

10x Genomics, Inc. Exhibit 2001
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: **1051**
Sydney Brenner et al.	Examiner: **Karla A. Dines**
Application No.: **15/677,957**	Art Unit: **1639**
Filed: **August 15, 2017**	
For: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	**RESPONSE TO OFFICE ACTION**

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

Commissioner:

In response to the Office Action mailed December 27, 2017, please enter the following amendments and remarks:

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

Remarks/Arguments begin on page **4** of this paper.

10x Genomics, Inc. Exhibit 2001
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PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

☒ Practitioners associated with Customer Number: 43850

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignments documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

☒ The address associated with Customer Number: 43850

OR

☐	Firm or Individual Name			
	Address			
	City		State	Zip
	Country			
	Telephone		Email	

Assignee Name and Address: 10X Genomics, Inc.
7068 Koll Center Parkway, Suite 401
Pleasanton, CA 94566

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/AIA/96 or equivalent) is required to be Filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of The practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature	[signature]	Date	8/13/2015
Name	Matthew Murphy	Telephone	(925) 401-7495
Title	Vice President, General Counsel		

This collection of information is required by 37 CFR 1.31, 1.32 and 1.33. 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 3 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.**

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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.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
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STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: 10X GENOMICS, INC.

Application No./Patent No.: 15/677,957 Filed/Issue Date: August 15, 2017

Titled: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

10X GENOMICS, INC., a corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

   ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached.

B. ☑ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

   1. From: Inventors To: Population Genetics Technologies Ltd.

      The document was recorded in the United States Patent and Trademark Office at

      Reel 044602, Frame 0905, or for which a copy thereof is attached.

   2. From: Population Genetics Technologies Ltd. To: 10X GENOMICS, INC.

      The document was recorded in the United States Patent and Trademark Office at

      Reel 044603, Frame 0040, or for which a copy thereof is attached.

This collection of information is required by 37 CFR 3.73(b). 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 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.

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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.

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

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6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☑ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Gargi Talukder — Signature

3/26/2018 — Date

Gargi Talukder — Printed or Typed Name

61,368 — Title or Registration Number

Electronic Acknowledgement Receipt	
EFS ID:	32162172
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Gargi Talukder/Sheila Gloss
Filer Authorized By:	Gargi Talukder
Attorney Docket Number:	104371-5016-US08
Receipt Date:	26-MAR-2018
Filing Date:	15-AUG-2017
Time Stamp:	20:01:06
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		104371-5016-US08_Response.pdf	140129 0bb4ddac73d2fb47a7bbab60c9ee839cae32a24b	yes	8

	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Applicant Arguments/Remarks Made in an Amendment		4	8	
	Claims		2	3	
	Amendment/Req. Reconsideration-After Non-Final Reject		1	1	
Warnings:					
Information:					
2	Power of Attorney	10X_POA.pdf	635234 211a33dbdc739b2aa0078dc2e064e08f8cd6b7ae	no	2
Warnings:					
Information:					
3	Assignee showing of ownership per 37 CFR 3.73	104371-5016-US08_STMT.pdf	125723 18d3db6a9081b4eb809abb9f82ee5698e22a1e0c	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	901086		

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.

Remarks/Arguments

Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Interview summary

Examiner Dines and Applicants' representative, Gargi Talukder, participated in a telephone interview on March 19, 2018.

Examiner Dines and Applicants' representative discussed the § 102 rejection and the cited Linnarsson reference (WO 2010/117620). Applicants' representative noted that Linnarsson does not describe the second tag element in the claims. Examiner Dines stated that she would need to review the reference further and recommended that a response be filed and a follow-up interview scheduled if needed. Examiner Dines further confirmed that if the § 102 rejection were overcome by Applicants' arguments, the § 101 rejection would also be rendered moot/overcome.

Applicants are grateful to the Examiner for her time and attention to this matter.

Status of the Claims

Claims 1-6 are pending and under consideration in this application.

Claim 1 is amended to clarify elements of the invention. This amendment is supported throughout the specification, for example in paragraph [0084] of the application as filed.

Applicants respectfully request entry of the claims as amended into the record.

Response to Office Action

Claim Rejections – 35 USC § 101

Claims 1-6 are rejected under 35 U.S.C. § 101 for the invention being allegedly directed to a judicial exception. Applicants respectfully disagree.

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IPR2023-00958
Page 00173

As discussed in the above Interview Summary, the Examiner has acknowledged that the § 101 rejection flows with the § 102 rejection. As such, Applicants defer discussion of this rejection in favor of the discussion provided below regarding the anticipation rejection. In light of the remarks related to the § 102 rejection, Applicants respectfully request that all rejections under § 101 be withdrawn.

Claim Rejections – 35 USC § 112 second paragraph

Claims 1-6 are rejected under 35 U.S.C. § 112 (pre-AIA), second paragraph, as allegedly being incomplete for omitting essential steps. Applicants respectfully disagree.

The Office has identified three allegedly omitted steps on page 6 of the Office Action. Applicants discuss each of the three below in accordance with the numbering utilized in the Office Action.

For allegedly omitted step (i), Applicants respectfully submit that exemplary methods of tagging MID sequences are provided throughout the specification, and that identifying the specific details of such tagging methods are not essential steps for the claimed method. The inventive feature of the claimed method is that the MIDs contain two tag sequences, one of which is associated with the single cell from which the sample polynucleotide is derived and the other distinguishes the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell. The specific method of tagging is not essential to that inventive feature. Applicants note that methods of tagging are described for example in paragraphs [0023] – [0024], [0030], [0059] – [0094].

For allegedly omitted step (ii), as discussed above for (i), exemplary methods of tagging MID sequences are provided throughout the specification, and identifying the specific details of such tagging methods are not essential steps for the claimed method. The skilled artisan would appreciate based on the methods known in the art and described in the present specification that multiple methods could be used to generate the tagged sequences of the presently claimed invention and that specifying the order of generating those tagged sequences is not a necessary technical element of the claimed invention.

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For allegedly omitted step (iii), to assist with clarifying elements of the claimed invention and without conceding to the propriety of this rejection, Applicants have amended claim 1 to recite that the first tag sequence is different for different single cells from the plurality of single cells.

For at least the foregoing reasons, Applicants respectfully request that all rejections under §112 be withdrawn.

Claim Rejections – 35 USC § 102

Claims 1-6 are rejected under pre-AIA 35 U.S.C. § 102(A)(1)(A)(2) as allegedly being anticipated by Linnarsson (WO2010117620). Applicants respectfully disagree.

As will be appreciated, to support a prima facie case of anticipation, a single prior art reference must expressly or inherently disclose each and every element as set forth in the claim. The identical invention must be shown in as complete detail as is contained in the claim. See MPEP § 2131. Applicants submit that Linnarsson fails to disclose every element of the present claims, and as such a rejection under § 102 cannot be maintained.

The Office appears to be equating the tags in the present claims to the template switching oligonucleotides in Linnarsson. Applicants submit that the template switching oligonucleotides (TSOs) described in Linnarsson do not have two tag sequences, one of which is associated with the single cell from which the sample polynucleotide is derived and the other distinguishes the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell, as is recited in the present claims. The TSOs in Linnarsson are essentially a single tag that is associated with a particular well, which may or may not contain a single cell. As such, Linnarsson does not describe a second tag that distinguishes the sample polynucleotides from other pluralities of sample polynucleotides derived from the same cell. For example, Linnarsson describes use of the TSOs on page 32 with a single cell being collected into each well of a 96-well capture plate and then associating a different TSO with each well: "Each well of the capture plate contained a different template-switching helper oligo (STRT-FW-n) with a distinct barcode." Similarly, the description on page 37 of Linnarsson also describes a different TSO used in each well: "A different helper oligo was used in each well, with distinct five-base

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barcodes and universal primer sequence." There is no disclosure or suggestion in Linnarsson of a second tag sequence distinguishing the sample polynucleotide from other pluralities of sample polynucleotides from the same single cell. Thus, Linnarsson cannot support a rejection for anticipation.

For at least the foregoing reasons, Applicants respectfully request that all rejections under §102 be withdrawn.

Claim Rejections – Double Patenting

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12 and 13 of U.S. Patent No. 9,410,149 in view of Linnarsson (WO 2010/117620). Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12, 13 and 19 of U.S. Patent No. 9,410,150 in view of Linnarsson (WO 2010/117620). Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 11 and 12 of U.S. Patent No. 8,679,756 in view of Linnarsson (WO 2010/117620). Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 8,563,274 in view of Linnarsson (WO 2010/117620). Claims 1-6 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 56-60 of co-pending Application No. 14/792,094.

Applicants request that this matter be held in abeyance until the present application is in condition for allowance.

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CONCLUSION

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Order No.: 104371-5016-US08).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: March 26, 2018 By: /Gargi Talukder/
Gargi Talukder, Reg. No. 61,368

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Amendments to the Claims:

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

Listing of Claims:

1. (Currently Amended) A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
   (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
   (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
      (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
      (ii) a multiplex identifier (MID) sequence comprising:
         I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and
         II. a second tag sequence distinguishing the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell;
   (c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;
   (d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the polynucleotide sequence is derived; and
   (e) using the second tag sequence to correlate the identified polynucleotide sequence with the plurality of sample polynucleotides from which the polynucleotide sequence is derived.

2. (Original) The method of claim 1, wherein the method further comprises amplifying the tagged polynucleotides prior to the sequencing step (c).

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3. (Original) The method of claim 1, wherein the sample polynucleotides are selected from DNA and RNA.

4. (Original) The method of claim 3, wherein the sample polynucleotides comprise mRNA.

5. (Original) The method of claim 1, wherein the tagged polynucleotides are generated through at least one ligation reaction.

6. (Original) The method of claim 1, wherein the tagged polynucleotides are generated through PCR or linear amplification of the plurality of sample polynucleotides using an adapter sequence comprising the MID sequence and an amplification primer.

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Remarks/Arguments

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Claims 1-6 are rejected under 35 U.S.C. § 101 for the invention being allegedly directed to a judicial exception. Applicants respectfully disagree.

10x Genomics, Inc. Exhibit 2001
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IPR2023-00958
Page 00180

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For allegedly omitted step (iii), to assist with clarifying elements of the claimed invention and without conceding to the propriety of this rejection, Applicants have amended claim 1 to recite that the first tag sequence is different for different single cells from the plurality of single cells.

For at least the foregoing reasons, Applicants respectfully request that all rejections under §112 be withdrawn.

Claim Rejections – 35 USC § 102

Claims 1-6 are rejected under pre-AIA 35 U.S.C. § 102(A)(1)(A)(2) as allegedly being anticipated by Linnarsson (WO2010117620). Applicants respectfully disagree.

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The Office appears to be equating the tags in the present claims to the template switching oligonucleotides in Linnarsson. Applicants submit that the template switching oligonucleotides (TSOs) described in Linnarsson do not have two tag sequences, one of which is associated with the single cell from which the sample polynucleotide is derived and the other distinguishes the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell, as is recited in the present claims. The TSOs in Linnarsson are essentially a single tag that is associated with a particular well, which may or may not contain a single cell. As such, Linnarsson does not describe a second tag that distinguishes the sample polynucleotides from other pluralities of sample polynucleotides derived from the same cell. For example, Linnarsson describes use of the TSOs on page 32 with a single cell being collected into each well of a 96-well capture plate and then associating a different TSO with each well: "Each well of the capture plate contained a different template-switching helper oligo (STRT-FW-n) with a distinct barcode." Similarly, the description on page 37 of Linnarsson also describes a different TSO used in each well: "A different helper oligo was used in each well, with distinct five-base

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For at least the foregoing reasons, Applicants respectfully request that all rejections under §102 be withdrawn.

Claim Rejections – Double Patenting

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12 and 13 of U.S. Patent No. 9,410,149 in view of Linnarsson (WO 2010/117620). Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12, 13 and 19 of U.S. Patent No. 9,410,150 in view of Linnarsson (WO 2010/117620). Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 11 and 12 of U.S. Patent No. 8,679,756 in view of Linnarsson (WO 2010/117620). Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 8,563,274 in view of Linnarsson (WO 2010/117620). Claims 1-6 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 56-60 of co-pending Application No. 14/792,094.

Applicants request that this matter be held in abeyance until the present application is in condition for allowance.

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CONCLUSION

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Order No.: 104371-5016-US08).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: March 26, 2018 By: /Gargi Talukder/
Gargi Talukder, Reg. No. 61,368

Customer No.: 43850
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One Market, Spear Street Tower
San Francisco, CA 94105
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PTO/SB/06 (09-11)
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/677,957	Filing Date 08/15/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

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

APPLICATION AS AMENDED – PART II

AMENDMENT	03/26/2018	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 6	Minus	** 20	= 0	X $50 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $230 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

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

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

LIE
CAROLYN THOMAS

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.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

43850 7590 03/27/2018

MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CALIFORNIA 94105
UNITED STATES OF AMERICA

EXAMINER	
DINES, KARLA A	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
03/27/2018	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

donald.mixon@morganlewis.com
sfipdocketing@morganlewis.com

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Applicant-Initiated Interview Summary	**Application No.** 15/677,957	**Applicant(s)** Brenner et al.	
	Examiner KARLA A DINES	**Art Unit** 1639	**AIA Status** No

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

(1) KARLA A. DINES. (3) _____.

(2) Gargi Talukder. (4) _____.

Date of Interview: 19 March 2018.

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

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

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

Claim(s) discussed: 1.

Identification of prior art discussed: Linnarsson.

