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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte GAVIN J. SHERLOCK, JAMES DUANE BROOKS, RICHARD M. MYERS, YUYA KOBAYASHI, and DEVIN M. ABSHER

Appeal 2017-011677
Application 14/008,480
Technology Center 1600

Before ULRIKE W. JENKS, RYAN H. FLAX, and DAVID COTTA, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge.*

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellants[1] appeal from Examiner's decision to reject claims as anticipated and as being directed to non-statutory subject matter. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] Appellants identify the real party in interest as The Board of Trustees of the Leland Stanford Junior University and Hudson Alpha Institute for Biotechnology. Br. 2. We have considered, and herein refer to, the Specification of September 27, 2013 ("Spec."); Final Office Action of August 17, 2016 ("Final Act."); Advisory Action of December 9, 2016; Appeal Brief of April 17, 2017 ("Br."); and Examiner's Answer of May 26, 2017 ("Ans.").

STATEMENT OF THE CASE

Claims 1, 3–6, and 8–16 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. Claim 1 is representative of the claims on appeal, and reads as follows:

> 1. A method detecting the presence of prostate cancer cells in a sample, the method comprising:
>
> obtaining a sample suspected of comprising prostate cancer cells from an individual;
>
> testing the sample for the presence of methylated cytosine in a CpG context in promoters of EIF5A2, EPHA2, RAB33A, SYNGR1, and EPSTl1 in DNA, and
>
> detecting prostate cancer cells by the presence of increased methylated cytosine in a CpG context in promoters of EIF5A2, EPHA2, RAB33A, SYNGR1, and EPSTl1 in DNA.

Appellants request review of following rejections made by Examiner:

I. Claims 1, 3–6, and 8–16 under pre-AIA 35 U.S.C. § 101, as being directed to non-statutory subject matter.

II. Claims 1, 3–6, and 8–16 under pre-AIA 35 U.S.C. § 102(a) as being anticipated by Sorensen.[2]

III. Claims 1, 3–6, and 8–16 under pre-AIA 35 U.S.C. § 102(b) as being anticipated by Vanaja.[3]

I. Patent Ineligible Subject Matter

Examiner rejected claims 1, 3–6, and 8–16 as being directed to a judicial exception. Ans. 4. In particular, Examiner finds:

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[2] Sorensen et al., US 2010/0303795 A1, published Dec. 2, 2010 ("Sorensen").

[3] Vanaja et al., *Abstract #5197: Comprehensive DNA methylation analysis*, 69 CANCER RESEARCH 5197 (2009) ("Vanaja").

> Claim 1 is directed to "a method detecting the presence of prostate cancer cells in a sample" by obtaining a sample and testing ["]the presence of methylated cytosine in a CpG context in promoters of E1F5A2, EPHA2, RAB33A, SYNGR1 and EPSTl1" in [the] sample and detecting prostate cancer cells by the presence of increased methylated cytosine in a CpG context in promoters of E1F5A2, EPHA2, RAB33A, SYNGR1 and EPSTI1. [This relates to] a correlation that preexists in the human body is an unpatentable phenomenon. Any association between increased methylation of EIF5A2, EPHA2, RAB33A, SYNGR1, and EPSTl1 and prostate cancer cells is a law of nature/natural phenomenon.

Ans. 4–5.

Appellants contend "that the present claims provide specific limitations other than what is well-understood, routine and conventional in the field." Br. 6. Citing the JUL-1 example from the USPTO May 2016 Guidelines for subject matter eligibility, Appellants contend that there is no need to move on to Step 2B. *Id.* Specifically, arguing that when viewing the claim as a whole the process of detecting JUL-1 is not focused on the product per se. *Id.* Appellants contend that the "claims very specifically call out a combination of genes that must be tested for methylation, as well as cytosine methylation specifically in a CpG context." *Id.* at 7.

