UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ATHENA DIAGONISTICS, INC., ISIS INNOVATION LIMITED, and MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN e.V.,	*	
Plaintiffs,	*	
v.	*	Civil Action No: 15-cv-40075-IT
MAYO COLLABORATIVE SERVICES, LLC, d/b/a MAYO MEDICAL LABORATORIES, and MAYO CLINIC,	*	
Defendants.	*	

MEMORANDUM & ORDER

August 4, 2017

TALWANI, D.J.

Plaintiffs Athena Diagnostics, Inc., Isis Innovation Limited, and Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., allege that two tests developed by Defendants Mayo Collaborative Services, LLC, and Mayo Clinic, infringe on Plaintiffs' patent, U.S. Patent No. 7,267,820 (the "'820 Patent"). Third Am. Compl. ("Complaint") [#92]. Defendants moved to dismiss Plaintiffs' complaint arguing that the '820 patent is invalid under 35 U.S.C. § 101 because the claimed method applies routine and conventional techniques to a law of nature. Defs.' Rule 12(b)(6) Mot. Dismiss ("Defs.' Mot. Dismiss") [#25]. The court was unable to determine on the papers before it whether the patent used standard techniques in the art, or whether it was sufficiently inventive to be patentable under § 101, and denied the motion. Mem. & Order 10 [#103]. At a subsequent hearing, Plaintiffs' counsel agreed that a statement in

the patent specification (that "[i]odination and immunoprecipitation are standard techniques in the art") was undisputed. See '820 Patent col. 4 l. 10-11; Tr. Oral Argument, at 17-18, Athena Diagnostics, Inc. v. Mayo Collaborative Servs., Inc., No. 15-cv-40075 (D. Mass. Oct. 6, 2016). Based on that statement, the court allowed Defendants the opportunity to renew their motion to dismiss, and allowed additional briefing by the parties. For the following reasons, the Renewed Motion to Dismiss [#131] is ALLOWED.

I. Facts

A. The '820 Patent

The '820 patent allows for the diagnosis of a form of Myasthenia Gravis, a chronic autoimmune disorder. '820 Patent col. 1 l. 13-14. Patients with Myasthenia Gravis experience waning muscle strength throughout the day, and symptoms include eye weakness (drooping eyelids, double vision), leg weakness, dysphagia (difficulty swallowing), and slurred or nasal speech. Id. col. 1 l. 15-23. In 1960, it was discovered that in 80% of patients with Myasthenia Gravis, antibodies attack the acetyle choline receptor (AChR) (a neurotransmitter). Id. col. 1 l. 24-26, 34-36. In those patients, diagnosis is achieved through tests which detect the presence of AChR autoantibodies. See id. col. 1 l. 34-36. Autoantibodies "are naturally occurring antibodies directed to an antigen which an individual's immune response recognizes as foreign even though that antigen actually originated in the individual." Id. col. 1 l. 42-45. However, 20% of Myasthenia Gravis patients do not have the AChR autoantibodies despite experiencing the same symptoms and responding to the same therapies. Id. col. 1 l. 36-40. For the 20% of Myasthenia Gravis patients who do not have the AChR autoantibodies, the '820 patent inventors discovered that they had IgG antibodies that attack the N-terminal domains of muscle specific tyrosine

kinase ("MuSK"), a receptor that is located on the surface of neuromuscular junctions. Id. col. 1 l. 55-61.

The patent describes the method for a more accurate and speedy diagnosis of these patients. Id. col. 3 l. 4-7. Specifically, the patent describes a method for diagnosing Myasthenia Gravis in which a radioactive label is attached to MuSK (or a fragment thereof) and is then introduced to a sample of bodily fluid. Id. col. 3 l. 66-67, col. 4 l. 1-10. The method specifies that ^{125}I be used as the radioactive label. Id. col. 4 l. 9-10. When ^{125}I-MuSK is introduced into the sample of bodily fluid, the MuSK autoantibodies, if present, attach to the labeled fragment. Id. col. 4 l. 2-9. After the bodily fluid is immunoprecipitated, the presence of the radioactive label on any antibody indicates that the person is suffering from Myasthenia Gravis. Id. col. 4 l. 8-10.