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

Applicant's representative stated that the prior art of Lnnarsson does not teach a second tag, and that on page 32 of the examples, each cell is in a well, so that the cells are labeled but each individual polynucleotide from that cell is not labeled. The 101 was discussed, with Applicant's representative suggesting possibly changing the wording so that the word "correlating" was changed to something else. However, the examiner pointed out that if the method itself is novel, and not known in the prior art, then the method would be patent eligible under 35 USC 101. Applicant indicated that a response would be filed in the next week. Another interview might take place after that time. No agreement was reached..

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

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

☐ Attachment

/KARLA A DINES/ Primary Examiner, Art Unit 1639	

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Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

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

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

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

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

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

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

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

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

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

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

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

Examiner to Check for Accuracy

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

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08

CONFIRMATION NO. 1051

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

POA ACCEPTANCE LETTER

OC000000098476281

Date Mailed: 04/03/2018

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 03/26/2018.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

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**.

/dgela/

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

43850 7590 07/10/2018

MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CALIFORNIA 94105
UNITED STATES OF AMERICA

EXAMINER	
DINES, KARLA A	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
07/10/2018	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

donald.mixon@morganlewis.com
sfipdocketing@morganlewis.com

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Office Action Summary	**Application No.** 15/677,957	**Applicant(s)** Brenner et al.	
	Examiner KARLA A DINES	**Art Unit** 1639	**AIA Status** No

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

Period for Reply

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

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

Status

1)☑ Responsive to communication(s) filed on 26 March 2018.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

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

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

Disposition of Claims*

5) ☑ Claim(s) 1-6 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) 1-6 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: _____.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Notice of Pre-AIA or AIA Status

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

Status of the Claims

Claims 1-6 are currently pending and examined on the merits.

Withdrawn Rejections/Objections

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn in view of the amendments filed 3/26/2018. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The 35 USC § 101 rejection of claims 1-6 is hereby withdrawn. The active steps in the claims, steps (a) and (b) were not usual and customary, well-understood and routine at the time of the instant invention.

The 35 USC § 112 rejection of claims 1-6 is hereby withdrawn in view of the amended claims.

The double patenting rejection over application 14/792,094 is withdrawn in view of the abandonment of application 14/792,094.

Claim Rejections - 35 USC § 102

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of

rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim(s) 1-6 is/are rejected under pre-AIA 35 U.S.C. 102(e) as being anticipated by Linnarsson (WO2010117620, cited in the IDS filed 12/19/2017).

Instant Claim 1 is drawn to a method of analyzing nucleic acids from a plurality of single cells.

Regarding claims 1 and 6, Linnarsson teaches a method of preparing nucleic acid libraries from a plurality of single cells, the method comprising the steps of:

releasing mRNA from each single cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell,

synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell,

pooling the tagged cDNA samples, and amplifying the pooled cDNA samples to generate a cDNA library comprising double-stranded cDNA, wherein the method further comprises processing the cDNA library to obtain a library suitable for sequencing, and sequencing the cDNA library to identify genes originated from the cell source; e.g. Figs. 1-4 and claims 1-5 and 9-11.

The cell specific tag (e.g. Figure 3) in the nucleic acid sample from each of the single cell is the first Multiplex Identifier (first MID) sequences associated with a segment of a nucleic acid molecule of (a) uniquely identifies the single isolated cell from which the nucleic acid molecule is provided. Linnarsson teaches on page 4, lines 8-13, that their method is a method of analyzing gene expression in a plurality of cells and that each single cell is placed in a separate well of a 96-well plate, lysed, further teaching tagging cDNA samples which are pooled and then sequenced. Taught is identification of expressed genes and identification of cells from which they are originated. Figure 3 depicts a “cell-tag”, “XXXXX”, which is reasonably interpreted to depict a tag that identifies a particular cell among a plurality of cells. Claim 14 teaches that each cDNA sample has a distinct tag or combination of tags.

Regarding claim 2, Linnarsson teach amplifying the tagged polynucleotide prior to sequencing; e.g. claim 1.

Regarding claims 3 and 4, Linnarsson teach mRNA sample polynucleotides; e.g. claim 1.

Regarding claim 5, Linnarsson teaches ligating the adaptor to the nucleic acid segments; e.g. pg. 29, lines 3-11.

Response to Arguments

Applicant's arguments filed 3/26/2018 have been fully considered but they are not persuasive.

Applicant argues on page 6, last 2 paragraphs, that Linnarsson does not teach each and every element of the present claims.

This argument is not found to be persuasive. Applicant cite an embodiment of the Linnarsson reference describing template switching oligonucleotides associated with individual wells, further explaining that the TSOs are a single tag that is associated with a particular well, which may or not contain a single cell. The particular embodiment to which Applicant refers and that accompanying argument is not persuasive for the following reasons:

1. Linnarsson teaches on page 4, lines 8-13, that their method is a method of analyzing gene expression in a plurality of cells and that each single cell is placed in a separate well of a 96-well plate, lysed, the cDNA is tagged, the cDNA is then pooled and sequenced. Taught is identification of expressed genes and identification of cells from which they are originated, which would necessarily require a means of identifying a particular nucleic acid sequence, as well as a tag for identifying the particular cell from which it came.
2. Figure 3 of Linnarsson depicts a cell-tag, XXXXX, which is reasonably interpreted to be a different tag for each cell, given that Linnarsson teach identification of genes and further teach identification of the cell from which the gene originated, the cell-tag clearly is present as a separate tag, used to identify a particular cell.

3. Linnarsson's Claim 14 teaches that each cDNA sample has a distinct tag or combination of tags, which is reasonably interpreted to mean that each cDNA sample comprised 2 distinct tags.

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 claims at issue 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); and *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 a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l) (1) - 706.02(l) (3) for

applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/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 http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 9,410,149 in view of Linnarsson (WO 2010/117620 published Oct. 14, 2010, priority date Mar. 30, 2009) for the following reasons.

Regarding instant claim 1 and 3 and claims 1, 10, 12 and 13 of ‘149 patent disclose a method of analyzing DNA. One having ordinary skill in the art would recognize that nucleic acid from a bacterium meets the limitation of an isolated single cell.

Claims of ‘149 patent do not disclose step of generating a tag sequence that distinguishes sample polynucleotides from the other pluralities of sample polynucleotides derived from the same single cell. However, this limitation is taught by Linnarsson, who teaches a method of preparing a nucleic acid libraries from a plurality of single cells, the method comprising the steps of: releasing mRNA from each single

cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell; synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell; pooling the tagged cDNA samples; and amplifying the pooled cDNA samples to generate a cDNA library comprising double-stranded cDNA, wherein the method further comprises processing the cDNA library to obtain a library suitable for sequencing and sequencing the cDNA library to identify genes originated from the cell source; e.g. Fig. 1 and its legend, and Linnarsson, claims 1-5 and 9-11. Linnarsson also teaches pooling the samples simplifies handling of the samples from each single cell and reduces the time required to analyze gene expression in the single cells, which allows high throughput analysis of gene expression. Pooling the samples prior to amplification also provides the advantage that technical variation between samples is virtually eliminated (pg. 11, paragraph 1), thus providing motivation to include the step of including the tagging the nucleic acid sample for each of the isolated single cell and pooling the plurality of isolated single cell nucleic acids in the claims of '149 patent.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include the step of including the tagging the nucleic acid sample for each of the isolated single cells and pooling the plurality of isolated single cell nucleic acids in the claims of '149 patent with a reasonable expectation of success with the expected benefit of allowing high throughput analysis of gene expression and eliminating the technical variation between samples as taught by

Linnarsson (pg. 11, paragraph 1). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves including additional step of tagging nucleic acid sample with identifier sequence which is routinely practiced in the art as exemplified Linnarsson.

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12, 13 and 19 of U.S. Patent No. 9,410,150 in view of Linnarsson (WO 2010/117620) for the following reasons.

Regarding instant claims 1 and 3 and claims 1, 10, 12, 13 and 19 of '150 patent, although the conflicting claims are not identical, they are not patentably distinct from each other because the difference between the instant claims and claims 1, 10, 12, 13 and 19 of '150 patent is that instant claim 1 recites a step of generating a tag sequence that distinguishes sample polynucleotides from the other pluralities of sample polynucleotides derived from the same single cell, a step not recited by the '150 patent. However, this limitation is taught by Linnarsson, who teaches a method of preparing a nucleic acid libraries from a plurality of single cells, the method comprising the steps of: releasing mRNA from each single cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell; synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell; pooling the tagged cDNA samples; and amplifying the pooled cDNA samples to generate a cDNA library comprising double-stranded cDNA, wherein the method further comprises

processing the cDNA library to obtain a library suitable for sequencing and sequencing the cDNA library to identify genes originated from the cell source; e.g. Fig. 1 and its legend, and Linnarsson, claims 1-5 and 9-11. Linnarsson also teaches pooling the samples simplifies handling of the samples from each single cell and reduces the time required to analyze gene expression in the single cells, which allows high throughput analysis of gene expression. Pooling the samples prior to amplification also provides the advantage that technical variation between samples is virtually eliminated (pg. 11, paragraph 1), thus providing motivation to include the step of including the tagging the nucleic acid sample for each of the isolated single cell and pooling the plurality of isolated single cell nucleic acids in the claims of '150 patent.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include the step of providing a plurality of nucleic acid samples each made from single isolated cells and analyzing the nucleic acid samples of Linnarsson in the claims of '150 patent with a reasonable expectation of success with the expected benefit of allowing high throughput analysis of gene expression and eliminating the technical variation between samples as taught by Linnarsson (pg. 11, paragraph 1). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves including additional step of tagging nucleic acid sample with identifier sequence which is routinely practiced in the art as exemplified Linnarsson.

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 11 and 12 of U.S. Patent No. 8,679,756 in view of Linnarsson (WO 2010/117620 as cited above) for the following reasons.

It is noted that the subject matter of claims 1-12 of '756 patent are similar to claims 1-13 and 12of '149 patent. Therefore analysis is very similar. Thus it is maintained that steps of instant claims 1 and 3 are not significantly different from claims 1, 11 and 12 of '756 patent in view of Linnarsson.

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 8,563,274 in view of Linnarsson (WO 2010/117620 as cited above) for the following reasons.

It is noted that the subject matter of claims 1-11 of '274 patent is similar to claims 1-13 of '149 patent. Therefore analysis is very similar. Thus it is maintained that steps of instant claims 1 and 3 are not significantly different from claims 1-11 of '274 patent in view of Linnarsson.

Response to Arguments

Applicant's arguments filed 3/26/2018 have been fully considered but they are not persuasive.

Applicant has requested that the non-statutory obviousness-type double patenting rejection be held in abeyance until allowable subject matter is indicated in the present application. However, said rejection must be maintained as a matter of record

until the appropriate terminal disclaimers have been filed, or until the applications have been amended in such a way as to not claim patently identical subject matter.

Conclusion

No claims are allowed.

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 mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLA A DINES whose telephone number is (571)272-6837. The examiner can normally be reached on Monday-Friday 7am-4pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

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

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

/KARLA A DINES/
Primary Examiner, Art Unit 1639
final

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	Art Unit
	KARLA A DINES	1639

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
EAST and PALM searches	12/18/2017	kd
EAST and PubMed Searches	12/18/2017	kd
EAST inventor search	12/20/2017	kd
EAST and PALM inventor searches	07/03/2018	kd
EAST and PubMed searches	07/02/2018	kd
Update EAST search	07/03/2018	kd

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

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	1227	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2017/12/18 09:26
S2	73	S1 and "single cell"	USPAT	OR	OFF	2017/12/18 09:27
S3	9	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))and "single cell sequencing"	USPAT	OR	OFF	2017/12/18 09:31
S4	8	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))same "single cell sequencing"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 09:33
S5	1227	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2017/12/18 11:54
S6	97	barcode same "nucleic acid" same "single cell" same sequenc$4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 12:30
S7	172	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:42
S8	49	S7 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:43
S9	48	S7 and "single cell" and sequenc$3	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/12/18 13:44

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			JPO; DERWENT; IBM_TDB			
S10	1	S7 and "single cell" and sequenc$3 and ("multiplex identifier" or "MID")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S11	5	S7 and ("single cell" and sequenc$3).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 14:22
S12	442	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:13
S13	3	S12 and ("single cell" and sequenc$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:33
S14	58	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 11:59
S15	27	mikawa-gi.in. and tags	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:05
S16	22	mikawa-gi.in. and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:06
S17	184	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
S18	14	S17 and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT;	OR	OFF	2017/12/20 12:09

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			USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			
S19	14	S17 and ((tags or barcodes) with "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:10
S20	44	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
S21	14	S20 and ((tags or barcodes) with "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
S22	19	S20 and (tags or barcodes)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:22
S23	0	S20 and (tags or barcodes)with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:23
S24	38	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:24
S25	2655	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:26
S26	0	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with "linear amplification" with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28

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S27	54	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with amplification with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S28	54	S27 not S24	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S29	22	"combinatorial barcoding"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 09:36
S30	8	"9410149".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 12:47
S31	8	"9410150".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 13:03
S32	2	"8679756".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 14:09
S33	3	"8563274".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 16:11
S34	246	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:07
S35	52	S34 and "single cell" and sequenc$3.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO;	OR	OFF	2018/07/02 14:08

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			DERWENT; IBM_TDB			
S36	0	S34 and "single cell" and "tagged sequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S37	0	S34 and "single cell" and "tagsequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S38	1	S34 and "single cell" and "tag sequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S39	10062	"single cell" and (tags or zipcode or "zip code" or barcode or "bar code")and sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:32
S40	28	"single cell" same (tags or zipcode or "zip code" or barcode or "bar code") same sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:34
S41	10	"single cells" same (tags or zipcode or "zip code" or barcode or "bar code") same sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:47
S42	2863	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 16:14
S43	32	S42 and ("single cells" with identif$7)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 16:15
S44	445	brenner-sydney.in.	US-PGPUB; USPAT; USOCR;	OR	OFF	2018/07/03 11:01

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			FPRS; EPO; JPO; DERWENT; IBM_TDB			
S45	31	S44 and "multiplex identifier"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:02
S46	4	S44 and "multiplex identifier" and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:10
S47	2	"7544473".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:13
S49	1	"multiplex identifier" same "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:23
S50	22	"multiplex identifier" and "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:23
S51	60	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:43
S52	195	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:46
S53	13	S52 and "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:52
S54	45	slatter-andrew.in.	US-PGPUB;	OR	OFF	2018/07/03

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			USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			11:53
S55	301	tag same sequence same "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:11
S56	19	S55 and "first tag"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:11
S57	18	S55 and ("first tag" same "second tag")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:12
S58	8	"9410149".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 14:08
S59	8	"9410150".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 14:13
S60	2	"8679756".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 14:34

EAST Search History (Interference)

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7/ 4/ 2018 10:40:53 AM
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: **1051**
Sydney Brenner et al.	Examiner: **Karla A. Dines**
Application No.: **15/677,957**	Art Unit: **1639**
Filed: **August 15, 2017**	
For: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	**RESPONSE TO OFFICE ACTION**

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

Commissioner:

In response to the Final Office Action mailed July 10, 2018, please enter the following remarks. As this response is being filed on or before September 10, 2018, which is two months from the issuance of the Final Office Action, Applicants kindly request the issuance of an Advisory Action.

