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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SHERI WILCOX, DEBORAH AYERS, NEBOJSA JANJIC, LARRY GOLD, MICHAEL RIEL-MEHAN, and THALE JARVIS[1]

Appeal 2017-005853
Application 13/808,751
Technology Center 1600

Before JEFFREY N. FREDMAN, JOHN G. NEW, and DAVID COTTA, *Administrative Patent Judges.*

NEW, *Administrative Patent Judge.*

DECISION ON APPEAL

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[1] Appellants identify SomaLogic, Inc., as the real party-in-interest is. App. Br. 3.

SUMMARY

Appellants file this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 1, 6–7, 10, 17, 24, 29–30, 33–38, 40–41, and 47. Specifically, the claims stand rejected as unpatentable under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

Claims 1, 6, 7, 10, and 17 stand rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of Gold et al. (US 2010/0070191 A1, March 18, 2010) ("Gold"), R.S. Stearman et al., *A Macrophage Gene Expression Signature Defines a Field Effect in the Lung Tumor Microenvironment*, 68(1) CANCER RESEARCH 34–43 (2008) ("Stearman"), H.W. Chen et al., *Molecular Recognition of Small-Cell Lung Cancer Cells Using Aptamers*, 3 CHEM. MED. CHEM. 991–1001 (2008) ("Chen"), and R.M. Ostroff et al., *Unlocking Biomarker Discovery: Large Scale Application of Aptamer Proteomic Technology for Early Detection of Lung Cancer*, 5(12) JOURNAL OF PROTEOMICS 649–66 (2010) ("Ostroff").

Claims 24, 29, 30, 33–38, and 40 stand rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of Gold, Stearman, C.W. Seder et al., *Upregulated INHBA expression may promote cell proliferation and is associated with poor survival*, 11(4) NEOPLASIA 388–96 (2009) ("Seder").

Claim 47 stands rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of Gold, Stearman, Seder, and E. Kettunen et al., *Differentially Expressed Genes in Nonsmall Cell Lung Cancer: Expression Profiling of Cancer-Related Genes in Squamous Cell Lung Cancer*, 149 CANCER GENETICS AND CYTOGENETICS 98–106 (2004) ("Kettunen").

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

NATURE OF THE CLAIMED INVENTION

Appellants' invention is directed to biomarkers, methods, devices, reagents, systems, and kits for the detection and diagnosis of lung cancer. Abstract.

REPRESENTATIVE CLAIM

Claim 1 is representative of the claims on appeal and recites:

> 1. A method for diagnosing lung cancer in an individual, the method comprising:
>
> contacting a tissue test sample from the individual with a capture reagent having specific affinity for the protein biomarker TrATPase, wherein the capture reagent is selected from the group consisting of an aptamer and an antibody, measuring the level of the protein biomarker TrATPase in the tissue test sample with a capture reagent-based assay; and wherein a decreased expression level of the protein biomarker TrATPase in the tissue test sample compared to the expression level of the protein biomarker TrATPase in a control non-tumor tissue, indicates a likelihood that the individual has lung cancer.

App. Br. 25.

ISSUES AND ANALYSES

We agree with, and adopt, the Examiner's findings and conclusion that the appealed claims are (1) directed to nonstatutory subject matter; and (2) obvious over the combined cited prior art. We address the arguments raised by Appellants below.

A. Rejection of claims 1, 6–7, 10, 17, 24, 29–30, 33–38, 40–41, and 47 under 35 U.S.C. § 101

Issue 1

Appellants argue that the Examiner erred in concluding that the claims are directed to a judicially-created exception to 35 U.S.C. § 101 and that the remaining claims do not add significantly more to the claim so as to render it patentable. App. Br. 8.

Analysis

The Examiner finds that the claims are directed to a judicial exception, *viz.*, a law of nature, and specifically the correlation between altered biomarker expression in an individual and the likelihood that the individual has lung cancer. Final Act. 4. The Examiner also finds that the claims do not recite something significantly more than the judicial exception, because the steps of measuring the claimed proteins in a test sample using aptamers or antibodies are known, routine procedures typically undertaken to perform testing of a sample. *Id.* at 4–6 (citing, e.g., Ostroff, Table 1).

Appellants argue that the claims are directed to a patent-eligible statutory category, *viz.,* a process. App. Br. 8. However, Appellants assert, the claims do not seek to monopolize the correlation between lung cancer and the specified biomarkers, because the claims are limited to a capture reagent-based assay. *Id.* Therefore, Appellants argue, other applications of the correlation are not tied up by the instant claims because there are non-infringing, alternative methods available to apply the correlation that are

beyond the scope of Appellants' claims, e.g., assays based on mass spectrometry. *Id.*

