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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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*Ex parte* BERT VOGELSTEIN, KENNETH W. KINZLER,  
D. WILLIAMS PARSONS, XIAOSONG ZHANG,  
JIMMY CHENG-HO LIN, REBECCA J. LEARY,  
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VICTOR VELCULESCU, GIOVANNI PARMIGIANI,  
RACHEL KARCHIN, SIAN JONES, HAI YAN, DARELL BIGNER,  
CHIEN-TSUN KUAN, and GREGORY J. RIGGINS

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Appeal 2014-006244  
Application 13/412,696<sup>1</sup>  
Technology Center 1600

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Before DONALD E. ADAMS, JOHN G. NEW, and  
KRISTI L. R. SAWERT, *Administrative Patent Judges*.

SAWERT, *Administrative Patent Judge*.

DECISION ON APPEAL

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<sup>1</sup> Appellants identify the Johns Hopkins University as the real party in interest. Appeal Br. 2. Appellants further note that Personal Genome Diagnostics, Inc. and Agios Pharmaceuticals have licensing rights in the claimed subject matter. *Id.*

This is an appeal under 35 U.S.C. § 134 from the rejection of claims 1, 2, 4, 12–14, 16–19, 22, and 96–102 of U.S. Patent Application No. 13/412,696 (“the ’696 application”). We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

#### STATEMENT OF THE CASE

Claims 1, 2, 4, 12–14, 16–19, 22, and 96–102 are on appeal and stand rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter. Final Act. 2–4.

We choose claim 1 as representative. *See* 37 C.F.R. § 41.37(c)(1)(iv). Claim 1 provides:

1. A method to aid in analyzing isocitrate dehydrogenase 1 (*IDH1*) or isocitrate dehydrogenase 2 (*IDH2*) in a sample from a human subject, comprising:
  - assaying the sample for the *IDH1* or *IDH2* gene or mRNA transcribed from the gene in the human subject or protein translated from the mRNA, to identify residue 132 or a codon for residue 132 of *IDH1* or residue 172 or a codon for residue 172 of *IDH2*,
  - wherein the residue or the codon for the residue is not arginine, and wherein if the sample is from a colorectal tumor then the residue or codon for the residue is not a cysteine at residue 132 of *IDH1*.

Appeal Br. 10.

#### DISCUSSION

##### *Background*

Isocitrate dehydrogenase 1 (*IDH1*) and isocitrate dehydrogenase 2 (*IDH2*) are genes encoding for isocitrate dehydrogenase enzymes. The isocitrate dehydrogenase enzymes catalyze the oxidative decarboxylation of isocitrate to alpha-ketoglutarate. *See, e.g.*, US 2010/0291590 A1 ¶ 9

(published Nov. 18, 2010). Mutations in the genetic sequences of IDH1 and IDH2 have been found in human subjects suffering from gliomas, a type of primary brain tumor. Spec. ¶ 3. Gliomas are classified into different grades—Grade I to Grade IV—depending on the severity of the patient’s condition. The most invasive form of gliomas, known as glioblastoma multiforme (GBM), are Grade IV tumors. *Id.* GBM tumors generally lead to death. *Id.*

The inventors of the ’696 application discovered two specific mutations in the genetic sequences of IDH1 and IDH2 in patients having GBM tumors. Those mutations are somatic (i.e., not inherited) in nature, and occur at codon 132 of IDH1 and at codon 172 of IDH2. *Id.* ¶¶ 35–37. In normal cells, codon 132 of IDH1 and codon 172 of IDH2 encode the amino acid arginine (R). *Id.* at ¶ 37. In gliomas, however, the inventors found that codon 132 in IDH1 encodes histidine (H), serine (S), cysteine (C), leucine (L), or glycine (G), and that codon 172 in IDH2 encodes methionine (M), lysine (K), or glycine (G). *Id.* The ’696 application teaches that the “mutations at codon 132 and codon 172 can be detected using any means known in the art, including at the DNA, mRNA, or protein levels.” *Id.*

The Examiner finally rejected the claims as directed to unpatentable subject matter. *See* Final Act. 2–4. The Examiner observed that the claims recite a method for “assaying for amino acids that are not normally found at codon position 132 in IDH1 and at codon position 172 in IDH2.” *Id.* at 3. The Examiner further observed that “alterations of the amino acids at codon position 132 in IDH1 and at codon position 172 in IDH2 are associated with cancer.” *Id.* (citing Spec. ¶ 6). Finally, the Examiner noted that the “method steps listed in the present claims are well known methods in the art as [are]

the sequences of the IDH1 and IDH2 genes and mRNA.” *Id.* Based on these facts, the Examiner concluded that the “method steps for assaying a sample from a subject to identify a residue of a protein or a codon for that residue” are not “transformative,” and hence unpatentable.<sup>2</sup> *Id.* at 3–4.