A **Listing of Claims** begins on page **2** of this paper.

Remarks/Arguments begin on page **4** of this paper.

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Listing of Claims:

1. (Previously Presented) A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
   (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
   (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
      (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
      (ii) a multiplex identifier (MID) sequence comprising:
         I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and
         II. a second tag sequence distinguishing the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell;
   (c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;
   (d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the polynucleotide sequence is derived; and
   (e) using the second tag sequence to correlate the identified polynucleotide sequence with the plurality of sample polynucleotides from which the polynucleotide sequence is derived.

2. (Original) The method of claim 1, wherein the method further comprises amplifying the tagged polynucleotides prior to the sequencing step (c).

3. (Original) The method of claim 1, wherein the sample polynucleotides are selected from DNA and RNA.

4. (Original) The method of claim 3, wherein the sample polynucleotides comprise mRNA.

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5. (Original) The method of claim 1, wherein the tagged polynucleotides are generated through at least one ligation reaction.

6. (Original) The method of claim 1, wherein the tagged polynucleotides are generated through PCR or linear amplification of the plurality of sample polynucleotides using an adapter sequence comprising the MID sequence and an amplification primer.

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Remarks/Arguments

Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Interview summary

Examiner Dines and Applicants' representatives, Gargi Talukder and Louis Nguyen, participated in a telephone interview on July 19, 2018.

Examiner Dines and Applicants' representatives discussed the § 102 rejection and the cited Linnarsson reference (WO 2010/117620). Applicants' representative noted that Linnarsson does not describe the "second tag sequence" element in the claims. Examiner Dines stated that she would need to review the reference further and recommended that Applicants file a response to the Final Office Action by the two-month period and schedule a follow-up interview if needed. Applicants kindly thank Examiner Dines for her time and attention to this matter.

Status of the Claims

Claims 1-6 are pending and under consideration in this application.

Response to Office Action

Claim Rejections – 35 USC § 102

Claims 1-6 remains rejected under pre-AIA 35 U.S.C. § 102(A)(1)(A)(2) as allegedly being anticipated by Linnarsson (WO2010117620). Applicants respectfully disagree.

As will be appreciated, to support a *prima facie* case of anticipation, a single prior art reference must expressly or inherently disclose each and every element as set forth in the claim. The identical invention must be shown in as complete detail as is contained in the claim. *See* MPEP § 2131.

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In maintaining this rejection, the Office focused on the following three sections from Linnarsson:

1. The Office alleges that Linnarsson page 4, lines 8-13 teaches a method of analyzing gene expression in a plurality of cells, where each single cell is placed in a separate well of a 96-well, the cells are lysed, cDNA is tagged and the cDNA is then pooled and sequenced. The Office further alleges that Linnarsson page 4, lines 8-13 teaches "the identification of expressed genes and identification of cells from which they are originated, which would necessarily require a means of identifying a particular nucleic acid sequences, as well as a tag for identifying the cell from which it came." Final Office Action at 5 (emphasis in original Final Office Action). Applicants note that Linnarsson page 4, lines 8-13 is a description of Figure 1 of Linnarsson.

2. The Office alleges that Figure 3 of Linnarsson depicts a "cell-tag," XXXXX. The Office alleges that such a cell-tag is reasonably interpreted to be a different tag for each cell and "used to identify a particular cell." *Id.*

3. The Office alleges that claim 14 teaches that "each cDNA sample has a distinct tag or combination of tags, which is reasonably interpreted to mean that each cDNA sample comprises two distinct tags." *Id.* at 6 (emphasis in original Final Office Action). Applicants believe this is a typographical error as Linnarsson claim 13 actually discloses "each cDNA sample has a distinct tag or combination of tags." As such, Applicants analysis in this response will focus on claim 13.

Applicants submit that these three particular sections from Linnarsson fail to disclose each and every element of the present claims, as explained below. As such, a rejection under § 102 cannot be maintained.

Linnarsson page 4, lines 8-13 and Figure 1 do not disclose each and every element of the present claims

Applicants submit that Linnarsson page 4, lines 8-13 and Figure 1, do not disclose each and every element of the present claims.

The pending claims include a step (b) of generating a plurality of tagged polynucleotides. Each of the tagged polynucleotide includes (b)(i) a sequence from a sample polynucleotide and a

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(b)(ii) multiplex identifier (MID) sequence. This MID includes a first tag sequence and a second tag sequence. The first tag sequence is associated with the single cell from which the sample polynucleotide is derived and is a different sequence for different single cells. The second tag sequence distinguishes the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell. After the plurality of tagged polynucleotides are sequenced to obtain a plurality of identified polynucleotide sequences in step (c), this second tag is used in step (e) to correlate the identified polynucleotide sequence with the plurality of sample polynucleotides from which the polynucleotide sequence is derived.

Applicants submit Linnarsson page 4, lines 8-13 and Figure 1 do not disclose an MID having such a second tag sequence that distinguishes the sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell. Moreover, Linnarsson page 4, lines 8-13 and Figure 1 do not disclose a step of using such a second tag sequence to correlate an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived.

Linnarsson page 4, lines 8-13 and Figure 1 are reproduced below:

Figure 1, panels A-F, show an overview of a method of analyzing gene expression in a plurality of single cells. (A) the tissue of interest is dissected; (B) a plurality of single cells are selected; (C) single cells are placed in separate wells of a 96-well plate and lysed; tagged reverse transcription is performed on each sample to produce cDNA; (D) cDNA samples are pooled and amplified; (E) sequencing is performed to obtain 100 million reads; and (F) identification of expressed genes and identification of cells from which they originated.

Linnarsson page 4, lines 8-13

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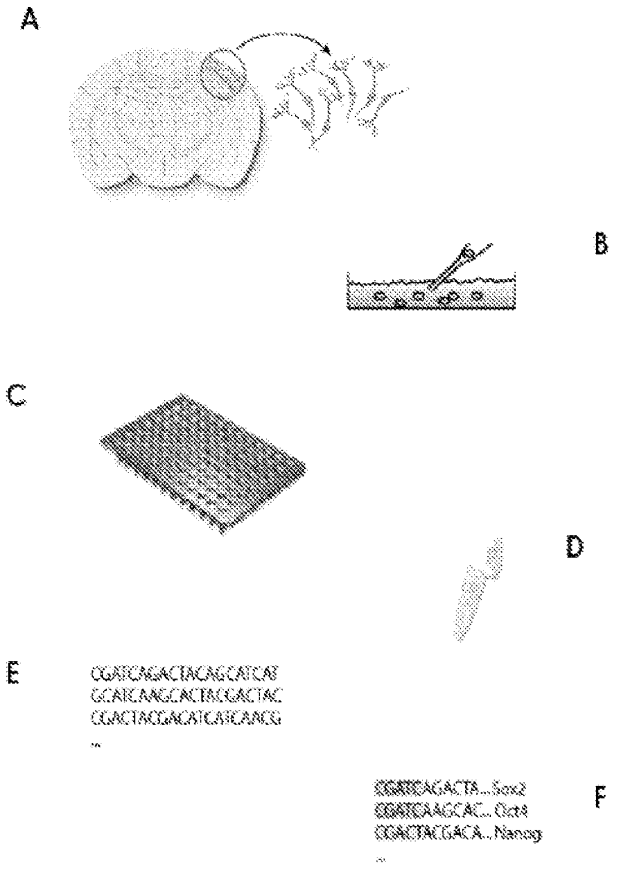


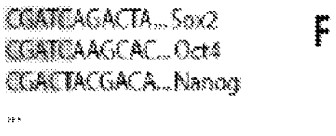
Figure 1

As shown, Linnarsson page 4, lines 8-13 describes a step (C) of performing "tagged reverse transcription" on lysed single cells in separate wells of a 96-well pate to produce cDNA. The cDNA samples are pooled and amplified and sequencing is performed to obtain 100 million reads (steps (E) and (D)). In step (F), expressed genes are identified, as well as the cells from which such expressed genes originated.

Linnarsson page 4, lines 8-13 and Figure 1, however, do not disclose a tagged nucleotide that includes a MID with two tag sequences as set forth in the present claims. Page 4, lines 8-13

simply mentions performing "tagged reverse transcription" and is silent with respect to the structure and function of such a tag. As page 4, lines 8-13 does not disclose an MID with two tag sequences, it necessarily follows that this disclosure also does not disclose a step of using a second tag sequence to correlate an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived, as set forth in the pending claims.

In maintaining this rejection, the Office alleges that step (F) of Linnarsson "*would necessarily require a means of identifying a particular nucleic acid sequences*, as well as a tag for identifying the cell from which it came." Final Office at 5 (emphasis added). Identification of a particular nucleic acid, however, does not necessarily require two tag sequences. Indeed, Figure 1 steps (E) and (F) of Linnarsson depict a plurality of cDNAs having the ***same tag***: CGATCA" (shaded boxes in step (F)).



As explained in Linnarsson, the tags in Figure 1 are used to identify the single cell from which the cDNAs came from, while sequencing of cDNA sequence derived from an expressed gene itself, as opposed to a second tag, are used for identification of the expressed gene. *See, e.g.*, Linnarsson at 22, ll. 26-28.

Applicants further note that the second tag sequence as set forth in the present claims is not cDNA derived from an expressed gene from a single cell. Rather, the claim clearly sets forth that the tagged polynucleotides includes a sequence from a sample polynucleotide ***and*** a MID sequence having two tag sequences, i.e., the sequence from the sample polynucleotide is distinct from the second tag sequence. Thus, the common tag and the cDNA sequence derived from the expressed gene in Figure 1F of Linnarsson cannot be reasonably interpreted to describe the MID having two tag sequences of the present claims.

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As such, Applicants submit that Linnarsson Figure 1 and page 4, lines 8-13 do not disclose each and every element of the present claims.

Linnarsson Figure 3 does not disclose each and every element of the present claims

Applicants submit that Linnarsson Figure 3 does not disclose each and every element of the present claims.

In particular, Applicants submit that Linnarsson Figure 3 does not disclose a second tag sequence or a step of using such a second tag sequence to correlate an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived.

Figure 3 and its accompanying description at page 4, lines 15-16 are reproduced below:

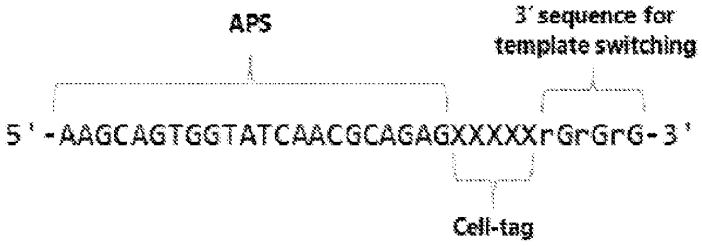


Figure 3

15 **Figure 3** shows an example of a template switching oligonucleotide comprising a 5' amplification primer sequence (APS), a cell tag and a 3' sequence for template switching.

Linnarsson page 4, lines 15-16

As shown, Figure 3 and page 4, lines 15-16 simply disclose a "cell-tag" XXXX. There is no description of the structure or function of such a tag based on this disclosure.

In maintaining this rejection, the Office alleges that "the cell-tag" clearly is present as a separate tag, used to identify a particular cell." Office Action at 5. Even assuming *arguendo* that the "cell-tag" in Figure 3 is for the identification of a particular cell, which is not conceded, Applicants note that Figure 3 and page 4, lines 15-16 fail to disclose a second tag sequence let alone a step of using such a tag for correlating an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived.

As such, Applicants submit that Linnarsson Figure 3 does not disclose each and every element of the present claims.

Linnarsson Claims 1 and 13 do not disclose each and every element of the present claims

The Office alleges that claim 13 of Linnarsson also discloses each and every element of the present claims. Claim 13 of Linnarsson is dependent from claim 1. Applicants submit that Linnarsson claims 1 and 13 do not disclose each and every element of the present claims.

Claims 1 and 13 of Linnarsson disclose:

1. A method of preparing a cDNA library from a plurality of single cells, the method comprising the steps of:

(i) releasing mRNA from each single cell to provide a plurality of individual mRNA samples, wherein the mRNA in each individual mRNA sample is from a single cell;

(ii) synthesizing a first strand of cDNA from the mRNA in each individual mRNA sample and incorporating a tag into the cDNA to provide a plurality of tagged cDNA samples, wherein the cDNA in each tagged cDNA sample is complementary to mRNA from a single cell;

(iii) pooling the tagged cDNA samples; and

(iv) amplifying the pooled cDNA samples to generate a cDNA library comprising double-stranded cDNA.

