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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KATRIN BITTER and CAROLINA RIBBING

Appeal 2017-011197
Application 14/125,991
Technology Center 1600

Before JEFFREY N. FREDMAN, TIMOTHY G. MAJORS, and DAVID COTTA, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1,2] under 35 U.S.C. § 134 involving claims to a method for cancer treatment planning. The Examiner rejected the claims as lacking patentable subject matter under 35 U.S.C. § 101. 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 Koninklijke Philips N.V., (App. Br. 2).

[2] We have considered and herein refer to the Specification of Dec. 13, 2013 ("Spec."); Final Office Action of Nov. 25, 2016 ("Final Act."); Appeal Brief of Apr. 11, 2017 ("App. Br."); Examiner's Answer of July 11, 2017 ("Ans."), and Reply Brief of Aug. 31, 2017 ("Reply Br.").

Statement of the Case

Background

"Mass spectrometry (MS) is a method for determining molecular mass . . . . During the last decades, MS has proven to be a viable technique for accurate and sensitive analysis of biological species like proteins and peptides" (Spec. 1). "From blood serum, diagnostic mass spectrometric proteomic patterns showing e.g. early cancer or host response to radiation can be obtained" (Spec. 3). "[R]adiotherapy planning targets the prostate cancer while minimizing dose to the very closely situated bowel and bladder. The frequent and serious side-effects of prostate cancer radiotherapy especially affect the bladder and the bowel." (*id.*).

The Claims

Claims 1, 5–9, 11–18, and 31–33 are on appeal. Claim 1 is representative and reads as follows:

> 1. A method for cancer treatment planning, comprising:
>
> determining molecular masses of polypeptides present in a serum sample of a patient using mass spectrometry;
>
> comparing the molecular masses of the determined polypeptides present in the serum sample with a pre-determined set of molecular masses of interest indicative of a difference in radiosensitivity from exposure to a radiotherapy treatment;
>
> classifying a radiosensitivity for the patient according to at least one molecular mass included in the determined molecular masses of polypeptides present in the serum sample that is included in the pre-determined set of molecular masses of interest indicative of the difference in radiosensitivity for the patient, wherein radiosensitivity includes an indication of a difference in a radiotoxicity to the patient induced by radiation from radiotherapy;
>
> at least one of creating a new treatment plan or modifying an existing treatment plan for the patient with a cancer based on the classified radiosensitivity for the patient

> according to the at least one molecular mass present in the serum sample and included in the pre-determined set of molecular masses, wherein the at least one of creating a new treatment plan or modifying an existing treatment plan for a patient with cancer includes planning one or more treatments for the patient, wherein the at least one of creating a new treatment plan or modifying an existing treatment plan for a patient with cancer is performed using a treatment planning device that includes one or more configured processors, wherein the at least one of creating a new treatment plan or modifying an existing treatment plan for the patient with a cancer based on the classified radiosensitivity for the patient includes at least one of selecting a treatment according to the classified radiosensitivity for the planned one or more treatments planned for the patient from a plurality treatments or modifying a planned radiotherapy dose according to the classified radiosensitivity.

The Rejection

The Examiner rejected claims 1, 5–9, 11–18, and 31–33 under 35 U.S.C. § 101 (Final Act. 2–7).

The Examiner finds that the claims on appeal are directed to "a naturally occurring correlation between masses of polypeptides in a serum sample and radiosensitivity of a patient" (Final Act. 3). The Examiner finds "the claims do not amount to significantly more than a statement of the natural principle with generalized directions to apply it to the relevant population" (*id.*). The Examiner also finds "the steps in addition to the judicial exception(s) do not do more than describe the judicial exception(s) with general instructions" (Final Act. 5).

Appellants contend the

> claims do not recite a naturally occurring correlation. The Applicant suggests that the claims are directed to creating a new treatment plan or modifying an existing treatment plan for a patient with a cancer based on a radiosensitivity for the patient

> classified according to molecular masses of polypeptides present in a serum sample determined by mass spectrometry and compared with a pre-determined set of molecular masses.