*Principle of Law*

Under § 101, “any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof” may be eligible for a patent, subject to the conditions and requirements of the Patent Act. 35 U.S.C. § 101. But, under Supreme Court precedent, “[I]aws of nature, natural phenomena, and abstract ideas are not patentable.” *Mayo Collaborative Services v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1293 (2012) (citation omitted). “Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry.” *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2117 (2013).

The Supreme Court articulated a two-step test for patent eligibility under § 101 that “distinguish[es] patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts.” *Alice Corp. Pty. Ltd. v. CLS Bank Int’l*, 134 S. Ct. 2347, 2355 (2014) (citing *Mayo*, 132 S. Ct. at 1296–97) (“the *Alice/Mayo* test”). “First, we determine whether the claims at issue are

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<sup>2</sup> In coming to this conclusion, the Examiner relied on the Federal Circuit’s decision in *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303 (Fed. Cir. 2012), aff’d in part, rev’d in part sub nom. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013), holding method claims for screening for somatic mutations in the BRCA1 gene unpatentable for reciting “abstract mental processes.” Final Act. 3–4.

directed to one of those patent-ineligible concepts. If so, we then ask, what else is there in the claims before us?” *Id.* (citation and quotations omitted). Second, we “search for an inventive concept—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself.” *Id.* (quotations and alterations omitted).

### *Analysis*

The issue in this case is whether the claims encompass patent-eligible subject matter under 35 U.S.C. § 101. We agree with the Examiner that the appealed claims are unpatentable. Indeed, the Federal Circuit’s recent decision in *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369 (Fed. Cir. 2016), compels us to affirm the Examiner’s rejection of the claims.

The patent-at-issue in *Genetic Technologies* disclosed methods for detecting a coding region of DNA based on its relationship to non-coding regions. 818 F.3d at 1372–73. The inventor of the patent discovered, contrary to prevailing thought, that coding regions (i.e., exons) correlated with non-coding regions (i.e., introns) within the same gene or elsewhere in the genome. *Id.* at 1372. The inventor claimed that discovery as a “method for detection of at least one coding region allele” that encompassed within its scope “detecting a coding region allele by amplifying and analyzing any linked non-coding region, which could be found within the same gene as the coding region, within a different gene, or within an intergenic region.” *Id.* at 1372–73.

Starting with step one of the *Mayo/Alice* test, the Federal Circuit observed that “claim 1 covers a method of detecting a coding region of a

person’s genome,” and that the “product of the method of claim 1 is information about a patient’s natural genetic makeup” that “relies on the existence of linkage disequilibrium between the non-coding and coding regions.” *Genetic Techs.*, 818 F.3d at 1374–75. The court further observed that “the patent claim focuses on a newly discovered fact about human biology (the linkage of coding and non-coding regions of DNA), involves no creation or alteration of DNA sequences, and does not purport to identify novel detection techniques.” *Id.* at 1376. Thus, the court concluded, the claims were directed to a law of nature. *Id.*

Turning to step two, the court “examine[d] the elements of the claim to determine whether it contains an inventive concept sufficient to transform . . . the law of nature into a patent-eligible application.” *Id.* at 1376 (citing *Alice*, 134 S. Ct. at 2357 (alternations omitted)). The court first noted that “a claim directed to a newly discovered law of nature . . . cannot rely on the novelty of that discovery for the inventive concept necessary for patent eligibility; instead, the application must provide something inventive, beyond mere well-understood, routine, conventional activity.” *Id.* The court then analyzed the two claimed method steps—“amplifying” genomic DNA and “analyzing” the amplified DNA—and found that both represented “well known, routine, and conventional” techniques. *Id.* at 1377. Thus, the court concluded, “the physical steps . . . do not, individually or in combination, provide sufficient inventive concept to render claim 1 patent eligible.” *Id.*

Just as in *Genetic Technologies*, the claimed subject matter in this case relies on a new discovery: that patients with GBM may possess amino

acids mutations at positions 132 of IDH1 and 172 of IDH2. The Specification explains this discovery:

In a genome-wide analysis of GBMs, we identified somatic mutations of codon 132 of the isocitrate dehydrogenase 1 gene (IDH1) in ~12% of GBMs analyzed. . . . Remarkably, we found IDH1 mutations in the majority of early malignant gliomas. Furthermore, many of the gliomas without IDH1 mutations had analogous mutations in the closely related IDH2 gene. These results suggest that IDH mutations play an early and essential role in malignant glioma development.