13. The method according to claim 1, wherein each cDNA sample has a distinct tag or combination of tags.

In maintaining this rejection, the Office alleges that claim 13 can be "reasonably interpreted to mean that each cDNA sample comprised 2 distinct tags." Final Office Action at 6.

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Even assuming *arguendo* that claim 13 discloses a cDNA sample that include two distinct tags, Applicants submit that claims 1 and 13 and the remaining claims of Linnarsson are silent with respect to multiple tags that are distinct from one another. Thus, claims 1 and 13 do not disclose a second tag that distinguishes a sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell, as set forth in the pending claims. As the cited claims do not disclose two tag sequences that are distinct from one another, it follows that Linnarsson also does not describe a step of using a second tag sequence for correlating an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived, as set for in the present claims. Thus, Applicants submit that Linnarsson claims 1 and 13 do not disclose each and every element of the present claims.

For at least the foregoing reasons, Applicants submit that the three sections of Linnarsson cited by the Office in maintaining this rejection collectively do not disclose each and every element of the pending claims. Accordingly, Applicants submit that Linnarsson does not anticipate the pending claims and, therefore, respectfully request the withdrawal of this rejection.

Claim Rejections – Double Patenting

The Office maintains the rejection of claims 1 and 3 on the grounds of nonstatutory double patenting as being unpatentable over claims of the following references below. Applicants respectfully traverse these rejections.

In determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is — does any claim in the application define an invention that is anticipated by, or is merely an obvious variation of, an invention claimed in the patent? M.P.E.P. §804.II.B.1.

A double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 U.S.P.Q. 29 (CCPA 1967). Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. §103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985).

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U.S. Patent No. 9,410,149 in view of Linnarsson

The Office maintains the rejection of claims 1 and 3 on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12 and 13 of U.S. Patent No. 9,410,149 (the "'149 patent") in view of Linnarsson.

As the '149 patent is cited solely for its disclosure of a method of analyzing DNA, the '149 patent does not cure the deficiencies of Linnarsson, as discussed above. Moreover, Linnarsson does not teach or suggest a second tag that distinguishes a sample polynucleotide from other pluralities of sample polynucleotides derived from the same single cell or a step of using such a second tag sequence to correlate an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived, as set for in the present claims.

Accordingly, Applicants respectfully request the withdrawal of this rejection.

U.S. Patent No. 9,410,150 in view of Linnarsson

The Office maintains the rejection of claims 1 and 3 on the ground of nonstatutory double patenting as being unpatentable over claims 1, 10, 12, 13 and 19 of U.S. Patent No. 9,410,150 (the "'150 patent") in view of Linnarsson. In making this rejection, the Office acknowledges that the '150 patent does not teach or suggest a step of generating a tag sequence that distinguishes sample polynucleotides from the other plurality of sample polynucleotides derived from the same single cell and relies on Linnarsson for teaching this element.

As discussed above, Linnarsson also does not disclose or teach or suggest a step of generating a tag sequence that distinguishes sample polynucleotides from the other plurality of sample polynucleotides derived from the same single cell. Moreover, Linnarsson and the '150 patent do not disclose or teach or suggest a step of using such a second tag sequence to correlate an identified polynucleotide sequence with a plurality of sample polynucleotides from which the polynucleotide sequence is derived.

As such, the pending claims are not anticipated or obviousness over the '150 patent claims in view of Linnarsson. Accordingly, Applicants respectfully request the withdrawal of this rejection.

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U.S. Patent No. 8,679,756 in view of Linnarsson

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 11 and 12 of U.S. Patent No. 8,679,756 (the "'756 patent") in view of Linnarsson. In making this rejection, the Office asserts that the claims of the '756 patent are similar to claims of the '149 patent. Final Office Action at 11. Thus, the Office asserts that this rejection is similar to the nonstatutory double patenting over the '149 patent and Linnarsson. *Id.* As discussed above, the claims of the '149 patent do not cure the deficiencies of Linnarsson. Therefore, it follows that the claims of the '756 patent also do not cure the cure the deficiencies of Linnarsson.

As such, the pending claims are not anticipated or obviousness over the '756 patent claims in view of Linnarsson. Accordingly, Applicants respectfully request the withdrawal of this rejection.

U.S. Patent No. 8,563,274 in view of Linnarsson

Claims 1 and 3 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 8,563,274 (the "'274 patent") in view of Linnarsson. In making this rejection, the Office asserts that the claims of the '274 patent are similar to claims of the '149 patent. Final Office Action at 11. Thus, the Office asserts that this rejection is similar to the nonstatutory double patenting over the '149 patent and Linnarsson. *Id.* As discussed above, the claims of the '149 patent do not cure the deficiencies of Linnarsson. Therefore, it follows that the claims of the '274 patent also do not cure the cure the deficiencies of Linnarsson.

As such, the pending claims are not anticipated or obviousness over the '274 patent claims in view of Linnarsson. Accordingly, Applicants respectfully request the withdrawal of this rejection.

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CONCLUSION

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Order No.: 104371-5016-US08).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: August 6, 2018 By: /Louis T. Nguyen/
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Gargi Talukder, Reg. No. 61,368

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Electronic Acknowledgement Receipt	
EFS ID:	33388054
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Louis-Vu T. Nguyen/Sheila Gloss
Filer Authorized By:	Louis-Vu T. Nguyen
Attorney Docket Number:	104371-5016-US08
Receipt Date:	06-AUG-2018
Filing Date:	15-AUG-2017
Time Stamp:	19:22:47
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		104371-5016-US08_AFResponse.pdf	366660 346e404b10ebad35c4679831883524ab63868fa	yes	14

	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	14
Warnings:			
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/677,957	Filing Date 08/15/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $40 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $210 =	
☐ 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	08/06/2018	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 6	Minus	** 20	= 0		x $50 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $230 =	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.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	Moliki I May
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The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

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Application Number	15/677,957
Filing Date	August 15, 2017
First Named Inventor	Sydney Brenner
Art Unit	1639
Examiner Name	DINES, KARLA A
Attorney Docket Number	104371-5016-US08

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Signature /Gargi Talukder/

Typed or Printed Name Gargi Talukder

Date	Telephone
August 7, 2018	415.442.1000

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☐ *Total of _____forms are submitted.

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

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 Acknowledgement Receipt

EFS ID:	33397409
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	43850
Filer:	Gargi Talukder/Sheila Gloss
Filer Authorized By:	Gargi Talukder
Attorney Docket Number:	104371-5016-US08
Receipt Date:	07-AUG-2018
Filing Date:	15-AUG-2017
Time Stamp:	17:15:24
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	Change of Address	5016-US08_aia0122.pdf	228830 07da0a89d4f8a86d78b92ff6d6910f0f9dab07da	no	2

Warnings:

Information:	
Total Files Size (in bytes):	228830

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.

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

156830 7590 08/28/2018

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

EXAMINER
DINES, KARLA A

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/28/2018

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

TITLE OF INVENTION: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	11/28/2018

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: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 02/11)

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00233

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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)

156830 7590 08/28/2018
MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

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 facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

TITLE OF INVENTION: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	11/28/2018

EXAMINER	ART UNIT	CLASS-SUBCLASS
DINES, KARLA A	1639	506-004000

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 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(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 has been filed for recordation as set forth in 37 CFR 3.11. 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. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

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

❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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. _____

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00234

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
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

156830 7590 08/28/2018

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

EXAMINER	
DINES, KARLA A	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/28/2018

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.

PTOL-85 (Rev. 02/11)

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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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 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, 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.
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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 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. 15/677,957	Applicant(s) Brenner et al.	
	Examiner KARLA A DINES	Art Unit 1639	AIA Status No

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

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

1. ☑ This communication is responsive to communication filed on August 6, 2018.
   ☐ 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 1-6 . 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 areply 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 _____.
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 _____.

/KARLA A DINES/
Primary Examiner, Art Unit 1639

10x Genomics, Inc. Exhibit 2001
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Notice of Pre-AIA or AIA Status

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

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

The 35 USC 102 rejection is hereby withdrawn. The closest prior art, Linnarsson (WO 2010/117620), does not teach or suggest generating a plurality of tagged polynucleotides comprising an identifier sequence of instant claim 1(ii). The claimed identifier sequence comprises a first tag sequence, which distinguishes each single cell in a sample of a plurality of cells, and a second tag sequence, which distinguishes a sample polynucleotide from other sample polynucleotides derived from a single cell, which is not taught by Linnarsson.

The double patenting rejections are withdrawn in view of the fact that the instant claims are neither obvious nor anticipated by 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

Claims 1-6 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLA A DINES whose telephone number is (571)272-6837. The examiner can normally be reached on Monday-Friday 7am-4pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

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

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

/KARLA A DINES/
Primary Examiner, Art Unit 1639

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	Art Unit
	KARLA A DINES	1639

CPC - Searched*		
Symbol	Date	Examiner
C12Q1/6874	08/22/2018	kd
C12N15/1065	08/22/2018	kd

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner
506	4	08/23/2018	kd

* 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
EAST and PALM searches	12/18/2017	kd
EAST and PubMed Searches	12/18/2017	kd
EAST inventor search	12/20/2017	kd
EAST and PALM inventor searches	07/03/2018	kd
EAST and PubMed searches	07/02/2018	kd
Update EAST search	07/03/2018	kd
EAST and PALM inventor searches	08/22/2018	kd
EAST and PubMed searches	08/22/2018	kd
C12Q1/6874	08/23/2018	kd
C12N15/1065	08/23/2018	kd
506/4	08/23/2018	kd

/KARLA A DINES/ Primary Examiner, Art Unit 1639	

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00241

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	Art Unit
	KARLA A DINES	1639

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
506	4	08/23/2018	kd
C12Q1	6874	08/23/2018	kd

/KARLA A DINES/ Primary Examiner, Art Unit 1639	

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Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
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Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	**Art Unit**
	KARLA A DINES	1639

CPC						
Symbol					**Type**	**Version**
C12Q	/	1	/	6874	F	2013-01-01
C12Q	/	1	/	6855	I	2013-01-01
C12Q	/	1	/	6806	I	2013-01-01
C12Q	/	1	/	686	I	2013-01-01
C12N	/	15	/	1065	I	2013-01-01

CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
C12Q	/	1	/	6855	I	1	1	2013-01-01
C12Q	/	2563	/	179	A	1	2	2013-01-01
C12Q	/	2537	/	143	A	1	3	2013-01-01
C12Q	/	2535	/	122	A	1	4	2013-01-01
C12Q	/	1	/	6855	I	2	1	2013-01-01
C12Q	/	2525	/	161	A	2	2	2013-01-01
C12Q	/	2525	/	155	A	2	3	2013-01-01
C12Q	/	2525	/	143	A	2	4	2013-01-01

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/KARLA A DINES/ Primary Examiner, Art Unit 1639	22 August 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20180822

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	15/677,957	Brenner et al.
	Examiner	**Art Unit**
	KARLA A DINES	1639

INTERNATIONAL CLASSIFICATION					
CLAIMED					
C12Q1/686	/	1	/	686	
NON-CLAIMED					
C12N15/10	/	15	/	10	

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**
506	4

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	6	
/KARLA A DINES/ Primary Examiner, Art Unit 1639	22 August 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20180822

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Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	**Art Unit**
	KARLA A DINES	1639

☑ 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)	6	
/KARLA A DINES/ Primary Examiner, Art Unit 1639	22 August 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20180822

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Bibliographic Data

Application No: 15/677,957

Foreign Priority claimed: ○ Yes ◉ No

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

Verified and Acknowledged: /KARLA A DINES/ Examiner's Signature | Initials

Title: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
08/15/2017	506	1639	104371-5016-US08
RULE			

APPLICANTS

10X Genomics, Inc., Pleasanton, CA, UNITED STATES

INVENTORS

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Gi Mikawa Great Shelford, UNITED KINGDOM

Robert Osborne Great Chesterford, UNITED KINGDOM

Andrew Slatter Lindon, UNITED KINGDOM

CONTINUING DATA

This application is a CON of 14792094 07/06/2015

14792094 is a CON of 14172694 02/04/2014 PAT 9102980

14172694 is a CON of 14021790 09/09/2013 PAT 8679756

14021790 is a CON of 13859450 04/09/2013 PAT 8563274

13859450 is a CON of 13622872 09/19/2012

13622872 is a CON of 13387343 02/15/2012 PAT 8298767

13387343 is a 371 of PCT/IB2010/002243 08/13/2010

PCT/IB2010/002243 has PRO of 61288792 12/21/2009

PCT/IB2010/002243 has PRO of 61235595 08/20/2009

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

08/22/2017

**** SMALL ENTITY ****

STATE OR COUNTRY

UNITED KINGDOM

ADDRESS

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105
UNITED STATES

FILING FEE RECEIVED

$2,800

#6	Add	Search **Slatter, Andrew[Author]**	5
#5	Add	Search **osborne, robert[Author]**	32
#4	Add	Search **(Mikawa[Author]) AND "single cell"**	3
#3	Add	Search **mikawa, gi[Author]**	0
#1	Add	Search **Brenner, Sydney[Author]**	100
#2	Add	Search **(#1) AND "single cell"**	0

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	91	"POPULATION GENETICS TECHNOLOGIES LTD"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:23
L2	2	l1 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:24
L3	1135	506/4.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:25
L6	9334	c12Q1/6874.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:37
L7	1211	l6 and (molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2018/08/23 10:41
L8	75	l7 and "single cells"	USPAT	OR	OFF	2018/08/23 10:41
L9	85	l7 and "single cell"	USPAT	OR	OFF	2018/08/23 10:41
L10	9334	c12Q1/6874.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:44
L11	2569	l10 and (molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT;	OR	OFF	2018/08/23 10:44