Issue Presented

Does a preponderance of the evidence of record support Examiner's conclusion that claims 1, 3–6, and 8–16 are directed to patent ineligible subject matter?

Analysis

Unless otherwise noted, we adopt Examiner's findings and reasoning as set out in the Final Office Action and Answer and agree that the claims

are unpatentable under 35 U.S.C. § 101. *See* Final Act. 3–10; *see* Ans. 2–8, 12–14.

We analyze this appeal under the framework set forth by the Supreme Court in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), and applied by our reviewing court in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015). As the *Ariosa* court explained:

> In *Mayo* . . . , the Supreme Court set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. First, we determine whether the claims at issue are directed to a patent-ineligible concept. If the answer is yes, then we next consider the elements of each claim both individually and "as an ordered combination" to determine whether additional elements "transform the nature of the claim" into a patent-eligible application. The Supreme Court has described the second step of this analysis as a 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. at 1375 (alteration in original) (internal citations omitted).

We begin with the first step of the *Mayo* test, namely, whether a claim is "directed to" a patent-ineligible concept. On January 7, 2019, the Director of the USPTO issued the "2019 Revised Patent Subject Matter Eligibility Guidance" ("Revised Guidance"), which provides further details regarding how the Patent Office analyzes patent-eligibility questions under 35 U.S.C. § 101. 84 Fed. Reg. 50–57 (Jan. 7, 2019). Under the Revised Guidance, the first step of the *Mayo* test (i.e., Step 2A of the Revised Guidance) is "a two-prong inquiry." *Id.* at 54. In prong one, we evaluate whether the claim recites a judicial exception, such as laws of nature, natural phenomena, or abstract

ideas. *Id.* If the claim recites a judicial exception, the claim is further analyzed under prong two, which requires "evaluat[ion of] whether the claim recites additional elements that integrate the exception into a practical application of that exception." *Id.* The Revised Guidance explains that, "[i]f the recited exception is integrated into a practical application of the exception, then the claim is eligible at Prong Two of . . . Step 2A [of the Revised Guidance]." *Id.*

Step 2A – Prong One

In our analysis, we must determine whether Appellants' claims are directed to a law of nature. We select claim 1 as representative. With respect to the first prong of Step 2A of the Revised Guidance, we agree with Examiner that independent claim 1 recites a patent-ineligible law of nature. Specifically, claim 1 recites the relationship between the presence of increased methylated cytosine in a CpG context in promoters of EIF5A2, EPHA2, RAB33A, SYNGR1, and EPSTl1 and a correlation with prostate cancer. Examiner points out that "[a] diagnosis step is an abstract mental process. It is further noted that the recitation of the determining step is an action than can be performed mentally." Final Act. 6. "[T]he process to predict the diagnosis of prostate cancer, amounts to no more than an 'instruction to apply the natural law.'" *Id.* at. 8. Examiner explains that "[a]ny association between increased methylation of EIF5A2, EPHA2, RAB33A, SYNGR1, and EPSTl1 and prostate cancer cells is a law of nature/natural phenomenon. With regard to the natural correlation, as in *Prometheus*, the relationship is itself a natural process that exists apart from any human action." Ans. 4–5.

We are not persuaded by Appellants contention that the active step of "detection" as recited in the claim cannot be a "mental step." Br. 7. We agree with Examiner's position that the claims are directed to patent-ineligible subject matter because they are directed to a law of nature and natural phenomenon, namely, the correlation between the presence of increased methylated cytosine in a CpG context of the recited promoters and the presence of prostate cancer cells.