Appellants argue further that the limitation requiring measuring the decreased expression of TrATPase protein with a capture reagent having specific affinity for TrATPase protein, as indicative of lung cancer, is not "well-understood, routine and conventional in the field" for at least the reason that the cited references do not teach or suggest this limitation. App. Br. 8–9 (citing *2014 Interim Guidance on Patent Subject Matter Eligibility*, 79(241) Fed. Reg. 74618, 74624 (December 16, 2014)). Appellants point to the Examiner's finding that Stearman teaches that the Acp5 gene, which encodes for the TrATPase protein, is up-regulated in lung tissue adjacent to tumor tissue when compared to that in normal tissue. *Id.* at 9. Appellants assert that Stearman therefore does not teach that decreased expression of TrATPase protein is indicative of lung cancer. *Id.* Consequently, argue Appellants, their claims on appeal do not seek to tie up a judicial exception and also include at least one limitation which adds significantly more to the claims than a judicial exception. *Id.*

We are not persuaded by Appellants' arguments. Appellants' claims are directed to the relationship between decreased expression of the biochemical marker TrATPase, when compared to a control, and a likelihood of lung cancer. *See* claim 1. As an initial matter, although the avoidance of preempting a judicially-created exception to Section 101 may be part of the purpose of the judicially-created exceptions to the statute, whether a claim actually preempts such an exception is not part of the two-part analysis that the Supreme Court has instructed us, in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012) and *Alice*

Corp. v. CLS Bank Int'l, 134 S.Ct. 2347 (2014), to perform in determining patentability in such cases. Rather, the analysis requires us to determine, first, whether the claims are directed to one of the judicially-created exceptions and, second, if the answer is yes, to determine whether the elements of each claim both individually and "as an ordered combination," possess additional elements that "transform the nature of the claim" into a patent-eligible application. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.,* 788 F.3d 1371, 1375 (2015) (citing *Mayo*, 566 U.S. at 78–79). The Supreme Court has likened this second step of the 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.* (citing *Mayo*, 566 U.S. at 72–73; *also citing Digitech Image Techs., LLC v. Elecs. for Imaging, Inc.*, 758 F.3d 1344, 1351 (Fed. Cir. 2014) ("Without additional limitations, a process that employs mathematical algorithms [an exception] to manipulate existing information to generate additional information is not patent eligible").

We find that the steps recited in Appellants' claims are directly analogous to those at issue in *Mayo*. In *Mayo*, the claim at issue similarly recited: (1) obtaining a sample; (2) analyzing the sample; and (3) determining a diagnosis and a plan of treatment based upon the results of that analysis.[2] *Mayo*, 566 U.S. at 74–75. The Supreme Court first found

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[2] The claims of the patent-in-suit of *Mayo* additionally recited the administration of a thiopurine compound prior to obtaining the sample. By way of example, claim 1 of *Mayo* recited:

that the *Mayo* claims were directed to a judicially-created exception to Section 101, *viz.*, a phenomenon of nature. *Id.* at 77. Specifically, the Court found that the claims recited relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm. *Id.*

In the appeal presently before us, we conclude that Appellants' claims are similarly directed to a phenomenon of nature: *viz.*, the relationship between decreased levels of expression of TrATPase in an individual and an increased likelihood of lung cancer. We conclude that this is a phenomenon of nature because the relationship occurs naturally in such an individual whether or not it is measure or observed.

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6–thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6–thioguanine in said subject having said immune-mediated gastrointestinal disorder,
>
> wherein the level of 6–thioguanine less than about 230 pmol per 8 x 10^8 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and
>
> wherein the level of 6–thioguanine greater than about 400 pmol per 8 x 10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

Mayo, 566 U.S. at 74–75.

Having so concluded, and continuing to follow the analysis set forth by the Court in *Mayo*, we are next required to determine whether the claims "do significantly more than simply describe these natural relations. To put the matter more precisely, do the patent claims add enough to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that apply natural laws?" *Mayo*, 566 U.S. at 77 (emphasis in original).

We conclude that they do not. We find that the additional recited steps of Appellants' claims are directly analogous to the steps of the claims at issue in *Mayo* which:

> [S]imply tell doctors to gather data from which they may draw an inference in light of the correlations. To put the matter more succinctly, the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons we believe that the steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities.

Mayo, 566 U.S. at 79–80.

Neither Appellants' claims nor their Specification recite a novel manner of obtaining or analyzing the collected samples; instead, the scope of the claim encompasses any and all methods of obtaining and analyzing the collected sample for TrATPase expression using antibodies or aptamers, including those commonly known in the art, and as taught by Gold and Stearman. *See, e.g.*, Gold ¶ 21, claims 1–4; Stearman 34–35, Table 1. And, having made such an analysis of the sample, the person performing it is required to do no more than understand the phenomenon of nature to which

the claim is directed, *viz.*, that an abnormally decreased level of TrATPase expression in the sample is a likely diagnostic indicator of lung cancer. As such, we conclude that the claims are not directed to significantly more than the natural phenomenon itself and are, consequently, unpatentable.

B. Rejection of claims 1, 6–7, 10, 17, 24, 29–30, 33–38, 40, and 47 under 35 U.S.C. § 103(a)

Issue

Appellants argue the Examiner erred because, in contrast to the teaching of Stearman with respect to up-regulation of the Acp5 gene in lung tissue adjacent to tumor tissue as compared to normal tissue, Appellants have found *decreased* expression of the TrATPase protein as indicative of lung cancer. App. Br. 12.

