

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TWINSTRAND BIOSCIENCES, INC.
Petitioner,

v.

GUARDANT HEALTH, INC.
Patent Owner.

Case IPR2022-01152
U.S. Patent No. 11,118,221

**PETITION FOR *INTER PARTES* REVIEW
OF U.S. PATENT NO. 11,118,221**

Mail Stop "PATENT BOARD"
Patent Trial and Appeal Board
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

I.	Introduction.....	1
II.	Statement of Precise Relief Requested and Reasons Therefor (37 C.F.R. §42.22(A))	2
III.	State of the art before December 2013	2
	A. Optimization techniques for DNA library preparation were well known.	3
	B. Cell-free DNA isolated from blood was widely used in NGS platforms.....	5
	1. The presence of cell-free tumor DNA in human blood was well known.....	6
	2. Isolating cfDNA from blood was routine with off-the-shelf kits.	7
	C. The prior art taught that Duplex Sequencing dramatically lowers NGS error rate.	7
	D. The prior art taught applying Duplex Sequencing to cfDNA.	14
IV.	The '221 patent and its prosecution history	15
V.	Person of ordinary skill in art	19
VI.	Claim construction.....	19
VII.	Identification of the challenge (37 C.F.R. §42.104(b))	20
VIII.	The facts and law weigh against discretionary denial of institution.	22
	A. This Petition satisfies 35 U.S.C. §325(d).....	22
	B. The <i>Fintiv</i> factors do not support discretionary denial.	26
IX.	Ground 1: claims 1-4, 6-7, 9-15, 18-22, and 24-28 would have been obvious over Narayan and Schmitt	27
	A. Claim 1	28
	1. “A method, comprising: (a) providing a population of cell-free deoxyribonucleic acid (cfDNA) molecules having first and second complementary strands...”	28
	2. “(b) tagging a plurality of the cfDNA molecules of the population with a set of duplex tags comprising molecular barcodes from a set of molecular barcodes to produce tagged parent polynucleotides, wherein duplex tags from the set of duplex tags are attached at both	

	ends of a molecule of the plurality of the cfDNA molecules...”	28
3.	“(c) amplifying a plurality of the tagged parent polynucleotides to produce amplified progeny polynucleotides...”	30
4.	“(d) sequencing at least a subset of the amplified progeny polynucleotides to produce a set of sequence reads...”	30
5.	“(e) reducing or tracking redundancy in the set of sequence reads using at least sequence information from the molecular barcodes to generate a plurality of consensus sequences representative of original cfDNA molecules from among the tagged parent polynucleotides, wherein the plurality of consensus sequences is generated from (i) paired reads corresponding to sequence reads generated from a first tagged strand and a second tagged complementary strand derived from a cfDNA molecule from among the tagged parent polynucleotides, and (ii) unpaired reads corresponding to sequence reads generated from a first tagged strand having no second tagged complementary strand derived from a cfDNA molecule from among the tagged parent polynucleotides.”	30
6.	A POSA would have had a reason to combine Narayan and Schmitt.	33
7.	A POSA would have had a reasonable expectation of success.	37
B.	Claim 18	38
1.	“A method, comprising: (a) providing a population of double-stranded cell-free deoxyribonucleic acid (cfDNA) molecules having first and second complementary strands...”	39
2.	“(b) non-uniquely tagging a plurality of the double-stranded cfDNA molecules of the population with a set of duplex tags comprising molecular barcodes from a set of molecular barcodes to produce non-uniquely tagged parent polynucleotides, wherein the double-stranded cfDNA molecules that map to a mappable base position of a reference sequence are tagged with a number of different molecular barcodes ranging from	

	at least 2 to fewer than a number of the double-stranded cfDNA molecules that map to the mappable base position...”	39
3.	“(c) amplifying a plurality of the non-uniquely tagged parent polynucleotides to produce amplified progeny polynucleotides...”	42
4.	“(d) sequencing at least a subset of the amplified progeny polynucleotides to produce a set of sequence reads...”	43
5.	“(e) reducing or tracking redundancy in the set of sequence reads using at least sequence information from the molecular barcodes...”	43
6.	“(f) sorting the set of sequence reads into paired reads and unpaired reads, wherein (i) a paired read corresponds to sequence reads generated from a first tagged strand and a second tagged complementary strand derived from a double-stranded cfDNA molecule from among the non-uniquely tagged parent polynucleotides, and (ii) an unpaired read corresponds to sequence reads generated from a first tagged strand having no second tagged complementary strand derived from a double-stranded cfDNA molecule from among the non-uniquely tagged parent polynucleotides...”	43
7.	“(g) determining, at one or more loci of a reference sequence, quantitative measures of at least two of (i) the paired reads, (ii) the unpaired reads, (iii) read depth of the paired reads, and (iv) read depth of the unpaired reads.”	46
C.	Claims 2 and 19	49
D.	Claims 3 and 20	50
E.	Claims 4 and 21	51
F.	Claim 6	52
G.	Claim 7	53
H.	Claim 22	53
I.	Claims 9-10 and 24-25	54
J.	Claims 11 and 26	55
K.	Claims 12 and 13	57
L.	Claim 14	58
M.	Claim 15	59

N. Claims 27 and 28.....60

X. Ground 2: claim 5 would have been obvious over Narayan, Schmitt, and Meyer 61

XI. Ground 3: claims 8 and 23 would have been obvious over Narayan, Schmitt, and Craig..... 63

XII. Ground 4: claims 16-17 and 29-30 would have been obvious over Narayan, Schmitt, and Kivioja. 65

XIII. Objective indicia do not support patentability..... 70

XIV. Certification of standing and Patent IPR eligibility (37 C.F.R. §42.104(a)) 70

XV. Mandatory Notices (37 C.F.R. §42.8(a)(1)) 70

XVI. Conclusion. 72

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.