

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): TALASAZ et al.	Confirmation No.: 4580
Serial Number: 15/669,779	Customer No.: 115823
Filing Date: August 4, 2017	Group Art Unit: 1637
Title: SYSTEMS AND METHODS TO DETECT RARE MUTATIONS AND COPY NUMBER VARIATION	Examiner: Cynthia B WILDER

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

AMENDMENT AND RESPONSE TO NON-FINAL OFFICE ACTION

Dear Commissioner:

This paper is in response to Office Action mailed on May 13, 2019. With the extension of time of 2 months filed concurrently herewith, this response is timely filed. Applicant respectfully requests reconsideration of the above-referenced application in view of the following remarks:

Amendments to the Specification begin on page 2 of this paper

Amendments to the Claims begin on page 3 of this paper.

Remarks begin on page 5 of this paper.

Conclusion begins on page 7 of this paper.

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

[0227] After collection of bodily fluid, cell free polynucleotides may be isolated and extracted using a variety of techniques known in the art. In some cases, cell free DNA may be isolated, extracted and prepared using commercially available kits such as the QIAGEN QIAamp® ~~Qiagen Qiamp®~~ Circulating Nucleic Acid Kit protocol. In other examples, ~~Qiagen~~ QIAGEN Qubit™ dsDNA HS Assay kit protocol, Agilent™ DNA 1000 kit, or TruSeq™ Sequencing Library Preparation; Low-Throughput (LT) protocol may be used.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings in the above-referenced patent application. The foregoing amendments are without prejudice and do not constitute an admission regarding the patentability of the amended subject matter and should not so be construed. Applicant reserves the right to pursue the subject matter of the cancelled claims in this or any other appropriate patent application.

Listing of Claims:

1. – 20. (Cancelled).
21. (New) A method for quantifying single nucleotide variant tumor markers in cell-free DNA (“cfDNA”) molecules from a subject, comprising:
 - (a) providing a plurality of cfDNA molecules obtained from a bodily sample of the subject;
 - (b) attaching tags comprising barcodes selected from a plurality of distinct barcode sequences to the cfDNA molecules obtained from the bodily sample of the subject, to generate non-uniquely tagged parent polynucleotides, wherein each non-uniquely tagged parent polynucleotide is substantially unique with respect to other non-uniquely tagged parent polynucleotides in the bodily sample;
 - (c) amplifying the non-uniquely tagged parent polynucleotides to produce amplified non-uniquely tagged progeny polynucleotides;
 - (d) sequencing the amplified non-uniquely tagged progeny polynucleotides to produce a plurality of sequence reads from each non-uniquely tagged parent polynucleotide, wherein each sequence read comprises a barcode sequence and a sequence derived from a cfDNA molecule;
 - (e) grouping the plurality of sequence reads produced from each non-uniquely tagged parent polynucleotide into families based on i) the barcode sequence and ii) sequence information derived from the cfDNA molecules, whereby each family comprises sequence reads of non-uniquely tagged progeny polynucleotides

amplified from a unique polynucleotide among the non-uniquely tagged parent polynucleotides;

- (f) comparing the sequence reads grouped within each family to each other to determine consensus sequences for each family, wherein each of the consensus sequences corresponds to a unique polynucleotide among the non-uniquely tagged parent polynucleotides;
- (g) providing a reference sequence from a human genome, the reference sequence comprising one or more loci;
- (h) identifying consensus sequences that map to a given locus of the one or more loci; and
- (i) calculating a number of consensus sequences that map to the given locus that include the single nucleotide variant thereby quantifying single nucleotide variant tumor markers in the cfDNA molecules from the bodily sample of the subject.

22. (New) The method of claim 21, wherein, in (b), at least 10% of the cfDNA molecules are tagged with the tags comprising the barcodes to generate the non-uniquely tagged parent polynucleotides.

REMARKS

Claims 1-20 were pending prior to entry of the above-referenced claim amendments. Claims 1-20 have been cancelled. Claims 21-22 have been newly added. Accordingly, claims 21-22 are now pending. No new matter is added.

Claim Amendments

New claims 21 and 22 are fully supported by the specification as filed in the instant application, U.S. Patent Application No. 15/669,779, now U.S. Patent Publication 2018/0023125A1 (hereinafter “Application”), at for example, paragraphs [0044], [0088], [0096], [0098], [0099], [0114], [0115], [0117], [0122], [0123], [0144], [0148], [0202], [0210], [0235], and [0243]. No new matter is being introduced by these amendments.

Specification Objection

The specification was objected to because of the following informality: the use of trade names and marks used in commerce should be identified and presented accordingly in the patent application. Applicant has amended the specification herein with the appropriate correction. No new matter is being introduced. Accordingly, Applicant respectfully requests that the objection be withdrawn.

35 U.S.C. §103

Claims 1-9 and 11-20 stand rejected under 35 U.S.C. § 103 over Schmitt et al. (US 9,752,188) (“Schmitt”) in view of Fan et al. (PNAS 2008, 105(42):16266-16271) (“Fan”) and further in view of Forshew (Sci. Transl. Med. 2012, 4(136):1-12) (“Forshew”). Without conceding to the basis of rejection, Applicant has cancelled claims 1-9 and 11-20. Accordingly, the § 103 rejections of claims 1-9 and 11-20 are now moot in view of the cancellation of these claims. Applicant respectfully requests that the § 103 rejections of claims 1-9 and 11-20 be withdrawn.

Claim 10 stands rejected under 35 U.S.C. § 103 over Schmitt in view of Fan and Forshew as applied above, and further in view of Pinter et al. (US 20040209299) (“Pinter”). Without conceding in the basis of rejection, Applicant has canceled claim 10. Accordingly, the §103

rejection of claim 10 is now moot in view of the cancellation of this claim. Applicant respectfully requests that the §103 rejection of this claim be withdrawn.

Nonstatutory Double Patenting

Claims 1-20 stand provisionally rejected on the ground of nonstatutory double patenting over claims 1-33 of U.S. Patent No. 9,902,992.

Claims 1, 2, 3, 9-11 stand provisionally rejected on the ground of nonstatutory double patenting over claims 1, 4, and 6-11 of U.S. Patent No. 9,598,731.

Claims 1, 2, 4, 10-15, and 17 stand provisionally rejected on the ground of nonstatutory double patenting over claims 1, 2, 4, 5, 9, 10, 21, 2, 41, and 44 of co-pending U.S. Patent Application No. 14/855,301.

Without conceding in the basis of rejection, Applicant has cancelled claims 1-20 rendering the nonstatutory rejections of these claims moot. Accordingly, Applicant respectfully requests that the rejections of these claims be withdrawn.

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

CONCLUSION

This paper fully addresses the rejections raised in the Office Action mailed May 13, 2019. Applicant believes that the present application is now in condition for allowance and respectfully requests that the Examiner expedite the prosecution of this application to allowance. The Commissioner is authorized to charge any underpayment, or credit any overpayment, to Deposit Account No. 23-2415, referencing Attorney Docket No. 42534-710.303.

Respectfully submitted,

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