Step 2A – Prong Two

Under the Revised Guidance, we must also determine "whether the claim recites additional elements that integrate the exception into a practical application of that exception." 84 Fed. Reg. at 54. Limitations that are indicative of integration into a practical application include applying the natural law to effect a particular treatment or prophylaxis for a disease or medical condition. *See, e.g., Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1134–35 (Fed. Cir. 2018) (holding that claims including a limitation of genotyping to determine if a patient is a CYP2D6 poor metabolizer and then administering a drug in certain amounts depending upon whether the patient is or is not a CYP2D6 poor metabolizer where risk of QTc prolongation is correlated to the amount of drug administered and status as CYP2D6 metabolizer is an application of the relationship between the drug, CYP2D6 metabolism, and QTc prolongation). On the other hand, diagnostic methods that simply measure the concentration of a drug after administration and determine whether a particular dosage of a drug will prove ineffective or cause harm is not a practical application. *Mayo*, 566 U.S. at 77. That is because the method itself does not recite a use of the natural relationship, it simply provides for an

observation based on that relationship. *Id.*; s*ee also Athena Diagnostics, Inc. v Mayo Collaborative Services, LLC*, No. 2017-2508, 2019 WL 453489, at *5 (Fed. Cir. Feb. 6, 2019) (noting that while the claims include certain concrete steps, those steps only apply conventional techniques to detect the natural law, i.e., "observe its operation").

We conclude, as Examiner did, that the steps of obtaining a sample, testing the sample for CpG levels, and "detecting prostate cancer cells by the presence of increased methylated cytosine in a CpG context in [the] promoters" as required by the claim amount to diagnosing the subject. *See* Ans. 5 ("[T]he claim is essentially diagnosing by the presence of prostate cancer cells."). "The testing step essentially tells users to determine the methylation through whatever known processes they wish to use." Ans. 7. The detecting step is thereby not an additional element that integrates the exception into a practical application, nor is the diagnostic observation. *See* Ans. 7 ("The detecting prostate cancer cells tells users of the process to predict the detection or diagnosis of prostate cancer cells which amounts to no more than an 'instruction to apply the natural law.'"). Similar to the claims in *Athena*, claim 1 is directed to measuring increased methylated cytosine in a CpG context in promoters and associating the increased levels with a diagnosis, as such the claims only encompass the natural law itself. *See Athena*, 2019 WL 453489, at *6 ("Claiming a natural cause of an ailment and well-known means of observing it is not eligible for patent because such a claim in effect only encompasses the natural law itself.").

Step 2B – Inventive Concept

Having determined that claim 1 is directed to a patent-ineligible law of nature without an integration into a practical application, we next consider

whether claim 1 recites "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.'" *Ariosa*, 788 F.3d at 1375 (citation omitted). We agree with Examiner that it does not. Ans. 5–6. Examiner finds that "[t]he claims also do not add a specific limitation other than what is well understood, routine and conventional in the field." Ans. 6 (citing the use the Illumina Human Methylation 27 Bead Chip[4]). The data gathering step of the claims does not add "significantly more" to the law of nature/natural phenomenon on which the claim is based so as to provide eligibility on its own. Appellants present no persuasive evidence to the contrary.

For the reasons discussed above we are not persuaded that Examiner erred in rejection claim 1 as patent ineligible. Claims 3–6 and 8–16 were not separately argued and fall with claim 1. *See* 37 C.F.R. § 41.37(c)(1)(iv).

II. Anticipation by Sorensen

Examiner finds that Sorensen teaches methods of diagnosing prostate cancer using Infinium Human Methylation 27 Bead Chip (Illumina). *See* Final Act. 13; Ans. 9–10 (citing Sorensen ¶¶ 55, 96, 270, claims), 15–19.

Appellants contend that "[t]he present claims are drawn to the identification of prostate cancer cells by specifically determining increased methylation in the promoter region of the recited genes." Br. 3. "[O]ne of skill in the art would not have reason to select the specific set for analysis . . . ." *Id.* at 4.

[4] *See, e.g.*, Sorensen ¶¶ 114, 116, 118, 433, 435, 440, 441.

Upon consideration of the evidence on this record, and Appellants' contentions, we find that the preponderance of evidence supports Examiner's finding that the subject matter of Appellants' claims is unpatentable. Accordingly, we affirm Examiner's rejections for the reasons set forth in the Answer and Final Action, which we adopt as our own, including Examiner's responses to Appellants' arguments.