(App. Br. 4). Appellants also contend the "claims, as a combination and in individual steps, recite limitations, which are significantly more" (*id.*).

We apply the test set out in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) based on the two-step *Alice* framework. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014).

In *Alice* step one, we ask whether the claims are directed to a patent ineligible concept, such as an abstract idea or natural phenomenon. *Alice*, 134 S.Ct. at 2355; *Mayo*, 566 U.S. at 75–77; *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015). While method claims are generally eligible subject matter, method claims that are directed only to abstract ideas and/or natural phenomena are directed to patent ineligible concepts. *Ariosa*, 788 F.3d at 1376. In *Alice* step two, we examine the elements of the claims to determine whether they contain an inventive concept sufficient to transform the claimed naturally occurring phenomena into a patent-eligible application. *Mayo*, 566 U.S. at 71–72 (quoting *Alice*, 134 S.Ct. at 2355).

Alice Step One

Claim 1 is directed to a natural phenomenon because the claim is "based on serum concentrations/amounts of a predetermined set of polypeptides of the patient that indicate a radiotoxicity of the patient to radiation" (Spec. 5). Claim 1 analyzes this information to develop a treatment plan, an abstract idea.

Therefore, the law of nature at issue is the relationship between changes in concentrations of particular polypeptides in a patient and the likelihood that radiotherapy will cause toxicity to the patient. *Cf. Mayo*, 566 U.S. at 77 (finding that claims at issue were directed to "laws of nature—namely, 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."). That the relationship is obtained using mass spectrometric methods and computer processing of the mass spectrometry data does not change the fact that the relationship between radiotoxicity and the presence of particular peptides "exists in principle apart from any human action." *Mayo*, 566 U.S. at 77.

The abstract idea is the use of an algorithm to analyze the law of nature, as the Specification teaches using a "set of polypeptide radiotoxicity markers along with data . . . and one or more algorithms 109, including treatment identification algorithms 110, optimization algorithms 112, and/or other algorithms" (Spec. 6). The recited steps of "comparing," "classifying," and "creating" or "modifying" treatment plans using "configured processors" all involve categorizing and/or analyzing information. Our reviewing Court has explained that "[i]nformation as such is an intangible" and "that collecting information, including when limited to particular content (which does not change its character as information)," analyzing it, and presenting the results of the collection and analysis without more are patent ineligible abstract concepts. *See, e.g., Electric Power Group, LLC v. Alstom S.A.*, 830 F.3d 1350, 1353–54 (Fed. Cir. 2016).

Because the claims are directed to a natural phenomenon, we turn to the second step of the *Alice* framework.

Alice Step Two

In *Alice* step two, we examine the elements of the claims to determine whether they contain an inventive concept sufficient to transform the claimed natural phenomenon or abstract idea into a patent-eligible application. *Mayo*, 566 U.S. at 71–72 (*quoting Alice*, 134 S.Ct. at 2355). We must consider the elements of the claims both individually and as an ordered combination to determine whether the additional elements transform the nature of the claims into a patent-eligible concept. *Ariosa*, 788 F.3d at 1375.

Weibrecht[3] teaches that "a method for generating a patient specific therapy plan includes generating an initial therapy plan" (Weibrecht 4:15–16). Weibrecht teaches a step of "determining a first set of patient specific markers" then administering "a dose of radiation," after which a "second set of patient specific biomarkers is determined," and then creating "relationship between the first set and second set of patient specific biomarkers" (*id.* at 5:2–6). Weibrecht teaches that a "radiation dose or treatment plan can be altered based on a patient's reaction to therapy" (*id.* at 5:13–14). Weibrecht teaches that the treatment plan is performed when a

> planning processor **70** integrates individual patient specific information derived from a single or plurality of biomarkers into the calculation of the NTCP [normal tissue complication probability] model and the TCP [tumor control probability] model using a patient specific calculation of an EUD [equivalent uniform dose] for each model considering the biomarkers.

(*id.* at 7:22–25). Thus, Weibrecht evidences that an automated method of

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[3] Weibrecht, WO 2010/109357 A1, published Sept. 30, 2010.

cancer treatment planning using comparisons of markers before and after radiotherapy was known in the prior art, including using processors to perform the analysis.