Analysis

The Examiner finds Gold teaches a method for diagnosing an individual as having an increased likelihood of lung cancer by employing an *in vitro* assay using aptamers as capture reagents. Final Act. 10 (citing, e.g., Gold claims 2, 3, and 4).

The Examiner finds that, whereas Gold does not teach the biomarker TrATPase, Stearman teaches that the level of Acp5 gene expression is a biomarker for a diagnosis of lung cancer. Final Act. 10 (citing Stearman 34–35, Table 1). The Examiner also notes that it was known in the art that Acp5 is the gene for the TrATPase protein biomarker. *Id. at* 10–11 (citing Spec. Table 18).

The Examiner concludes that it would have been obvious to one of ordinary skill in the art to modify the method and system of Gold with the use of Acp5, as taught by Stearman. Final Act. 11. The Examiner finds that a skilled artisan would have been motivated to employ Acp5 as a biomarker because Stearman teaches that the altered expression levels of Acp5 suggest that the gene expression information is informative for predicting tumor status. *Id.* The Examiner acknowledges that Stearman teaches that the Acp5 gene is up-regulated in lung cancer cases, whereas Appellants claim that the expression level of the TrATPase, which is synthesized by the Acp5 gene, states that decreased expression of the protein is diagnostic of possible lung cancer. *Id.* Nevertheless, the Examiner finds that Chen teaches that genetic changes do not always correlate with changes at the protein level and that it would have been obvious to one of ordinary skill in the art to include the use of a known biomarker in the diagnosis of lung cancer. *Id.* (citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

Appellants agree with the Examiner that, in contrast to the teaching of Stearman with respect to relative up-regulation of the Acp5 gene in lung tissue adjacent to tumor tissue, Appellants have found decreased expression of the TrATPase protein is indicative of lung cancer. App. Br. 13. Appellants argue the Examiner's reliance on Chen as teaching that genetic changes do not always correlate with changes at the protein level is misplaced, because this teaching of Chen demonstrates that the teachings of Stearman with respect to the Acp5 gene do not provide any reasonably reliable information with respect to the TrATPase protein. *Id.*

Appellants emphasize that they have determined the lack of correlation between gene expression and protein expression in its own

research and that, consequently, Stearman in combination with Chen would not provide one of ordinary skill in the art any reasonably reliable teaching or suggestion that decreased expression of TrATPase protein is indicative of lung cancer. App. Br. 13.

We are not persuaded by Appellants' arguments. Stearman expressly teaches that altered regulation of the Acp5 gene is consistent with a diagnosis of lung cancer. *See, e.g.*, Stearman 39. We agree with the Examiner that a person of ordinary skill in the art, understanding the teachings of Stearman, would look to the expression of the TrATPase protein expressed by the Acp5 gene teaching as a diagnostic indicator of lung cancer with a reasonable expectation of success. Such an expectation would be reasonable because the direct link between Acp5 expression and TrATPase synthesis was well known in the contemporary art. *See* Spec. Table 18. The fact, discovered by Appellants, that TrATPase expression is decreased, rather than increased, in individuals likely to have lung cancer, may well have been unexpected, even though Chen expressly teaches that: "[g]enetic changes can be detected reproducibly by PCR and genomic hybridization, but they do not always correlate with changes at the protein level." Chen 991. Nevertheless, Chen also teaches that: "multiple aptamers can be readily developed for any cancer cells of interest without prior knowledge of cell-surface marker proteins, and are more predictive of cancer progression than single probes used in previous studies." *Id.* at 992. We find that these combined teachings would have motivated the skilled artisan to arrive at the claimed invention.

We consequently conclude that a person of ordinary skill in the art would, knowing that the gene responsible for transcribing TrATPase is a

useful marker for lung cancer, would have found it obvious to use TrATPase as a marker for a lung cancer diagnosis based upon the combined teachings of Gold and Stearman. We consequently affirm the Examiner's rejection of claims 1, 6, 7, 10, and 17, which Appellants argue together. *See* App. Br. 12.

Furthermore, Appellants argue claims 24, 29, 30, 33–38, and 40 and claim 47 separately, but rely upon the same arguments presented with respect to claims 1, 6, 7, 10, and 17. *See* App. Br. 13–14. For the same reasons, we affirm the Examiner's rejection of these claims.

DECISION

The Examiner's rejection of claims 1, 6–7, 10, 17, 24, 29–30, 33–38, 40–41, and 47 as unpatentable under 35 U.S.C. § 101 is affirmed.

The Examiner's rejection of claims 1, 6–7, 10, 17, 24, 29–30, 33–38, 40, and 47 as unpatentable under 35 U.S.C. § 103(a) is affirmed.

The Examiner's rejection of claims as unpatentable under the judicially-created doctrine of obviousness-type double patenting is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED