UNITED STATES	PATENT AND	TRADEMARK OFFI	CE
BEFORE THE PA	ATENT TRIAL A	AND APPEAL BOAR	D

TWINSTRAND BIOSCIENCES, INC. Petitioner,

v.

GUARDANT HEALTH, INC. Patent Owner.

Case IPR2022-01116 U.S. Patent No. 10,889,858

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PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 10,889,858

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Patent Trial and Appeal Board U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450



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	B.	Cell-free DNA isolated from blood was widely used in next-generation sequencing platforms.	5
		1. The presence of cell-free tumor DNA in human blood was well known.	
		2. Isolating cfDNA from blood was routine with commercially available kits.	6
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		1. "A method for analyzing sequencing reads of double-stranded cell-free deoxyribonucleic acid (cfDNA) molecules from a sample of a subject"	. 26
		2. "(a) tagging a plurality of double-stranded cfDNA molecules from a population of double-stranded cfDNA molecules from the sample with a set of library adaptors comprising a plurality of molecular barcodes to generate tagged parent polynucleotides, wherein the	



	tagging comprises ligating a plurality of library	
	adaptors from the set of library adaptors to the plurality	
	of double-stranded cfDNA molecules from the	
	population using more than a 10× molar excess of	
	library adaptors as compared to the double-stranded	
	cfDNA molecules of the population"	27
3.	"wherein the tagging produces at least 20% of the	
	double-stranded cfDNA molecules of the populations	
	having library adaptors ligated to both ends of a	
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4.	"(b) amplifying a plurality of the tagged parent	
	polynucleotides to produce progeny	
	polynucleotides"	30
5.	"(c) sequencing a plurality of the progeny	
	polynucleotides to produce a set of sequencing	
	reads"	30
6.	"and (d) determining, based at least on sequence	
	information from the molecular barcodes, individual	
	double-stranded cfDNA molecules from among the	
	tagged parent polynucleotides for which either (1) both	
	a Watson strand and a Crick strand of the individual	
	double-stranded cfDNA molecule are detected or (2)	
	only one of a Watson strand or a Crick strand of the	
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1.	"A method for analyzing double-stranded cell-free	
	deoxyribonucleic acid (cfDNA) molecules from a	
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2.	"(a) tagging a plurality of double-stranded cfDNA	
	molecules from a population of double-stranded	
	cfDNA molecules from the sample with a set of library	
	adaptors comprising a plurality of molecular barcodes	
	to generate tagged parent polynucleotides, wherein the	



B.

	tagging comprises ligating a plurality of library	
	adaptors from the set of library adaptors to the plurality	
	of double-stranded cfDNA molecules from the	
1	population using more than a 10× molar excess of	
	library adaptors as compared to the double-stranded	
(cfDNA molecules of the population"	40
3.	"wherein the tagging produces at least 20% of the	
(double-stranded cfDNA molecules of the population	
1	having library adaptors ligated to both ends of a	
1	molecule of the double-stranded cfDNA molecules"	40
4.	"(b) amplifying a plurality of the tagged parent	
1	polynucleotides to produce progeny	
1	polynucleotides"	41
5.	"(c) determining nucleotide sequences of a plurality of	
1	the progeny polynucleotides"	41
6.	"(d) analyzing a plurality of the nucleotide sequences	
•	with a programmed computer processor the analyzing	
(comprising mapping a plurality of the nucleotide	
5	sequences to a reference sequence to produce mapped	
5	sequences"	41
7. '	"grouping a plurality of the mapped sequences into	
i	families based on a combination of sequence	
i	information from the molecular barcodes and start and	
5	stop positions of the mapped sequences, wherein a	
1	family of the families is representative of an individual	
(double-stranded cfDNA molecule from among the	
1	tagged parent polynucleotides"	42
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1	nucleotide sequences representing either (1) both a	
•	Watson strand and a Crick strand of an individual	
(double-stranded cfDNA molecule from among the	
1	tagged parent polynucleotides or (2) only one of a	
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