Pietrowska[4] teaches "MALDI-TOF [Matrix-Assisted Laser Desorption Ionization spectrometry coupled to a Time of Flight analyzer] based analyses for detection of dynamic changes in serum proteome mass profiles that result from therapy of breast cancer patients" (Pietrowska 10, col. 1). Pietrowska teaches, "the most significant changes in proteome patterns were observed in serum samples collected one year after the end of adjuvant radio/chemotherapy" (*id.* at 8, col. 1). Pietrowska teaches these "changes in the proteome pattern . . . reflects a long-term response of patients' organs to the toxic effects of adjuvant radio/chemotherapy" (*id.* at 8, col. 2). Pietrowska suggests the "applicability of mass spectrometry-based serum proteome pattern analyses in monitoring the toxicity of therapy" (*id.* at 10, col. 2). Thus, Pietrowska evidences that the technology of determining and comparing molecular masses of polypeptides in serum using mass spectrometry was well known in the prior art, as was the concept of using such comparisons to inform about patient toxicity to radiation and consequent choice of therapy.

Espina[5] teaches, "real time monitoring of the cellular and serum proteome information content, which will provide diagnostic and prognostic windows to guide patient management" (Espina 84, col. 2). Espina teaches

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[4] Monika Pietrowska et al., *Mass spectrometry-based analysis of therapy-related changes in serum proteome patterns of patients with early-stage breast cancer*, J. OF TRANSLATIONAL MEDICINE 8:66 (2010).
[5] Virginia Espina et al., *Use of proteomic analysis to monitor responses to biological therapies*, EXPERT OPIN. BIOL. THER. 4(1): 83–93 (2004)

"SELDI-TOF [surface-enhanced laser desorption/ionisation time of flight] mass spectrometry technology consists of three major components: protein chip arrays, a mass analyser and data analysis software" (*id.* at 86, col. 1). Espina teaches, "mass spectrometry is well-established as a routine clinical diagnostic tool" (*id.* at 89, col. 2). Espina teaches that using these techniques "the effect of the treatment can be monitored in real time" (*id.* at 90, col. 1). Espina teaches, "[t]hese data are suitable for traditional unsupervised and supervised learning algorithms" (*id.* at 88, col. 2). Thus, Espina also evidences that the use of mass spectrometry for analyzing polypeptides in serum was a well-established tool, that data analysis software and traditional algorithms for performing such analysis were well-known, and that monitoring treatment using these approaches was a known approach.

Therefore, the evidence of record supports the position that the claims do not add something "significantly more" to the natural phenomenon and abstract idea. Instead, the evidence shows that the additional elements in the claims (e.g., using mass spectrometry to measure polypeptides in patient serum, creating treatment plans using processors, and modifying treatment based on such analyses) are conventional, routine, and well-known. We conclude that the method claim does not result in an inventive concept that transforms the natural phenomenon and abstract idea described above into a patentable invention.

Appellants contend:

> The claims do not recite a naturally occurring correlation. The Applicant suggests that the claims are directed to creating a new treatment plan or modifying an existing treatment plan for a patient with a cancer based on a radiosensitivity for the patient

> classified according to molecular masses of polypeptides present in a serum sample determined by mass spectrometry and compared with a pre-determined set of molecular masses.

(App. Br. 4).

We find this argument unpersuasive because, even in Appellants' argument itself, the natural correlation between patient radiosensitivity and changes in concentrations of particular polypeptides in a patient is the essential element of the treatment plan. That is, the treatment plan determines whether there is a natural correlation between changes in polypeptide levels and radiotoxicity for a particular patient and selects treatment based on the presence or absence of that correlation (*cf.* Spec. 5 "creating and/or adapting a treatment plan for a patient based on serum concentrations/amounts of a predetermined set of polypeptides of the patient that indicate a radiotoxicity of the patient to radiation from radiotherapy").