Specifically, we agree with Examiner that the claims, by virtue of using the transitional phrase "comprising," are not limited to determining the methylated cytosine in a CpG context of the recited promoters. Accordingly, the broadest reasonable interpretation of the claims does not exclude identification of the methylation status in additional genes. *See* Ans. 18. Because the claims are not limited to the five recited promoters, we agree with Examiner that Sorensen's disclosure of using the Infinium Human Methylation 27 Bead Chip (Illumina) (*see, e.g.,* Sorensen ¶¶ 114, 116, 118, 433, 435, 440, 441) meets the claim limitation. We note that Appellants Specification discloses using same Illumina chip as the one disclosed in Sorensen. *See* Spec. ¶ 81. Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. *In re King*, 801 F.2d 1324, 1326–27 (Fed. Cir. 1986). We agree with Examiner's position that the Illumina chip contains the recited promotors (as well as other promotors not recited in claim 1), and that Sorensen's process of determining the methylation state of promotors in patient derived samples would simultaneously include detecting the methylation state of the recited promoters. *See* Ans. 15–19. Accordingly, we agree with Examiner's finding that testing patient samples

for methylation patterns using the Illumina chip for the purpose of detecting prostate cancer as disclosed in Sorensen would anticipate the claims. We affirm the rejection of claims 1 and 14 under 35 U.S.C. § 102 by Sorensen. Claims 3–6, 8–13, 15, and 16 were not separately argued and fall with claims 1 and 14.

III. Anticipation by Vanaja

Examiner finds that Vanaja teaches methods of diagnosing prostate cancer using Infinium Human Methylation 27 Bead Chip (Illumina). *See* Final Act. 15–16; Ans. 10–11, 19–22.

Appellants contend that "[t]he present claims are drawn to the identification of prostate cancer cells by specifically determining increased methylation in the promoter region of the recited genes." Br. 4. Appellants further argue, "[o]ne of skill in the art cannot determine from the teachings of Vanaja anything more than a general indication that there may be a change, but is not informed where and what the change is." *Id.* at 5.

Upon consideration of the evidence on this record, and Appellants' contentions, we find that the preponderance of evidence supports Examiner's finding that the subject matter of Appellants' claims is unpatentable. Accordingly, we affirm Examiner's rejections for the reasons set forth in the Answer and Final Action, which we adopt as our own, including Examiner's responses to Appellants' arguments.

As discussed above, we agree with Examiner that the claims, by virtue of using the transitional phrase "comprising," are not limited to the recited promoters. Accordingly, the broadest reasonable interpretation of the claims does not exclude additional genes. *See* Ans. 21–22. Because the claims are

not limited to the five recited promoters, we agree with Examiner that Vanaja's disclosure of using the Infinium Human Methylation 27 Bead Chip (Illumina) meets the claim limitation. Because the Illumina chip contains the recited promotors (as well as others promotors not recited in claim 1), we agree with Examiner that Vanaja's process of determining the methylation state of promotors in patient derived samples would simultaneously include detecting the methylation state of the recited promotors. *See* Ans. 19–22. Accordingly, we agree with Examiner's finding that testing patient samples for methylation patterns using the Illumina chip for the purpose of detecting prostate cancer as disclosed in Vanaja would anticipate the claims. *See King*, 801 F.2d at 1326–27. We affirm the rejection of claims 1 and 14 under 35 U.S.C. § 102 by Vanaja. Claims 3–6, 8–13, 15, and 16 were not separately argued and fall with claims 1 and 14.

SUMMARY

We affirm the rejection of claims 1, 3–6, and 8–16 as being patent ineligible.

We affirm the rejection of claims 1, 3–6, and 8–16 as anticipated by Sorensen.

We affirm the rejection of claims 1, 3–6, and 8–16 as anticipated by Vanaja.

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