

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

10X GENOMICS, INC. and THE BOARD OF	)	
TRUSTEES OF THE LELAND STANFORD	)	
JUNIOR UNIVERSITY	)	
	)	
Plaintiffs,	)	
	)	
v.	)	
	)	C.A. No. 22-1117 (JHS)
PARSE BIOSCIENCES, INC.,	)	
	)	
Defendant.	)	

OPENING REPORT OF JOHN QUACKENBUSH, Ph.D.

May 17, 2024

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Additionally, to the extent Parse argues it does not infringe because two sample polynucleotides may have the same second tag sequence, that is incorrect. The claim does not require perfection, just that the “second tag sequence distinguish[es] the sample polynucleotide from other sample polynucleotides derived from the same single cell.” ’981 Patent at 30:35-37. Thus, since there are up to a million unique sequence in Parse’s method, there are different sequences for at least some of the sample polynucleotides derived from the same single cell that can be used to distinguish between them.

158. In my opinion, Parse infringes a method to append to the sample polynucleotide a second tag sequence distinguishing the sample polynucleotide from other sample polynucleotides derived from the same single cell satisfying this claim element of claim 1 of the ’981 Patent.

Claim 1. A method of analyzing nucleic acids from a plurality of single cells, the method comprising:

(a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;

(b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:

(i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and

(ii) a multiplex identifier (MID) sequence comprising:

I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and

II. a second tag sequence distinguishing the sample polynucleotide from other sample polynucleotides derived from the same single cell;

(c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;

(d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the identified polynucleotide sequence is derived; and

(e) using the second tag sequence to correlate the identified polynucleotide sequence with the sample polynucleotide from which the identified polynucleotide sequence is derived.

159. Claim 1 of the '981 Patent requires sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences. The '981 Patent states that “the nucleic acid may be sequenced directly using a sequencing primer specific for the primer site. This sequencing reaction will read through the MID and desired site in the insert.” '197 Patent at 19:29-32.

160. In my opinion, Parse’s Evercode Products require sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences. “After sequencing, each single cell transcriptome is assembled by combining reads containing the same four-barcode combination.” *See, e.g.*, PARSE10X0000412, at 424, 456 (Evercode WT v2 Manual); *see also* PARSE10X0000343, at 355, 387 (Evercode WT Mini v2 Manual); PARSE10X0000481, at 493, 525 (Evercode WT Mega v2 Manual); WT v3 at 5-7, 33-35, 63-65; PARSE10X0000097, at 109, 141 (Evercode TCR Mega, Human TCR + WT Manual); *see also* PARSE10X0000179, at 191, 223 (Evercode TCR Mini, Human TCR + WT Manual); PARSE10X0000261, at 273, 305 (Evercode TCR, Human TCR + WT Manual). Parse’s Evercode Products require the use of sequencing machines. *See, e.g.*, PARSE10X0000012, at 028 ([REDACTED]); PARSE10X0000046, at 050 (Evercode Brochure) (sequencing data); PARSE10X0061542, at 614 ([REDACTED]);

PARSE10X0662818, at 826 ([REDACTED]); *see also* Parse Biosciences, *Evercode Combinatorial Barcoding* (2024), <https://www.parsebiosciences.com/technology/>.

161. To the extent Parse argues it does not infringe because it sequences fragments of the tagged polynucleotides, this is incorrect. The claims do not require sequencing the entirety of the tagged polynucleotides.

162. In my opinion, Parse infringes a method to sequence the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences satisfying this claim element of claim 1 of the '981 Patent.

Claim 1. A method of analyzing nucleic acids from a plurality of single cells, the method comprising:

(a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;

(b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:

(i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and

(ii) a multiplex identifier (MID) sequence comprising:

I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and

II. a second tag sequence distinguishing the sample polynucleotide from other sample polynucleotides derived from the same single cell;

(c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;

(d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the identified polynucleotide sequence is derived; and

exists between the Giresi Patents and my opinions regarding long-felt unmet need, failure of others, industry praise, and copying.

XV. Supplementation

595. I reserve the right to consider additional materials and to amend or supplement my opinions in light of additional information that may come to my attention, including any Court rulings and/or new arguments raised by Parse directly or through its experts or any critique of my report or opinions advanced by or on behalf of Parse.

596. If I am called to testify, I may explain principles and terminology referred to in this report as well as documents referenced or cited herein. I reserve the right to utilize visual aids, animations, demonstrative exhibits, trial exhibits, and other such testimonial aids in support of my testimony to illustrate the bases for my opinions.

HIGHLY CONFIDENTIAL – ATTORNEYS’ EYES ONLY

I declare under penalty of perjury that the foregoing is true and correct.

Dated: May 17, 2024.

A handwritten signature in black ink, appearing to read 'J. Quackenbush', written above a horizontal line.

JOHN QUACKENBUSH, Ph.D.