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			IBM_TDB			
L12	283	l11 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:44
L19	216	c12n15/1065.cpc.	USPAT	OR	OFF	2018/08/23 10:52
L20	2278	c12n15/1065.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:52
L21	437	l20 and (molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:53
S1	1227	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2017/12/18 09:26
S2	73	S1 and "single cell"	USPAT	OR	OFF	2017/12/18 09:27
S3	9	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))and "single cell sequencing"	USPAT	OR	OFF	2017/12/18 09:31
S4	8	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))same "single cell sequencing"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 09:33
S5	1227	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2017/12/18 11:54
S6	97	barcode same "nucleic acid" same "single cell" same sequenc$4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 12:30
S7	172	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/12/18 13:42

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			JPO; DERWENT; IBM_TDB			
S8	49	S7 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:43
S9	48	S7 and "single cell" and sequenc$3	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S10	1	S7 and "single cell" and sequenc$3 and ("multiplex identifier" or "MID")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S11	5	S7 and ("single cell" and sequenc$3).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 14:22
S12	442	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:13
S13	3	S12 and ("single cell" and sequenc$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:33
S14	58	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 11:59
S15	27	mikawa-gi.in. and tags	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:05
S16	22	mikawa-gi.in. and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT;	OR	OFF	2017/12/20 12:06

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			USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			
S17	184	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
S18	14	S17 and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
S19	14	S17 and ((tags or barcodes) with "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:10
S20	44	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
S21	14	S20 and ((tags or barcodes) with "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
S22	19	S20 and (tags or barcodes)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:22
S23	0	S20 and (tags or barcodes)with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:23
S24	38	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:24

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S25	2655	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:26
S26	0	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with "linear amplification" with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S27	54	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with amplification with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S28	54	S27 not S24	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S29	22	"combinatorial barcoding"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 09:36
S30	8	"9410149".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 12:47
S31	8	"9410150".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 13:03
S32	2	"8679756".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 14:09
S33	3	"8563274".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO;	OR	OFF	2017/12/21 16:11

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			DERWENT; IBM_TDB			
S34	246	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:07
S35	52	S34 and "single cell" and sequenc$3.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:08
S36	0	S34 and "single cell" and "tagged sequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S37	0	S34 and "single cell" and "tagsequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S38	1	S34 and "single cell" and "tag sequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S39	10062	"single cell" and (tags or zipcode or "zip code" or barcode or "bar code")and sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:32
S40	28	"single cell" same (tags or zipcode or "zip code" or barcode or "bar code") same sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:34
S41	10	"single cells" same (tags or zipcode or "zip code" or barcode or "bar code") same sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:47
S42	2863	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj	US-PGPUB; USPAT; USOCR;	OR	OFF	2018/07/02 16:14

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		tagging) or (stochastic adj attachment) or (digital adj counting)	FPRS; EPO; JPO; DERWENT; IBM_TDB			
S43	32	S42 and ("single cells" with identif$7)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 16:15
S44	445	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:01
S45	31	S44 and "multiplex identifier"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:02
S46	4	S44 and "multiplex identifier" and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:10
S47	2	"7544473".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:13
S49	1	"multiplex identifier" same "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:23
S50	22	"multiplex identifier" and "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:23
S51	60	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:43
S52	195	osborne-robert.in.	US-PGPUB;	OR	OFF	2018/07/03

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			USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			11:46
S53	13	S52 and "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:52
S54	45	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:53
S55	301	tag same sequence same "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:11
S56	19	S55 and "first tag"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:11
S57	18	S55 and ("first tag" same "second tag")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:12
S58	8	"9410149".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 14:08
S59	8	"9410150".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 14:13
S60	2	"8679756".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT;	OR	OFF	2018/07/03 14:34

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			IBM_TDB			
S61	69	"10x genomics".asn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 14:27
S62	445	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 14:36
S63	4	S62 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 14:37
S64	60	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 14:43
S65	196	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:30
S66	4	S65 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:30
S67	45	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:31
S68	4	S67 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:31
S70	1135	506/4.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2018/08/22 15:33

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			JPO; DERWENT; IBM_TDB			
S71	78	S70 and (barcode or "bar code")and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:34

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L4	196	506/4.ccls.	USPAT	OR	OFF	2018/08/23 10:26
L5	21	l4 and "single cell"	USPAT	OR	OFF	2018/08/23 10:26
L13	1198	c12Q1/6874.cpc.	USPAT	OR	OFF	2018/08/23 10:46
L14	1211	l13 and(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2018/08/23 10:46
L16	85	l14 and "single cell"	USPAT	OR	OFF	2018/08/23 10:48
L17	208	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)and "single cell"	USPAT	OR	OFF	2018/08/23 10:49
L18	163	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)and "single cell"	USPAT	OR	OFF	2018/08/23 10:50
L22	216	c12n15/1065.cpc.	USPAT	OR	OFF	2018/08/23 10:55
L23	9	l22 and ((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)) and "single cell"	USPAT	OR	OFF	2018/08/23 10:55
L24	196	506/4.ccls.	USPAT	OR	OFF	2018/08/23 10:57
L25	91	l24 and (molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)and "single cell"	USPAT	OR	OFF	2018/08/23 10:57

8/ 23/ 2018 10:58:24 AM
C:\ Users\ kdines\ Documents\ EAST\ Workspaces\ 15677957.wsp

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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 15/677,957	Filing Date 08/15/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)
☒ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	**140**
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	**140**

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT	**09/11/2018**	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 6	Minus	** 20	= 0	X $50 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $230 =	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 $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

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

LIE
GLORIA J. TRAMMELL

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.

Doc code: RCEX
Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (02-18)
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REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	15/677,957	Filing Date	2017-08-15	Docket Number (if applicable)	104371-5016-US08	Art Unit	1639
First Named Inventor	Sydney Brenner et al.			Examiner Name	Karla A. Dines		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☒ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

☒ **The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**
The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 500310

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

X Patent Practitioner Signature

Applicant Signature

PTO/SB/30EFS (02-18)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Signature of Registered U.S. Patent Practitioner			
Signature	/Louis-Vu Nguyen/	Date (YYYY-MM-DD)	2018-09-11
Name	Louis-Vu Nguyen	Registration Number	58729

This collection of information is required by 37 CFR 1.114. 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 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.

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

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 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.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: **1051**
Sydney Brenner et al.	Examiner: **Karla A. Dines**
Application No.: **15/677,957**	Art Unit: **1639**
Filed: **August 15, 2017**	
For: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	**AMENDMENT**

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

Commissioner:

Applicant requests entry the following Amendment.

Amendments to the Claims are reflected in the listing of claims that begins on page **2** of this paper.

Remarks/Arguments begin on page **4** of this paper.

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Parse Biosciences, Inc. v. 10x Genomics, Inc.
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AMENDMENTS TO THE CLAIMS

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

Listing of Claims:

1. (Currently amended) A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
   (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
   (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
      (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
      (ii) a multiplex identifier (MID) sequence comprising:
         I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and
         II. a second tag sequence distinguishing the sample polynucleotide from other ~~pluralities of~~ sample polynucleotides derived from the same single cell;
   (c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;
   (d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the identified polynucleotide sequence is derived; and
   (e) using the second tag sequence to correlate the identified polynucleotide sequence with the ~~plurality of~~ sample polynucleotide[[s]] from which the identified polynucleotide sequence is derived.

2. (Original) The method of claim 1, wherein the method further comprises amplifying the tagged polynucleotides prior to the sequencing step (c).

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3. (Original) The method of claim 1, wherein the sample polynucleotides are selected from DNA and RNA.

4. (Original) The method of claim 3, wherein the sample polynucleotides comprise mRNA.

5. (Original) The method of claim 1, wherein the tagged polynucleotides are generated through at least one ligation reaction.

6. (Original) The method of claim 1, wherein the tagged polynucleotides are generated through PCR or linear amplification of the plurality of sample polynucleotides using an adapter sequence comprising the MID sequence and an amplification primer.

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Remarks/Arguments

Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Status of the Claims

Claims 1-6 are pending and under consideration in this application.

Claim 1, steps (d) and (e) have been amended to provide continuity with respect to the term "identified polynucleotide," as recited in these steps. In addition, steps (b) and (e) of claim 1 have been amended for clarity to reflect the discussion of the allowable subject matter set forth in the Notice of Allowance mailed August 28, 2018. Accordingly, Applicants respectfully request entry of these amendments.

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CONCLUSION

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Order No.: 104371-5016-US08).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: September 11, 2018 By: /Louis T. Nguyen/
Louis T. Nguyen, Reg. No. 58,729 *for*
Gargi Talukder, Reg. No. 61,368

Customer No.: 43850
Morgan, Lewis & Bockius LLP
One Market, Spear Street Tower
San Francisco, CA 94105
Telephone: (415) 442-1000
Facsimile: (415) 442-1001

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Parse Biosciences, Inc. v. 10x Genomics, Inc.
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: **Karla A. Dines**
Sydney Brenner et al.	Art Unit: **1639**
Application No. **15/677,957**	Confirmation No. **1051**
Filed: **August 15, 2017**	Attorney Docket No. **104371-5016-US08**
Title: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	

REQUEST FOR CORRECTED FILING RECEIPT

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

Commissioner:

Applicants request correction of the official Filing Receipt for the above-captioned application. Attached hereto is a copy of the Filing Receipt indicating the following requested correction:

In the **Inventor(s)**, after Andrew Slatter, please delete "Lindon" and insert therefor --London--.

Support for this change can be found on the Supplemental Application Data Sheet submitted herewith.

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CONCLUSION

Although Applicant does not believe any additional fees are required, the Commissioner is authorized to charge any additional required fees or to credit any overpayment to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 (File No. 104371-5016-US08).

Please direct any calls in connection with this application to the undersigned at (415) 442-1000.

Respectfully submitted,

Dated: September 11, 2018

/Louis-Vu Nguyen/

Louis-Vu Nguyen, Reg. No. 58,729, for
Gargi Talukder, Reg. No. 61,368
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One Market, Spear Street Tower
San Francisco, CA 94105
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UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/677,957	08/15/2017	1639	800	104371-5016-US08	6	1

CONFIRMATION NO. 1051

CORRECTED FILING RECEIPT

43850
MORGAN, LEWIS & BOCKIUS LLP (SF)
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

OC000000098118838

Date Mailed: 12/22/2017

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

Inventor(s)

Sydney Brenner, Ely, UNITED KINGDOM;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, ~~Lindon~~ London, UNITED KINGDOM;

Applicant(s)

10X Genomics, Inc., Pleasanton, CA;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 14/792,094 07/06/2015
which is a CON of 14/172,694 02/04/2014 PAT 9102980
which is a CON of 14/021,790 09/09/2013 PAT 8679756
which is a CON of 13/859,450 04/09/2013 PAT 8563274
which is a CON of 13/622,872 09/19/2012 ABN
which is a CON of 13/387,343 02/15/2012 PAT 8298767
which is a 371 of PCT/IB2010/002243 08/13/2010
which claims benefit of 61/288,792 12/21/2009
and claims benefit of 61/235,595 08/20/2009

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.

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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: 08/22/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/677,957**

Projected Publication Date: 03/22/2018

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

Preliminary Class

506

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.

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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

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).

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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

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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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PTO/AIA/14 (11-15)
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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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
	Sydney		Brenner	

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

City	Ely	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	3 Barton Square		
Address 2			
City	Ely	**State/Province**	
Postal Code	CB7 4PJ	**Country** [i]	GB

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gi		Mikawa	

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

City	Great Shelford	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	104 High Street		
Address 2			
City	Great Shelford	**State/Province**	
Postal Code	CB1 6A3	**Country** [i]	GB

Inventor 3 Remove

Legal Name

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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		Osborne	

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

City	Great Chesterford	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	38 Pilgrim Close		
Address 2			
City	Great Chesterford	**State/Province**	
Postal Code	CB10 1QB	**Country** [i]	GB

Remove

Inventor 4
Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Andrew		Slatter	

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

City	~~Lindon~~ London	Country of Residence [i]	GB

Mailing Address of Inventor:

Address 1	65a Huddleston Road		
Address 2			
City	London	**State/Province**	
Postal Code	N7 0AE	**Country** [i]	GB

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	~~43850~~ 156830		
Email Address	sfipdocketing@morganlewis.com	Add Email	Remove Email

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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Application Information:

Title of the Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS		
Attorney Docket Number	104371-5016-US08	**Small Entity Status Claimed** ☒	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	13	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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

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

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

Publication Information:

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

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

Representative Information:

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

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	43850		

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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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	14/792094	2015-07-06

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14/792094	Continuation of	14/172694	2014-02-04	9102980	2015-08-11

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14/172694	Continuation of	14/021790	2013-09-09	8679756	2014-03-25

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
14/021790	Continuation of	13/859450	2013-04-09	8563274	2013-10-22

Prior Application Status	Abandoned		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13/859450	Continuation of	13/622872	2012-09-19

Prior Application Status	Patented			Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13/622872	Continuation of	13/387343	2012-02-15	8298767	2012-10-30

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13/387343	a 371 of international	PCTIB2010002243	2010-08-13

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
PCTIB2010002243	Claims benefit of provisional	61/288792	2009-12-21

PTO/AIA/14 (11-15)
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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
PCTIB2010002243	Claims benefit of provisional	61/235595	2009-08-20
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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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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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	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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	10X Genomics, Inc.		
Mailing Address Information For Applicant:			
Address 1	7068 Koll Center Parkway, Suite 401		
Address 2			
City	Pleasanton	**State/Province**	CA
Country	US	Postal Code	94566
Phone Number		Fax Number	
Email Address			

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.

