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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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AMBRY GENETICS CORPORATION,
Petitioner

v.

THE JOHNS HOPKINS UNIVERSITY
Patent Owner

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Case IPR2017-02096
Patent 8,859,206 B2

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Before LORA M. GREEN, TINA E. HULSE, and RICHARD J. SMITH, *Administrative Patent Judges.*

GREEN, *Administrative Patent Judge*.

# DECISION
Denying Institution of *Inter Partes* Review
*37 C.F.R. § 42.108*

# I. INTRODUCTION

Ambry Genetics Corporation ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1, 3, 15, 20, and 21 of U.S. Patent 8,859,206 B2 (the "'206 patent"). Paper 1 ("Pet.") The Johns Hopkins University ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp.").

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314; *see* 37 C.F.R. §§ 42.4, 42.108. Upon considering the Petition and Preliminary Response, we determine that Petitioner has not shown a reasonable likelihood that it would prevail in showing the unpatentability of challenged claims 1, 3, 15, 20, and 21. Accordingly, we decline to institute an *inter partes* review of those claims.

## *A. Related Proceedings*

The '206 patent has been asserted in pending district court proceedings: *Esoterix Genetic Laboratories, LLC and The Johns Hopkins University v. Ambry Genetics Corporation*, United States District Court for the Middle District of North Carolina, Case No. 1:16-cv-1111-WO-JEP. Pet. 1–2; Paper 3, 2. The '206 patent was also asserted in *Esoterix Genetic Laboratories, LLC and The Johns Hopkins University v. Myriad Genetics, Inc. and Myriad Genetics Laboratories, Inc.*, United States District Court for the Middle District of North Carolina, Case No. 1:16-cv-1112-WE-JEP, but that case has been dismissed. Pet. 2; Paper 3, 2.

Petitioner also filed petitions for *inter partes* review of certain claims

of related U.S. Patent No. 6,440,706 (IPR2017-02086); U.S. Patent No. 7,915,015 (IPR2017-02095); and U.S. Patent No. 7,824,889 (IPR2017-02093). Pet. 2; Paper 3, 2.

### *B. The '206 Patent*

The '206 patent issued on October 14, 2014, with Bert Vogelstein and Kenneth W. Kinzler as the listed co-inventors. Ex. 1001. The '206 patent relates to diagnostic genetic analyses. *Id.* at 1:12. With the understanding that somatic mutations are the primary cause of cancer, new opportunities for basic research into the pathogenesis of cancer have arisen. *Id.* at 1:19–22. For example, in some cases, detecting neoplastic cells in urine, stool, and sputum is possible at a stage when the primary tumors are still curable and the patients are asymptomatic. *Id.* at 1:27–33. Thus, it is important to be able to detect small populations of mutant cells among a large excess of normal cells. *Id.* at 1:25–27. Accordingly, the specification states that "[i]t is an object of the present invention to provide methods for determining the presence of a selected genetic sequence in a population of genetic sequences." *Id.* at 1:65–67.

The claimed method involves diluting a biological sample to a point where a practically usable number of the diluted samples contain a proportion of the selected genetic sequence (analyte) relative to total template molecules. *Id.* at 4:12–16. The diluted samples are separately amplified so that the amplified products have a proportion of the analyte sequence that is detectable by the detection means chosen. *Id.* at 3:66–4:2. With this method, single template molecules can be amplified so that the products are completely mutant or completely wild-type. *Id.* at 4:3–5.

The specification refers to this method as "[d]igital amplification." *Id.* at 4:34–35. According to the specification, "[t]he ultimate utility of Digital Amplification lies in its ability to convert the intrinsically exponential nature of PCR to a linear one." *Id.* at 5:51–53. The specification states further that "[i]t should thereby prove useful for experiments requiring the investigation of individual alleles, rare variants/mutations, or quantitative analysis of PCR products." *Id.* at 5:53–55.

### *C. Illustrative Claim*

Petitioner challenges claims 1, 3, 15, 20, and 21 of the '206 patent, of which claim 1 is an independent claim. Claim 1 is reproduced below:

> 1. A method for detecting quantity of a genetic sequence in a mixed population of human genomic nucleic acid sequences comprising at least a first and a second human genomic sequence, wherein the first sequence is a sequence of a wild-type allele of a locus and a second sequence is a sequence of a mutant allele of the locus, comprising:
>
> [(a)] distributing or diluting a mixed population of cell-free, human genomic nucleic acid template molecules from a sample in which the fraction of mutant alleles is less than 20%, into a set comprising at least fifteen assay samples such that said at least fifteen assay samples each comprises less than ten template molecules;
>
> [(b)] amplifying the template molecules in the assay samples, wherein an assay sample with a single template molecule forms homogeneous amplification products in the assay sample;
>
> [(c)] analyzing by determining nucleic acid sequence of amplification products in the assay samples of the set with homogeneous amplification products to determine a first number of assay samples in the set which contain the

first sequence and a second number of assay samples in the set which contain the second sequence;

[(d)] comparing the first number to the second number to ascertain a ratio which reflects the composition of the mixed population;

[(e)] identifying a mutation in the mixed population if a statistically significant fraction of assay samples comprises the second sequence.

Ex. 1001, 15:43–67; 16:41–43 (with step designations used by Petitioner added in brackets).

*D. The Asserted Grounds of Unpatentability*

Petitioner contends that the challenged claims are unpatentable under 35 U.S.C. §§ 102(b) and/or 103 based on the following specific grounds. Pet. 4.

| **Reference[s]** | **Basis** | **Claims challenged** |
|---|---|---|
| Sykes[1] | § 102(b) | 1, 3, 20, 21 |
| Sykes and Brown[2] | §103 | 15 |

Petitioner also relies on the Declaration of Gregory A. Buck, Ph.D. Ex. 1007.

Patent Owner submitted the Declaration of its expert, Fred Russell Kramer, Ph.D. (Ex. 2001), with its Preliminary Response.

[1] P.J. Sykes et al., *Quantitation of Targets for PCR by Use of Limiting Dilution*, 13 BIOTECHNIQUES 444–49 (1992) ("Sykes") (Ex. 1011).

[2] Brown et al., US Patent No. 6,143,496, issued Nov. 7, 2000 ("Brown") (Ex. 1010).

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