Spec. ¶ 35.

And, just as in *Genetic Technologies*, claim 1 “covers a method of detecting a coding region of a person’s genome” by assaying for specific residues in the IDH1 and IDH2 genes, the product of which “is information about a patient’s natural genetic makeup,” i.e., whether the IDH1 and IDH2 genes encode an amino acid other than arginine at positions 132 and 172, respectively.<sup>3</sup>

Finally, just as in *Genetic Technologies*, “the patent claim focuses on a newly discovered fact about human biology,” i.e., the presence of amino acids other than arginine at specific codon positions in IDH1 and IDH2, “involves no creation or alteration of DNA sequences, and does not purport to identify novel detection techniques.” *Id.* at 1376. Thus, we conclude that the claims are directed to a law of nature under step one of the *Alice/Mayo* test.

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<sup>3</sup> Alternatively, if the human sample is from a colorectal tumor, then the method assays for an amino acid other than cysteine at residue 132 of IDH1. Appeal Br. 10 (claim 1).

Under step two of the *Alice/Mayo* test, we turn to the single method step of claim 1. This step recites “assaying” a human sample for the IDH1 and IDH2 genes to determine whether the amino acid encoded at codon 132 of IDH1 or at codon 172 of IDH2 is other than arginine. Appeal Br. 10. As the Examiner explained, this step is performed with well known, routine, and conventional techniques. Ans. 4 (noting that assaying “includes the amplification and hybridization steps as well as immunoassay steps,” all of which “are well-understood, purely conventional routine procedures”). Thus, we conclude, just as the court in *Genetic Technologies*, that the “assaying” step does not “provide sufficient inventive concept to render claim 1 patent eligible.” *Genetic Techs.*, 818 F.3d at 1377.

We are not persuaded by Appellants’ arguments as to patentability. First, Appellants argue that the claims recite patentable subject matter because the assaying step cannot “be performed using *purely* mental steps,” and that the Examiner erred by “shoehorn[ing] a mental step into the claimed method.” Appeal Br. 5–6; *see also* Reply Br. 3–6 (arguing that the Examiner erred by reading a “comparison” step into claim 1).

We again find that *Genetic Technologies* forecloses this argument. In *Genetic Technologies*, the claim-at-issue recited the term “to detect the allele,” but as in the claim here, did not include an explicit “comparison step.” 818 F.3d at 1372, 1378. Nevertheless, the court characterized “to detect the allele” as “a mental process step, one that provides claim 1 with a purpose but does not create the requisite inventive concept, because it merely sets forth a routine comparison that can be performed by the human mind.” *Id.* at 1378.

Similarly here, “to identify residue 132 or a codon for residue 132 of IDH1 or residue 172 or a codon for residue 172 of IDH2,” as recited in claim 1, does not provide the “requisite inventive concept.” We view “to identify”—like the Federal Circuit characterized “to detect”—as instructing the relevant audience to determine whether the amino acid at residue 132 of IDH1 or residue 172 of IDH2 is an amino acid other than arginine. This instruction necessarily involves a comparison between the amino acid arginine and the amino acid in the sample, and “does not represent an unconventional, inventive application sufficient to make the claim patent-eligible.” *Genetic Techs.*, 818 F.3d at 1379.

Next, Appellants appear to argue that the Examiner failed to sufficiently show that the methods for assaying encompassed by the claim are not novel or non-obvious. Appeal Br. 8. We disagree. The specification describes methods for assaying by, for example, PCR amplification and sequencing. Spec. ¶ 60. Again, there can be no serious dispute that these techniques were well known in the art before the earliest-effective filing date of the '696 application. *See Genetic Techs.*, 818 F.3d at 1377 (characterizing PCR and sequencing as “clearly well known, routine, and conventional” in 1989).

For these reasons, we determine that the Examiner’s rejection of claim 1 under § 101 is supported by a preponderance of the evidence, and therefore we affirm this rejection.

SUMMARY

We affirm the rejection of claim 1. Claims 2, 4, 12–14, 16–19, 22, and 96–102 fall with claim 1. No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED