



Letter accompanying subsequently filed items

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The document(s) listed below is (are) subsequently filed documents pertaining to the following application:

Application number	20183626.9
Applicant's or representative's reference	P078152EP

	Description of document	Original file name	Assigned file name
1	Maintenance of the application	ES002_P078152EP-O-Filing claims-3c4a27e7 (signed).pdf	MEPA-1.pdf
2	Claims	ES002_P078152EP C001.pdf	CLMS-1.pdf

	Fees	Factor applied	Fee schedule	Amount to be paid
15-1	501 Additional filing fee for the 36th and each subsequent page	75	16.00	1 200.00
	Total:		EUR	1 200.00

	Payment	
1	Method of payment	Debit from deposit account
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	The European Patent Office is hereby authorised, to debit from the deposit account with the EPO any fees and costs indicated on the fees page.	
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Signatures

Place: **LONDON**
 Date: **11 September 2020**
 Signed by: **/MARSHALL, Cameron John/**

P078152EP

Guardant - EXHIBIT 2002
 Tempus AI, Inc. v. Guardant Health, Inc.
 IPR2025-01434

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Electronically submitted

Your Ref 20183626.9
Our Ref P078152EP:CJM/JNE
Date 11th September 2020

**Re: European Patent Application No. 20183626.9
Guardant Health, Inc.**

I refer to your communication under Rule 58 EPC of 13th July 2020 and I enclose a set of claims for this application.

As there are only 15 claims in the enclosed claim set, no excess claims fee is due.

Any outstanding additional pages fees for this application should be debited from our Deposit Account No. 2805.0059 (Carpmaels & Ransford LLP).

Basis for the enclosed set of claims is summarised in the table below.

Claim	Basis
1	PCT claim 87 & paragraph [0095]
2	Paragraph [0055]
3	Paragraph [0055]
4	Paragraph [0055]
5	Paragraph [0096], penultimate sentence
6	Paragraphs [0210] & [0227]
7	Paragraph [0257]
8	Paragraph [0104]
9	Paragraphs [0235], last sentence & [0105], third last sentence
10	Paragraph [0107]
11	Page 30, lines 4-6
12	Paragraph [0104], fourth sentence
13	Paragraph [0214]

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Claim	Basis
14	Paragraph [0225]
15	Paragraph [0212]

Yours faithfully,

// ELECTRONICALLY SIGNED AND SUBMITTED //

MARSHALL, Cameron John
Carpmaels & Ransford LLP Professional Association No. 182

Encl. Claims

CLAIMS:

1. A method, comprising:

(a) providing a sample comprising a set of double-stranded polynucleotide molecules, each double-stranded polynucleotide molecule including first and second complementary strands, wherein the polynucleotide molecules are cell-free DNA;

(b) tagging said double-stranded polynucleotide molecules with a set of duplex tags, wherein each duplex tag differently tags said first and second complementary strands of a double-stranded polynucleotide molecule in said set;

(c) sequencing at least some of said tagged strands to produce a set of sequence reads;

(d) reducing and/or tracking redundancy in said set of sequence reads;

(e) sorting sequence reads into paired reads and unpaired reads, wherein:

(i) each paired read corresponds to sequence reads generated from a first tagged strand and a second differently tagged complementary strand derived from a double-stranded polynucleotide molecule in said set; and

(ii) each unpaired read represents a first tagged strand having no second differently tag complementary strand derived from a double-stranded polynucleotide molecule represented among said sequence reads in said set of sequence reads; and

(f) determining quantitative measures of at least two of:

(i) said paired reads;

(ii) said unpaired reads that map to each of one or more genetic loci;

(iii) read depth of said paired reads; and

(iv) read depth of unpaired reads.

2. The method of claim 1, wherein (f) comprises determining quantitative measures of at least three of (i)-(iv).

3. The method of claim 1, wherein (f) comprises determining quantitative measures of all of (i)-(iv).

4. The method of any one of claims 1-3, wherein the method further comprises (g) estimating with a programmed computer processor a quantitative measure of total double-stranded polynucleotide molecules in the set that map to each of the one or more genetic loci based on the quantitative measure of paired reads and unpaired reads and their read depths mapping to each locus.

5. The method of any one of claims 1-4, wherein the cell-free DNA has been isolated from a bodily fluid, such as blood or serum.
6. The method of any one of claims 1-5, wherein the tagging uses an excess amount of tags as compared to the double-stranded polynucleotide molecules, optionally wherein the excess is at least 1.25, 1.5, 1.75, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more fold excess, optionally wherein the tagging yields the tagged polynucleotides with a conversion efficiency of at least 30%, optionally at least 50%.
7. The method of any one of claims 1-6, wherein the tagging is by blunt-end ligation or sticky-end ligation of tags to the polynucleotides.
8. The method of any one of claims 1-7, wherein the tags comprise molecular barcodes.
9. The method of claim 8, wherein the tagging is non-unique tagging, optionally wherein at least 1%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, or at least or about 50% of the tagged double-stranded polynucleotide molecules bear a molecular barcode that is shared by at least one other double-stranded polynucleotide molecule.
10. The method of claim 8 or claim 9, wherein no more than 100, 50, 40, 30, 20 or 10 molecular barcodes are used to tag the double-stranded polynucleotide molecules.
11. The method of any one of claims 8-10, wherein the barcodes in combination with sequence data of beginning (start) and/or end (stop) portions of sequence reads are used to assign a unique identity to a particular molecule.
12. The method of any one of claims 8-11, wherein the molecular barcodes have a minimum edit distance of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.
13. The method of any one of claims 1-12, wherein the reducing or tracking redundancy comprises determining consensus reads that are representative of single-strands of the original double-stranded polynucleotide molecules.

14. The method of any one of claims 1-13, wherein the sample is derived from a subject suspected of having a disease, optionally wherein the disease is cancer.

15. The method of any one of claims 1-14, wherein the method further comprises selectively enriching a subset of the tagged DNA, optionally wherein the selective enrichment is performed by hybridisation or amplification techniques, optionally wherein selective enrichment is performed by hybridisation using a solid support, optionally wherein the solid support comprises probes which specifically hybridise to genomic regions associated with cancer.

Acknowledgement of receipt

We hereby acknowledge receipt of the following subsequently filed document(s):

Submission number	9009741	
Application number	EP20183626.9	
Date of receipt	11 September 2020	
Receiving Office	European Patent Office, The Hague	
Your reference	P078152EP	
Applicant	All applicants as on file	
Documents submitted	package-data.xml epf1038.pdf (2 p.) CLMS-1.pdf\ES002_P078152EP C001.pdf (3 p.)	ep-sfd-request.xml MEPA-1.pdf\ES002_P078152EP-O-Fil ing claims-3c4a27e7 (signed).pdf (2 p.)
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