Appellants contend:

> The claims, as a combination and in individual steps, recite limitations, which are significantly more. . . . Conventional practice does not include treatment planning for a patient with a cancer based on a radiosensitivity determined from a serum sample. Furthermore, as a combination from a serum sample analyzed by mass spectrometry to a planned selection of a treatment or a planned modification of a radiotherapy dose is significantly more.

(App. Br. 4).

We find this argument unpersuasive because Weibrecht, Pietrowska, and Espina evidence that the steps are conventional. As already noted, Weibrecht teaches treatment planning based on a patient's reaction to radiation therapy using biomarkers (Weibrecht 5:1–14) including in vitro tests (*id.* at 8:25–27). Pietrowska teaches the use of mass spectrometry to

analyze changes in the proteome associated with radiotoxicity from serum samples (Pietrowska 8, col. 1 and 2) and directly suggests the "applicability of mass spectrometry-based serum proteome pattern analyses in monitoring the toxicity of therapy" (*id.* at 10, col. 2). Lastly, Espina establishes that mass spectrometry is well established as a diagnostic tool (Espina 89, col. 2). Espina also evidences that computer processors are routinely used to analyze proteome data, teaching, "statistical programs can use the mass spectrometry output to identify protein patterns associated with disease and healthy states" (Espina 86, col. 1).

Appellants contend:

> The concern of the courts has been whether the claims tie up technology. The claims do not tie up the use of polypeptides in serum samples as a measurement of responses to treatments, such as with previously cited prior art Pietrowska. The claims do not tie up treatment planning, such as with previously cited prior art Weibrecht. The claims do not tie up cancer treatment planning and/or delivery.

(App. Br. 4).

While preemption is a concern underlying the judicial exceptions, it is not a stand-alone test for determining eligibility. *Rapid Litig. Mgmt. v. CellzDirect, Inc.*, 827 F.3d 1042, 1052 (Fed. Cir. 2016). "[W]e have consistently held that claims that are otherwise directed to patent-ineligible subject matter cannot be saved by arguing the absence of complete preemption." *Return Mail, Inc. v. United States Postal Service*, 868 F.3d 1350, 1370 (Fed. Cir. 2017). Moreover, where claims are deemed only to disclose patent ineligible subject matter under the *Mayo* and *Alice* framework, as they are in this case, preemption concerns are fully addressed and made moot. *See Ariosa*, 788 F.3d at 1379.

Appellants contend that "the claims should be patent eligible according to what is more in *In re Abele*, [684 F.2d 902 (CCPA 1982)]" because the CCPA found a claim "eligible because it required 'X-ray attenuation data.'" (App. Br. 4–5; *citing Abele*, 684 F.2d at 908).

We find this argument unpersuasive. The Federal Circuit relied on this same reasoning in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*, 628 F.3d 1347, 1358 (Fed. Cir. 2010), noting their "analysis is consistent with *In re Abele*, 684 F.2d 902 (CCPA 1982)" because "the presence of mental steps similarly does not detract from the patentability of the administering and determining steps." *Id.* However, the Supreme Court reversed the Federal Circuit in *Mayo*, finding that while the claim "recites an 'administering' step, a 'determining' step, and a 'wherein' step. These additional steps are not themselves natural laws but neither are they sufficient to transform the nature of the claim." *Mayo*, 566 U.S. at 78. *Mayo* concluded that "appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Id.* at 82. Appellants' claim 1 is such a situation, where conventional steps of mass spectrometry, data analysis, and treatment planning are appended to the natural correlation of particular polypeptides in serum with a patient's radiosensitivity.

Appellants contend, "the facts of *Smartgene* do not match the facts of the present application. On page 4 of *Smartgene*, the court provides claim 1 of the '786 patent, which does not include any mass spectrometry or serum samples" (App. Br. 5).

