UNITED STATES	PATENT AND 7	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	
		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	
	C.	The prior art taught that Duplex Sequencing could dramatically lower the error rate of NGS	
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IX.		nd 1: claims 1-7 and 10-27 would have been obvious over Narayan itt, and Meyer26	
	A.	Claim 1	
		1. "A method for analyzing sequencing reads of double-stranded cell-free deoxyribonucleic acid (cfDNA) molecules from a sample of a subject"	
		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	



	adaptors from the set of library adaptors to the plurality	
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	polynucleotides"	30
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	reads"	30
6.	"and (d) determining, based at least on sequence	
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	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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۷.	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	
	to generate tagged parent polynderedides, 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	
population using more than a 10× molar excess of	
library adaptors as compared to the double-stranded	
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double-stranded cfDNA molecules of the population	
having library adaptors ligated to both ends of a	
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4. "(b) amplifying a plurality of the tagged parent	40
polynucleotides to produce progeny	
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Watson strand and a Crick strand of an individual	
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Watson strand or a Crick strand of an individual	
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Claims 2 and 19	
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