PTO/AIA/14 (11-15)
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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

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

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

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	/Louis-Vu Nguyen/			Date (YYYY-MM-DD)	2018-09-11
First Name	Louis-Vu	Last Name	Nguyen	Registration Number	58729

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

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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2nd Supplemental **Application Data Sheet 37 CFR 1.76**	Attorney Docket Number	104371-5016-US08
	Application Number	15/677,957
Title of Invention	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS	

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.**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor: **Sidney BRENNER**	Conf. No.: **1051**
Application No.: **15/677,957**	Art Unit: **1639**
Filed: **August 15, 2017**	Examiner: **Karla A. Dines**
For: **Methods for Analyzing Nucleic Acids from Single Cells**	Docket No.: **104371-5016-US08**

Certificate of Transmission (37 C.F.R. § 1.8)
I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office electronic filing system (EFS-Web) to the USPTO on September 11, 2018.

/ Sheila R. Gloss /
Sheila R. Gloss

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

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner:

This Information Disclosure Statement is hereby submitted in accordance with 37 C.F.R. 1.98 and pursuant to Applicant's continuing duty under 37 C.F.R. 1.56 to bring any information which may be material to patentability of this application to the Examiner's attention.

Applicant makes no representation that a search has been conducted by the Applicant, or that there is not possibly more relevant art. 37 C.F.R. § 1.97(g). Applicant also makes no representation that the information submitted herewith is in fact material to patentability. The filing of this Information Disclosure Statement shall not be construed as an admission against interest in any manner. 37 C.F.R. § 1.97(h).

The Examiner's attention is directed to the reference(s) cited on the accompanying substitute for forms 1449A/PTO and PTO/SB/08. Except for U.S. Patents and U.S. Patent Application Publications, *see* 37 C.F.R. § 1.98(a)(2)(i), copies of the cited references are enclosed, unless otherwise noted below.

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00283

This Information Disclosure Statement is being filed within three months of the filing date of a national application other than a continued prosecution application, within three months of the date of entry of a national stage, before the mailing of a first Office action on the merits, or before the mailing of a first Office action after the filing of a request for continued examination. 37 C.F.R. § 1.97(b). No fee is required.

This Application relies on the earlier filing date of prior Application No. 14/792,094, filed July 6, 2015; Application No. 14/021,790, filed September 9, 2013; Application No. 13/859,450, filed April 9, 2013; Application No. 13/622,872, filed September 19, 2012; and Application No. 13/387,343, filed February 12, 2012, under 35 U.S.C. § 120. It is understood that the Examiner will consider information that was submitted to or cited by the Office in such prior applications. M.P.E.P. § 609.02(A)(2). Copies of documents previously submitted to or cited by the Office in the prior application are not required to be provided in this application and thus are not attached. 37 C.F.R. § 1.98(d).

The Commissioner is hereby authorized to charge any underpayment of the following fees associated with this communication, including any necessary fees for the submission of an information disclosure statement under 37 CFR § 1.17(p) or for the extension of time, or credit any overpayment to Deposit Account No. 50-0310.

Respectfully submitted,

Date: September 11, 2018
MORGAN LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
San Francisco, California 94105
Tel: 415.442.1000
Fax: 415.442.1001

By: /Louis-Vu Nguyen /
Louis-Vu Nguyen, Reg. No. 58,729, for
Gargi Talukder, Reg. No. 61,368
Filed Under 37 C.F.R. § 1.34

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00284

Substitute for form 1449A/PTO
(Substitute PTO/SB/8A)

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	1

Complete if Known	
Application Number	15/677,957
Filing Date	August 15, 2017
First Named Inventor	Sidney BRENNER
Art Unit	1639
Examiner Name	Karla A. Dines
Attorney Docket Number	104371-5016-US08

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	B1	US 5,846,719		Brenner et al.	
	B2	US 6,677,121		Lizardi et al.	
	B3	US 7,217,522		Brenner	
	B4	US 7,393,665		Brenner	
	B5	US 7,537,897		Brenner et al.	
	B6	US 9,085,798		Chee	
	B7	US 2003/0050453		Sorge	
	B8	US 2003/0207300		Matray et al.	
	B9	US 2005/0250147		Macevicz	
	B10	US 2008/0274458		Latham et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[2] Number[4] Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	B11					
	B12					
	B13					
	B14					
	B15					

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	B16	BRENNER, S. et al. “In vitro cloning of complex mixtures of DNA on microbeads: Physical separation of differentially expressed cDNAs” PNAS 2000 Feb. 15; 97(4):1665-70.	
	B17	HUG, H. et al. "Measurement of the number of molecules of a single mRNA species in a complex mRNA preparation" J Theor Biol. 2003 Apr 21; 221(4):615-24.	
	B18	MINER et al. “Molecular barcodes detect redundancy and contamination in hairpin-bisulfite PCR” Nucleic Acids Res. 2004 Sep 30; 32(17):e135.	
	B19		

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.[1] Applicant's unique citation designation number (optional).[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).[4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.[6] Applicant is to place a check mark here if English language Translation is attached.

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

DB2/ 34423567.1

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00286

Electronic Patent Application Fee Transmittal

Application Number:	15677957
Filing Date:	15-Aug-2017
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Filer:	Louis-Vu T. Nguyen/Sheila Gloss
Attorney Docket Number:	104371-5016-US08

Filed as Small 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($)
Miscellaneous:				
RCE- 1ST REQUEST	2801	1	650	650
		Total in USD ($)		**650**

Electronic Acknowledgement Receipt	
EFS ID:	33683529
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	156830
Filer:	Louis-Vu T. Nguyen/Sheila Gloss
Filer Authorized By:	Louis-Vu T. Nguyen
Attorney Docket Number:	104371-5016-US08
Receipt Date:	11-SEP-2018
Filing Date:	15-AUG-2017
Time Stamp:	20:08:34
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$650
RAM confirmation Number	091218INTEFSW00006202500310
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	Request for Corrected Filing Receipt	104371-5016-US08_RequestCorrFR.pdf	377059 ce030721c1e5ffaa2320a838554941fd9cbc7a5f	no	6
Warnings:					
Information:					
2	Application Data Sheet	104371-5016-US08_2SuppADS.pdf	1129181 5a1d79f0898ef5d7cade3d7f7fad1ed120e428b2	no	9
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
3	Non Patent Literature	BRENNER_PNAS_2000.pdf	182308 4a56788c0a2c415cca6386e67d1ae2482e560046	no	1
Warnings:					
Information:					
4	Non Patent Literature	HUG_JTheorBiol_2003_615-624.PDF	808630 ca327182902344ddfbe41ec68550671af65cc7a7	no	10
Warnings:					
Information:					
5	Non Patent Literature	Miner_2004.pdf	224391 0277f76eeda9eb2c25e65d6fd25819314b427d28	no	4
Warnings:					
Information:					
6	Request for Continued Examination (RCE)	104371-5016-US08_RCE.pdf	1349956 e36034e2fdfd36adadcbc879768b87cc0c008943	no	3
Warnings:					

Information:					
7		104371-5016-US08_AmendwRCE.pdf	181303 222b604ab1e29f8f388face4fddaaf6ef7bea814	yes	5
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Amendment Submitted/Entered with Filing of CPA/RCE		1	1	
	Claims		2	3	
	Applicant Arguments/Remarks Made in an Amendment		4	5	
Warnings:					
Information:					
8	Information Disclosure Statement (IDS) Form (SB08)	104371-5016-US08_SIDS.pdf	334248 1881058ac04d1ed6ff870d2d3208eec03a342580	no	4
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
9	Fee Worksheet (SB06)	fee-info.pdf	30545 f541d4f1f52d498f8c0632388b1f0e0acfc54c85	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	4617621		

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.

UNITED STATES PATENT AND TRADEMARK OFFICE

USPTO Automated Interview Request (AIR)

Sep 13 2018

This paper requesting to schedule and/or conduct an interview is appropriate because:

This submission is requested to be accepted as an authorization for this interview to communicate via the internet. Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with the undersigned concerning scheduling of the interview via video conference, instant messaging, or electronic mail, and to conduct the interview in accordance with office practice including video conferencing.

Name(s):
Louis Nguyen

S-signature:
/Louis Nguyen/

Registration Number:
58729

U.S. Application Number:
15677957

Confirmation Number:
1051

E-mail Address:
louis.nguyen@morganlewis.com

Phone Number:
4154421303

Proposed Time of Interview:
9-19-2018 1:30 PM ET

Alternative Proposed Time(s) of Interview:
9-20-2018 1:30 PM ET

Alternative Proposed Time(s) of Interview:
9-21-2018 1:30 PM ET

Prefered Interview Type:
Telephonic

I am the applicant or applicant's representative for this application.

Topic for Discussion:
Claim amendments and IDS filed on September 11, 2018

uspto UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/677,957	08/15/2017	1639	800	104371-5016-US08	6	1

CONFIRMATION NO. 1051

CORRECTED FILING RECEIPT

156830
MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

OC000000102284448

Date Mailed: 09/14/2018

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

Inventor(s)

Sydney Brenner, Ely, UNITED KINGDOM;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, London, UNITED KINGDOM;

Applicant(s)

10X Genomics, Inc., Pleasanton, CA;

Power of Attorney: The patent practitioners associated with Customer Number 43850

Domestic Priority data as claimed by applicant

This application is a CON of 14/792,094 07/06/2015 ABN
which is a CON of 14/172,694 02/04/2014 PAT 9102980
which is a CON of 14/021,790 09/09/2013 PAT 8679756
which is a CON of 13/859,450 04/09/2013 PAT 8563274
which is a CON of 13/622,872 09/19/2012 ABN
which is a CON of 13/387,343 02/15/2012 PAT 8298767
which is a 371 of PCT/IB2010/002243 08/13/2010
which claims benefit of 61/288,792 12/21/2009
and claims benefit of 61/235,595 08/20/2009

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.

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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: 08/22/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/677,957**

Projected Publication Date: Not Applicable

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

Preliminary Class

506

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.

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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

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

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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 PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

156830 7590 09/28/2018

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

EXAMINER
DINES, KARLA A

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
09/28/2018	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

donald.mixon@morganlewis.com
sfipdocketing@morganlewis.com

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Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00298

Applicant-Initiated Interview Summary	**Application No.** 15/677,957	**Applicant(s)** Brenner et al.	
	Examiner KARLA A DINES	**Art Unit** 1639	**AIA Status** No

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

(1) KARLA A. DINES. (3) _____.

(2) Louis Nguyen, Applicant's representatitve. (4) _____.

Date of Interview: 19 September 2018.

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

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

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

Claim(s) discussed: _____.

Identification of prior art discussed: none.

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

Applicant's representative explained the reasons for the RCE after the Notice of Allowance, stating that the claims were amended to correct antecedent basis issues and that an IDS was filed..

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

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

☐ Attachment

/KARLA A DINES/ Primary Examiner, Art Unit 1639	

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Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

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

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

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

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

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

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

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

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

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

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

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

Examiner to Check for Accuracy

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

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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NOTICE OF ALLOWANCE AND FEE(S) DUE

156830 7590 10/03/2018

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

EXAMINER
DINES, KARLA A

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/03/2018

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

TITLE OF INVENTION: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	01/03/2019

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

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

HOW TO REPLY TO THIS NOTICE:

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

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

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

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

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

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

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 02/11)

10x Genomics, Inc. Exhibit 2001
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PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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)

156830 7590 10/03/2018
MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

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 facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

TITLE OF INVENTION: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	01/03/2019

EXAMINER	ART UNIT	CLASS-SUBCLASS
DINES, KARLA A	1639	506-004000

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 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(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 has been filed for recordation as set forth in 37 CFR 3.11. 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. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

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

❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00302

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

156830 7590 10/03/2018

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

EXAMINER	
DINES, KARLA A	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/03/2018

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.

PTOL-85 (Rev. 02/11)

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00303

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 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, 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. 15/677,957	Applicant(s) Brenner et al.	
	Examiner KARLA A DINES	Art Unit 1639	AIA Status No

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

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

1. ☑ This communication is responsive to the RCE filed on 9/11/2018.
   ☐ 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 1-6 . 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 areply 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 9/11/2018.
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 _____.