We find this argument unpersuasive because, like the Examiner, we agree that *SmartGene* is instructive here. *SmartGene, Inc. v. Advanced Biological Laboratories, SA*, 555 Fed. Appx. 950, 955 (Fed. Cir. 2014); *see* Ans. 10. In *SmartGene*, the claims were directed towards selection of a treatment regimen by using a computer with knowledge bases and expert rules to create a ranked list of treatments and advisory information. *SmartGene*, 555 Fed. Appx. at 952. Just as in *SmartGene*, the current claim 1 "does not purport to identify new computer hardware: it assumes the availability of physical components for input, memory, look-up, comparison, and output. Nor does it purport to identify any steps beyond those which doctors routinely and consciously perform." *Id.* at 955. Similarly, neither claim 1 nor the Specification identify any new mass spectrometric device, computer, or even mathematical algorithm for performing the comparison of mass spectrometry data. Moreover, neither claim 1 nor the Specification demonstrate that the method of cancer treatment planning encompasses any technology beyond that disclosed by Weibrecht, Pietrowska, and Espina as discussed above.

Appellants contend that "*Digitech* is also distinguished from the present claims" (App. Br. 5), apparently relying upon the interim eligibility guidelines (*see id.*).

We find this argument unpersuasive. The Federal Circuit has explained that "[i]nformation as such is an intangible" and "that collecting information, including when limited to particular content (which does not change its character as information)," analyzing it, and presenting the results of the collection and analysis are patent ineligible abstract concepts. *See,*

e.g, *Electric Power Group, LLC v. Alstom S.A.*, 830 F.3d 1350, 1353–54 (Fed. Cir. 2016).

> This case is similar to *Digitech Image Technologies, LLC v. Electronics for Imaging, Inc.*, 758 F.3d 1344 (Fed. Cir. 2014). There, the claims of the challenged patent were directed to the abstract idea of organizing information through mathematical correlations. *Id.* at 1350–51. . . . A process that started with data, added an algorithm, and ended with a new form of data was directed to an abstract idea. *Id.*

RecogniCorp LLC v. Nintendo Co., Ltd, 855 F.3d 1322, 1327 (Fed. Cir. 2017). Additionally, in *Digitech*, the Federal Circuit stated that:

> [w]ithout additional limitations, a process that employs mathematical algorithms to manipulate existing information to generate additional information is not patent eligible. "If a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory"

Digitech Image Technologies, LLC v. Electronics for Imaging, Inc., 758 F.3d 1344, 1351 (Fed. Cir. 2014) (citation omitted). Here, the process of claim 1 collects information by conventional mass spectrometric methods, compares and classifies that information to develop treatment plans using standard processors, and at best adds the natural correlation of particular polypeptides in serum with a patient's radiosensitivity.

Appellants separately argue claim 18, which includes specific molecular masses, contending, "the polypeptides that occur in the serum sample are not abstract. The measurement of the masses is not abstract, but rather requires the recited mass spectrometry. The specific masses of polypeptides in a serum sample are indicative of radiosensitivity, which are enumerated and are not abstract" (App. Br. 7).

We find this argument unpersuasive because the use of specific data points does not render the claims patent eligible. In *Mayo*, the claim recited specific data points, including a need to increase drug dosage where "the level of 6–thioguanine less than about 230 pmol per $8x10^8$ red blood cell" but decrease dosage when "the level of 6–thioguanine less than about 230 pmol per $8x10^8$ red blood cell." *Mayo*, 566 U.S. at 75. However, in spite of the fact that specific data values were recited, *Mayo* concluded these specific values are "a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes. And so a patent that simply describes that relation sets forth a natural law." *Id.* at 77. That is similar to claim 18, where the particular proteins whose molecular masses are associated with radiosensitivity is a consequence of the patient's response to radiation therapy, a process that fails to provide substantially more to the natural phenomenon and is no more patent eligible than the administration of thiopurine compounds of *Mayo*. Therefore, claim 18 simply describes more detail of the radiosensitivity relationship that sets forth natural phenomena.

We therefore conclude that all of the claims on appeal are directed to patent-ineligible subject matter.

SUMMARY

In summary, we affirm the rejection of claims 1 and 18 under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Pursuant to 37 C.F.R. § 41.37(c)(1), we also affirm the rejection of claims 5–9, 11–17, and 31–33 as being directed to non-statutory subject matter as these claims were not argued separately.

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