/KARLA A DINES/
Primary Examiner, Art Unit 1639

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Notice of Pre-AIA or AIA Status

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

Information Disclosure Statement

The information disclosure statement filed 9/11/2018 is acknowledged. A signed copy of the corresponding 1449 form has been included with this Office action.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

Applicants filed a new IDS on 9/11/2018. A thorough search of the prior art, including the prior art submitted in the newly filed IDS, filed after the Notice of Allowance mailed on 8/28/2018, shows no art that teaches or reasonably suggests the claimed invention. Likewise, amendments to the claims filed 9/11/2018, only serves to further clarify the claimed invention, which is free of the 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

Claims 1-6 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLA A DINES whose telephone number is (571)272-6837. The examiner can normally be reached on Monday-Friday 7am-4pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

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

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

/KARLA A DINES/
Primary Examiner, Art Unit 1639

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	Art Unit
	KARLA A DINES	1639

CPC - Searched*		
Symbol	Date	Examiner
C12Q1/6874	08/22/2018	kd
C12N15/1065	08/22/2018	kd
C12Q1/6874	09/30/2018	kd
C12N15/1065	09/30/2018	kd

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner
506	4	09/30/2018	kd
506	4	09/30/2018	kd

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

/KARLA A DINES/ Primary Examiner, Art Unit 1639	

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00308

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	Art Unit
	KARLA A DINES	1639

Search Notes		
Search Notes	**Date**	**Examiner**
EAST and PALM searches	12/18/2017	kd
EAST and PubMed Searches	12/18/2017	kd
EAST inventor search	12/20/2017	kd
EAST and PALM inventor searches	07/03/2018	kd
EAST and PubMed searches	07/02/2018	kd
Update EAST search	07/03/2018	kd
EAST and PALM inventor searches	08/22/2018	kd
EAST and PubMed searches	08/22/2018	kd
C12Q1/6874	08/23/2018	kd
C12N15/1065	08/23/2018	kd
506/4	08/23/2018	kd
EAST and PALM inventor searches	09/29/2018	kd
EAST and PubMed searches	09/30/2018	kd
506/4	09/30/2018	kd
C12Q1/6874	09/30/2018	kd
C12N15/1065	09/30/2018	kd

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
506	4	08/23/2018	kd
C12Q1	6874	08/23/2018	kd
506	4	09/30/2018	kd
C12Q1	6874	09/30/2018	kd

/KARLA A DINES/ Primary Examiner, Art Unit 1639	

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00309

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	**Art Unit**
	KARLA A DINES	1639

CPC						
Symbol					**Type**	**Version**
C12Q	/	1	/	6874	F	2013-01-01
C12Q	/	1	/	6855	I	2013-01-01
C12Q	/	1	/	6806	I	2013-01-01
C12Q	/	1	/	686	I	2013-01-01
C12N	/	15	/	1065	I	2013-01-01

CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
C12Q	/	1	/	6855	I	1	1	2013-01-01
C12Q	/	2563	/	179	A	1	2	2013-01-01
C12Q	/	2537	/	143	A	1	3	2013-01-01
C12Q	/	2535	/	122	A	1	4	2013-01-01
C12Q	/	1	/	6855	I	2	1	2013-01-01
C12Q	/	2525	/	161	A	2	2	2013-01-01
C12Q	/	2525	/	155	A	2	3	2013-01-01
C12Q	/	2525	/	143	A	2	4	2013-01-01

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/KARLA A DINES/ Primary Examiner, Art Unit 1639	30 September 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20180929

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00310

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	**Art Unit**
	KARLA A DINES	1639

INTERNATIONAL CLASSIFICATION				
CLAIMED				
C12Q1/686	/	1	/	686

NON-CLAIMED				
C12N15/10	/	15	/	10

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**
506	4

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/KARLA A DINES/ Primary Examiner, Art Unit 1639	30 September 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20180929

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00311

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/677,957	Brenner et al.
	Examiner	**Art Unit**
	KARLA A DINES	1639

☑ 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
1	1														
2	2														
3	3														
4	4														
5	5														
6	6														

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/KARLA A DINES/ Primary Examiner, Art Unit 1639	30 September 2018	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20180929

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00312

PATENT

Application No. 15/677,957
Attorney Docket No. 104371-5016-US08

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Conf. No.: **1051**
Sidney BRENNER	Art Unit: **1639**
Application No.: **15/677,957**	Examiner: **Karla A. Dines**
Filed: **August 15, 2017**	Docket No.: **104371-5016-US08**
For: **Methods for Analyzing Nucleic Acids from Single Cells**	*Certificate of Transmission (37 C.F.R. § 1.8)* *I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office electronic filing system (EFS-Web) to the USPTO on September 11, 2018.* / Sheila R. Gloss / *Sheila R. Gloss*

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

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner:

This Information Disclosure Statement is hereby submitted in accordance with 37 C.F.R. 1.98 and pursuant to Applicant's continuing duty under 37 C.F.R. 1.56 to bring any information which may be material to patentability of this application to the Examiner's attention.

Applicant makes no representation that a search has been conducted by the Applicant, or that there is not possibly more relevant art. 37 C.F.R. § 1.97(g). Applicant also makes no representation that the information submitted herewith is in fact material to patentability. The filing of this Information Disclosure Statement shall not be construed as an admission against interest in any manner. 37 C.F.R. § 1.97(h).

The Examiner's attention is directed to the reference(s) cited on the accompanying substitute for forms 1449A/PTO and PTO/SB/08. Except for U.S. Patents and U.S. Patent Application Publications, *see* 37 C.F.R. § 1.98(a)(2)(i), copies of the cited references are enclosed, unless otherwise noted below.

All References Considered Except Where Lined Through. /K.A.D/

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
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Page 00313

This Information Disclosure Statement is being filed within three months of the filing date of a national application other than a continued prosecution application, within three months of the date of entry of a national stage, before the mailing of a first Office action on the merits, or before the mailing of a first Office action after the filing of a request for continued examination. 37 C.F.R. § 1.97(b). No fee is required.

This Application relies on the earlier filing date of prior Application No. 14/792,094, filed July 6, 2015; Application No. 14/021,790, filed September 9, 2013; Application No. 13/859,450, filed April 9, 2013; Application No. 13/622,872, filed September 19, 2012; and Application No. 13/387,343, filed February 12, 2012, under 35 U.S.C. § 120. It is understood that the Examiner will consider information that was submitted to or cited by the Office in such prior applications. M.P.E.P. § 609.02(A)(2). Copies of documents previously submitted to or cited by the Office in the prior application are not required to be provided in this application and thus are not attached. 37 C.F.R. § 1.98(d).

The Commissioner is hereby authorized to charge any underpayment of the following fees associated with this communication, including any necessary fees for the submission of an information disclosure statement under 37 CFR § 1.17(p) or for the extension of time, or credit any overpayment to Deposit Account No. 50-0310.

Respectfully submitted,

Date: September 11, 2018
MORGAN LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
San Francisco, California 94105
Tel: 415.442.1000
Fax: 415.442.1001

By: /Louis-Vu Nguyen /
Louis-Vu Nguyen, Reg. No. 58,729, for
Gargi Talukder, Reg. No. 61,368
Filed Under 37 C.F.R. § 1.34

All References Considered Except Where Lined Through. /K.A.D/

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00314

Substitute for form 1449A/PTO (Substitute PTO/SB/8A)				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	**15/677,957**
				Filing Date	**August 15, 2017**
(use as many sheets as necessary)				First Named Inventor	**Sidney BRENNER**
				Art Unit	**1639**
				Examiner Name	**Karla A. Dines**
Sheet	**1**	of	**1**	Attorney Docket Number	**104371-5016-US08**

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	B1	US 5,846,719		Brenner et al.	
	B2	US 6,677,121		Lizardi et al.	
	B3	US 7,217,522		Brenner	
	B4	US 7,393,665		Brenner	
	B5	US 7,537,897		Brenner et al.	
	B6	US 9,085,798		Chee	
	B7	US 2003/0050453		Sorge	
	B8	US 2003/0207300		Matray et al.	
	B9	US 2005/0250147		Macevicz	
	B10	US 2008/0274458		Latham et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[2] Number[4] Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	B11					
	B12					
	B13					
	B14					
	B15					

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	B16	BRENNER, S. et al. “In vitro cloning of complex mixtures of DNA on microbeads: Physical separation of differentially expressed cDNAs” PNAS 2000 Feb. 15; 97(4):1665-70.	
	B17	HUG, H. et al. "Measurement of the number of molecules of a single mRNA species in a complex mRNA preparation" J Theor Biol. 2003 Apr 21; 221(4):615-24.	
	B18	MINER et al. “Molecular barcodes detect redundancy and contamination in hairpin-bisulfite PCR” Nucleic Acids Res. 2004 Sep 30; 32(17):e135.	
	B19		

Examiner Signature	/KARLA A DINES/	Date Considered	09/29/2018

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.[1] Applicant's unique citation designation number (optional).[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).[4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.[6] Applicant is to place a check mark here if English language Translation is attached.

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

DB2/ 34423567.1

All References Considered Except Where Lined Through. /K.A.D/

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	46	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 08:50
L2	9507	c12q1/6874.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 09:26
L3	443	l2 and "single cell" and (barcode or zipcode or "bar code" or identifier)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 09:48
L11	2343	c12n15/1065.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 11:49
L12	244	l11 and "single cell" and (barcode or zipcode or "bar code" or identifier)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 11:50
L15	1150	506/4.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 12:16
L16	93	l15 and "single cell" and (barcode or zipcode or "bar code" or identifier)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/09/30 12:17
S1	1227	(molecul$2 adj identifier) or (random	USPAT	OR	OFF	2017/12/18

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		adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)				09:26
S2	73	S1 and "single cell"	USPAT	OR	OFF	2017/12/18 09:27
S3	9	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))and "single cell sequencing"	USPAT	OR	OFF	2017/12/18 09:31
S4	8	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting))same "single cell sequencing"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 09:33
S5	1227	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2017/12/18 11:54
S6	97	barcode same "nucleic acid" same "single cell" same sequenc$4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 12:30
S7	172	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:42
S8	49	S7 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:43
S9	48	S7 and "single cell" and sequenc$3	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S10	1	S7 and "single cell" and sequenc$3 and ("multiplex identifier" or "MID")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 13:44
S11	5	S7 and ("single cell" and	US-PGPUB;	OR	OFF	2017/12/18

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		sequenc$3).clm.	USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			14:22
S12	442	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:13
S13	3	S12 and ("single cell" and sequenc$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/18 17:33
S14	58	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 11:59
S15	27	mikawa-gi.in. and tags	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:05
S16	22	mikawa-gi.in. and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:06
S17	184	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
S18	14	S17 and ((tags or barcodes) same "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:09
S19	14	S17 and ((tags or barcodes) with "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT;	OR	OFF	2017/12/20 12:10

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			IBM_TDB			
S20	44	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
S21	14	S20 and ((tags or barcodes) with "linear amplification")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:11
S22	19	S20 and (tags or barcodes)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:22
S23	0	S20 and (tags or barcodes)with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:23
S24	38	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:24
S25	2655	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with pcr	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:26
S26	0	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with "linear amplification" with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S27	54	((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting) or barcode or tag) with generat$3 with amplification with adapter	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/20 12:28
S28	54	S27 not S24	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/12/20 12:28

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			JPO; DERWENT; IBM_TDB			
S29	22	"combinatorial barcoding"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 09:36
S30	8	"9410149".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 12:47
S31	8	"9410150".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 13:03
S32	2	"8679756".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 14:09
S33	3	"8563274".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2017/12/21 16:11
S34	246	"10x genomics"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:07
S35	52	S34 and "single cell" and sequenc$3.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:08
S36	0	S34 and "single cell" and "tagged sequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S37	0	S34 and "single cell" and "tagsequence".clm.	US-PGPUB; USPAT;	OR	OFF	2018/07/02 14:57

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			USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			
S38	1	S34 and "single cell" and "tag sequence".clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 14:57
S39	10062	"single cell" and (tags or zipcode or "zip code" or barcode or "bar code")and sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:32
S40	28	"single cell" same (tags or zipcode or "zip code" or barcode or "bar code") same sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:34
S41	10	"single cells" same (tags or zipcode or "zip code" or barcode or "bar code") same sequence.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 15:47
S42	2863	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 16:14
S43	32	S42 and ("single cells" with identif$7)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/02 16:15
S44	445	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:01
S45	31	S44 and "multiplex identifier"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:02

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S46	4	S44 and "multiplex identifier" and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:10
S47	2	"7544473".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:13
S49	1	"multiplex identifier" same "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:23
S50	22	"multiplex identifier" and "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:23
S51	60	mikawa-gi.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:43
S52	195	osborne-robert.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:46
S53	13	S52 and "single cells"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:52
S54	45	slatter-andrew.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 11:53
S55	301	tag same sequence same "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO;	OR	OFF	2018/07/03 12:11

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			DERWENT; IBM_TDB			
S56	19	S55 and "first tag"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:11
S57	18	S55 and ("first tag" same "second tag")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/07/03 12:12
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S61	69	"10x genomics".asn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 14:27
S62	445	brenner-sydney.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 14:36
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S64	60	mikawa-gi.in.	US-PGPUB; USPAT; USOCR;	OR	OFF	2018/08/22 14:43

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			FPRS; EPO; JPO; DERWENT; IBM_TDB			
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S68	4	S67 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:31
S70	1135	506/4.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:33
S71	78	S70 and (barcode or "bar code")and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/22 15:34
S72	91	"POPULATION GENETICS TECHNOLOGIES LTD"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:23
S73	2	S72 and "single cell"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:24
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			USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			10:25
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S76	1211	S75 and (molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2018/08/23 10:41
S77	75	S76 and "single cells"	USPAT	OR	OFF	2018/08/23 10:41
S78	85	S76 and "single cell"	USPAT	OR	OFF	2018/08/23 10:41
S79	9334	c12Q1/6874.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:44
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S82	216	c12n15/1065.cpc.	USPAT	OR	OFF	2018/08/23 10:52
S83	2278	c12n15/1065.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2018/08/23 10:52
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EAST Search History (Interference)

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L10	15	l4 and ("single cell" same (barcode or zipcode or "bar code"))	USPAT	OR	OFF	2018/09/30 11:15
L13	221	c12n15/1065.cpc.	USPAT	OR	OFF	2018/09/30 11:59
L14	12	l13 and ("single cell" same (barcode or zipcode or "bar code"))	USPAT	OR	OFF	2018/09/30 12:00
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L18	0	l17 and ("single cell" same (barcode or zipcode or "bar code"))	USPAT	OR	OFF	2018/09/30 12:18
L19	20	l17 and (barcode or zipcode or "bar code")	USPAT	OR	OFF	2018/09/30 12:18

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L20	5	l19 and "single cell"	USPAT	OR	OFF	2018/09/30 12:19
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L22	1	"6677121".pn.	USPAT	OR	OFF	2018/09/30 12:25
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L24	0	"7217522".pn. and "single cell"	USPAT	OR	OFF	2018/09/30 12:26
L25	1	"7393665".pn.	USPAT	OR	OFF	2018/09/30 12:26
L26	1	"7537897".pn.	USPAT	OR	OFF	2018/09/30 12:28
L27	1	"9085798".pn.	USPAT	OR	OFF	2018/09/30 12:29
S85	196	506/4.ccls.	USPAT	OR	OFF	2018/08/23 10:26
S86	21	S85 and "single cell"	USPAT	OR	OFF	2018/08/23 10:26
S87	1198	c12Q1/6874.cpc.	USPAT	OR	OFF	2018/08/23 10:46
S88	1211	S87 and(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)	USPAT	OR	OFF	2018/08/23 10:46
S89	85	S88 and "single cell"	USPAT	OR	OFF	2018/08/23 10:48
S90	208	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (stochastic adj attachment) or (digital adj counting)and "single cell"	USPAT	OR	OFF	2018/08/23 10:49
S91	163	(molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)and "single cell"	USPAT	OR	OFF	2018/08/23 10:50
S92	216	c12n15/1065.cpc.	USPAT	OR	OFF	2018/08/23 10:55
S93	9	S92 and ((molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)) and "single cell"	USPAT	OR	OFF	2018/08/23 10:55
S94	196	506/4.ccls.	USPAT	OR	OFF	2018/08/23 10:57
S95	91	S94 and (molecul$2 adj identifier) or (random adj molecul$2 adj tag) or (molecular adj index) or (single adj molecule adj tagging) or (digital adj counting)and "single cell"	USPAT	OR	OFF	2018/08/23 10:57

9/ 30/ 2018 12:32:07 PM
C:\ Users\ kdines\ Documents\ EAST\ Workspaces\ 15677957.wsp

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00328

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00329

Bibliographic Data

Application No: 15/677,957

Foreign Priority claimed: ○ Yes ◉ No

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

Verified and Acknowledged: /KARLA A DINES/ Examiner's Signature | Initials

Title: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
08/15/2017	506	1639	104371-5016-US08
RULE			

APPLICANTS

10X Genomics, Inc., Pleasanton, CA, UNITED STATES

INVENTORS

Sydney Brenner Ely, UNITED KINGDOM

Gi Mikawa Great Shelford, UNITED KINGDOM

Robert Osborne Great Chesterford, UNITED KINGDOM

Andrew Slatter London, UNITED KINGDOM

CONTINUING DATA

This application is a CON of 14792094 07/06/2015

14792094 is a CON of 14172694 02/04/2014 PAT 9102980

14172694 is a CON of 14021790 09/09/2013 PAT 8679756

14021790 is a CON of 13859450 04/09/2013 PAT 8563274

13859450 is a CON of 13622872 09/19/2012

13622872 is a CON of 13387343 02/15/2012 PAT 8298767

13387343 is a 371 of PCT/IB2010/002243 08/13/2010

PCT/IB2010/002243 has PRO of 61288792 12/21/2009

PCT/IB2010/002243 has PRO of 61235595 08/20/2009

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

08/22/2017

**** SMALL ENTITY ****

STATE OR COUNTRY

UNITED KINGDOM

ADDRESS

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105
UNITED STATES

FILING FEE RECEIVED

$2,800

#17	Add	Search **(#1) AND #16**	0
#16	Add	Search **vann[Author]**	696
#15	Add	Search **(#1) AND #14**	0
#14	Add	Search **Hunkapiller[Author]**	138
#13	Add	Search **hunkapiller, t[Author]**	0
#12	Add	Search **Bridgham, John[Author]**	1
#11	Add	Search **Inman, Christina E[Author]**	5
#10	Add	Search **(#1) AND #8**	0
#9	Add	Search **(#6) AND #8**	0
#8	Add	Search **fry, george[Author]**	161
#7	Add	Search **(#2) AND #6**	11
#6	Add	Search **(#1) AND sequencing**	244
#4	Add	Search **((#1) AND #2) AND #3**	76
#3	Add	Search **(microarray) OR array**	245090
#2	Add	Search **(((beads) OR particles) OR microparticles) OR nanoparticles**	384857
#1	Add	Search **(("poly ethylene glycol") OR "polyethylene glcol") OR "PEG"**	42495

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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)

156830 7590 10/03/2018
MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

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 facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

Sheila R. Gloss	(Depositor's name)
/ Sheila R. Gloss /	(Signature)
October 11, 2018	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	1051

TITLE OF INVENTION: METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$500	$0.00	$0.00	$500	01/03/2019

EXAMINER	ART UNIT	CLASS-SUBCLASS
DINES, KARLA A	1639	506-004000

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 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(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 Morgan, Lewis & Bockius LLP
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 has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: 10X GENOMICS, INC.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Pleasanton, CA

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

4a. The following fee(s) are submitted:

☒ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

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

☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 50-0310 (enclose an extra copy of this form).

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 /Louis-Vu Nguyen/ Date October 11, 2018

Typed or printed name Louis-Vu Nguyen Registration No. 58,729

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00333

Electronic Patent Application Fee Transmittal

Application Number:	15677957
Filing Date:	15-Aug-2017
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Filer:	Louis-Vu T. Nguyen/Sheila Gloss
Attorney Docket Number:	104371-5016-US08

Filed as Small 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:				
UTILITY APPL ISSUE FEE	2501	1	500	500

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**500**

Electronic Acknowledgement Receipt	
EFS ID:	33988443
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	156830
Filer:	Louis-Vu T. Nguyen/Sheila Gloss
Filer Authorized By:	Louis-Vu T. Nguyen
Attorney Docket Number:	104371-5016-US08
Receipt Date:	11-OCT-2018
Filing Date:	15-AUG-2017
Time Stamp:	19:51:10
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$500
RAM confirmation Number	101218INTEFSW00005940500310
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	Issue Fee Payment (PTO-85B)	104371-5016-US08_IssueFeeTrans.pdf	799364 1487f68d1269fe8b2e9e01d08b4881bb50342382	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30428 3aea74034b7ec084a89d4ea87513b3a05bb0cba3	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	829792		

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

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

Attorney Docket No.: 104371-5016-US08

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: **1051**
Sydney Brenner et al.	Examiner: **Karla A. Dines**
Application No.: **15/677,957**	Art Unit: **1639**
Filed: **August 15, 2017**	
For: **METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS**	**STATEMENT OF SUBSTANCE OF INTERVIEW**

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

Sir:

Applicant notes that the substance of the INTERVIEW SUMMARY mailed September 28, 2018 appears accurate.

Respectfully submitted,

Dated: October 12, 2018 By: /Louis T. Nguyen/
Louis T. Nguyen, Reg. No. 58,729 *for*
Gargi Talukder, Reg. No. 61,368

Customer No.: 43850
Morgan, Lewis & Bockius LLP
One Market, Spear Street Tower
San Francisco, CA 94105
Telephone: (415) 442-1000
Facsimile: (415) 442-1001

DB2/ 35113432.1

Electronic Acknowledgement Receipt

EFS ID:	33995885
Application Number:	15677957
International Application Number:	
Confirmation Number:	1051
Title of Invention:	METHODS FOR ANALYZING NUCLEIC ACIDS FROM SINGLE CELLS
First Named Inventor/Applicant Name:	Sydney Brenner
Customer Number:	156830
Filer:	Louis-Vu T. Nguyen/Sheila Gloss
Filer Authorized By:	Louis-Vu T. Nguyen
Attorney Docket Number:	104371-5016-US08
Receipt Date:	12-OCT-2018
Filing Date:	15-AUG-2017
Time Stamp:	17:34:34
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 summary of interview with examiner	104371-5016-US08_IntSummary.pdf	107371 3f4eb6f1d63b92378e9b32f0c82b71a009a76411	no	1

Warnings:

10x Genomics, Inc. Exhibit 2001
Parse Biosciences, Inc. v. 10x Genomics, Inc.
IPR2023-00958
Page 00339

Information:	
Total Files Size (in bytes):	107371

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.

Substitute for form 1449A/PTO
(Substitute PTO/SB/8A)

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	1

Complete if Known	
Application Number	15/677,957
Filing Date	August 15, 2017
First Named Inventor	Sidney BRENNER
Art Unit	1639
Examiner Name	Karla A. Dines
Attorney Docket Number	104371-5016-US08

U.S. PATENT DOCUMENTS

Change(s) applied to document, /T.W./ 11/1/2018

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	B1	US 5,846,719	12/1998	Brenner et al.	
	B2	US 6,677,121	01/2004	Lizardi et al.	
	B3	US 7,217,522	05/2007	Brenner	
	B4	US 7,393,665	07/2008	Brenner	
	B5	US 7,537,897	05/2009	Brenner et al.	
	B6	US 9,085,798	07/2015	Chee	
	B7	US 2003/0050453	03/2003	Sorge	
	B8	US 2003/0207300	11/2003	Matray et al.	
	B9	US 2005/0250147	11/2005	Macevicz	
	B10	US 2008/0274458	11/2008	Latham et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[2] Number[4] Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	B11					
	B12					
	B13					
	B14					
	B15					

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	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[6]
	B16	BRENNER, S. et al. "In vitro cloning of complex mixtures of DNA on microbeads: Physical separation of differentially expressed cDNAs" PNAS 2000 Feb. 15; 97(4):1665-70.	
	B17	HUG, H. et al. "Measurement of the number of molecules of a single mRNA species in a complex mRNA preparation" J Theor Biol. 2003 Apr 21; 221(4):615-24.	
	B18	MINER et al. "Molecular barcodes detect redundancy and contamination in hairpin-bisulfite PCR" Nucleic Acids Res. 2004 Sep 30; 32(17):e135.	
	B19		

Examiner Signature	/KARLA A DINES/	Date Considered	09/29/2018

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.[1] Applicant's unique citation designation number (optional).[2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.[3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).[4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.[5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible.[6] Applicant is to place a check mark here if English language Translation is attached.

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

DB2/ 34423567.1

All References Considered Except Where Lined Through. /K.A.D/

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.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/677,957	12/18/2018	10155981	104371-5016-US08	1051

156830 7590 11/28/2018

MORGAN, LEWIS & BOCKIUS LLP - 10X Genomics
One Market, Spear Street Tower, Suite 2800
San Francisco, CA 94105

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

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

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

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 Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Sydney Brenner, Ely, UNITED KINGDOM;
10X Genomics, Inc., Pleasanton, CA;
Gi Mikawa, Great Shelford, UNITED KINGDOM;
Robert Osborne, Great Chesterford, UNITED KINGDOM;
Andrew Slatter, London, UNITED KINGDOM;

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 USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

AO 120 (Rev. 08/10)

TO:	**Mail Stop 8** **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	5/8/2019	for the District of Delaware

PLAINTIFF	DEFENDANT
10x Genomics, Inc.	Celsee, Inc.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	10,155,981 B2	12/18/2018	10X Genomics, Inc.
2	10,227,648 B2	3/12/2019	10X Genomics, Inc.
3	10,240,197 B1	3/26/2019	10X Genomics, Inc.
4	10,273,541 B2	4/30/2019	10X Genomics, Inc.
5	10,280,459 B1	5/7/2019	10X Genomics, Inc.

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
2		
3		
4		
5		

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
19-862-CFC-SRF	5/8/2019	for the District of Delaware

PLAINTIFF	DEFENDANT
10x Genomics, Inc.	Celsee, Inc.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	10,155,981 B2	12/18/2018	10X Genomics, Inc.
2	10,227,648 B2	3/12/2019	10X Genomics, Inc.
3	10,240,197 B1	3/26/2019	10X Genomics, Inc.
4	10,273,541 B2	4/30/2019	10X Genomics, Inc.
5	10,280,459 B1	5/7/2019	10X Genomics, Inc.

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
2		
3		
4		
5		

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

Chief Judge Connolly signed the Stipulation of Dismissal on 7/27/2021.

CLERK	(BY) DEPUTY CLERK	DATE
John A. Cerino		7/28/2021

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
19-862-CFC-SRF	5/8/2019	for the District of Delaware

PLAINTIFF	DEFENDANT
10x Genomics, Inc.	Celsee, Inc.

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☑ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 10,392,662 B1	8/27/2019	10x Genomics, Inc.
2 10,400,280 B2	9/3/2019	10x Genomics, Inc.
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

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Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

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	REQUEST ID
15/677,957	08/15/2017	Sydney Brenner	104371-5016-US08	157829

Acknowledgement of Loss of Entitlement to Entity Status Discount

The entity status change request below filed through Private PAIR on 02/02/2022 has been accepted.

CERTIFICATIONS:

Change of Entity Status:

X Applicant changing to regular undiscounted fee status.

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

This portion must be completed by the signatory or signatories making the entity status change in accordance with 37 CFR 1.4(d)(4).

Signature:	/Jason Schultz/
Name:	Jason Schultz
Registration Number:	74740

AO 120 (Rev. 08/10)

TO:	**Mail Stop 8** **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	8/24/2022	for the District of Delaware

PLAINTIFF	DEFENDANT
10X GENOMICS, INC.	PARSE BIOSCIENCES, INC. and THE BOARD OF TRUSTEES OF LELAND STANFORD JUNIOR UNIVERSITY

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	10,155,981	12/18/2018	10x Genomics, Inc.
2	10,697,013	6/30/2020	10x Genomics, Inc.
3	10,240,197	3/26/2019	10x Genomics, Inc.
4	10,150,995	12/11/2018	The Board of Trustees of the Leland Stanford Junior University
5	10,619,207	4/14/2020	The Board of Trustees of the Leland Stanford Junior University

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

ADDENDUM TO AO 120 (ADDITIONAL PATENTS)

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	8/24/2022	for the District of Delaware
PLAINTIFF		DEFENDANT
10X GENOMICS, INC.		PARSE BIOSCIENCES, INC. and THE BOARD OF TRUSTEES OF LELAND STANFORD JUNIOR UNIVERSITY

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
6	10,738,357	August 11, 2020	The Board of Trustees of the Leland Stanford Junior University
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading		
	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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