B. Infringement Allegations

Athena's test, "FMUSK," uses the patented method to diagnose neurotransmission or developmental disorders related to MuSK. Compl. ¶ 16 [#92]; '820 Patent Claim 1. Plaintiffs allege that "Defendants, with specific knowledge of the '820 patent and the method it covers, surreptitiously and purposefully designed an alternate test to avoid paying Athena for Athena's licensed FMUSK test." Compl. ¶ 20 [#92]. Plaintiffs allege that Defendants availed themselves of the technology disclosed in the '820 patent, and developed two tests for diagnosing Myasthenia Gravis patients. Id. ¶ 18. Plaintiffs argue that Defendants' actions directly or indirectly, and literally or under the doctrine of equivalents, infringe the '820 patent. Id. ¶ 24. The claims at issue are those listed in Claims 6-9 of the '820 patent. Pls.' Mem. Opp'n Defs.' Mot. Dismiss. 24 [#37]. Plaintiffs concede that they will not pursue infringement claims against Defendants based on the other claims in the patent. Id. at 8.

II. Motion to Dismiss

Defendants moved to dismiss the complaint on the ground that the patent seeks to patent a law of nature, and it uses techniques standard in the art. Defs.' Mem. Supp. Mot. Dismiss 5-6 [#26]; Defs.' Renewed Mem. Supp. Mot. Dismiss 4-5 [#132]. Plaintiffs argue that the patent is not directed at a law of nature because the patent requires the production and use of ^{125}I-MuSK, a non-naturally occurring protein. Pls.' Mem. Opp'n Defs.' Mot. Dismiss 17 [#37]. Plaintiffs also argue that applying various known types of procedures to a non-naturally occurring protein transforms the claim and makes it patent eligible. Id. at 13-14.

A. Standard of Review under 35 U.S.C. § 101

In applying § 101 at the pleading stage, the court construes the patent claims in a manner most favorable to the non-moving party. See Content Extraction & Transmission LLC v. Wells Fargo Bank, Nat'l Ass'n, 776 F.3d 1343, 1349 (Fed. Cir. 2014). As a threshold requirement for patent protection, the subject matter of a patent must be patentable under § 101; otherwise, the patent is invalid. § 101 states that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. The Supreme Court has held that this section contains an implicit exception: "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." Alice Corp. Pty. Ltd. v. CLS Bank Intern., 134 S. Ct. 2347, 2354 (2014) (quoting Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116 (2013)). Although "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas," these three patent-ineligible exceptions prevent "monopolization" of the "basic tools of scientific and

technological work" and the impeding of innovation. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 71 (2012).

To distinguish between patents that claim laws of nature, natural phenomena, and abstract ideas from patent-eligible inventions, the court must first determine whether the claims at issue are directed to one of those patent-ineligible concepts. Alice, 134 S. Ct. at 2355. If the concept is patent ineligible, the court then considers the elements of each claim both "individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." Id. at 2355 (quoting Mayo, 566 U.S. at 78-79). "We have described step two 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 2355 (quoting Mayo, 566 U.S. at 72-73). At step two, more is required than well-understood, routine, conventional activity already engaged in by the scientific community. Rapid Litig. Mgmt., Ltd. v. CellzDirect, Inc., 827 F.3d 1042, 1047 (Fed. Cir. 2016).

B. Step One: Are Claims Directed to a Patent Ineligible Concept?

Defendants argue that the '820 patent is directed at a law of nature: that the bodily fluid of some people with Myasthenia Gravis have autoantibodies to MuSK. Defs.' Renewed Mem. Supp. Mot. Dismiss 4-5 [#132]. Plaintiffs argue that the patent method uses a man-made, patent eligible molecule, and uses that chemical complex in an innovative and transformative manner. Pls.' Surreply Opp'n Mot. Dismiss 4 [#46]. Per Plaintiffs, "the claims are not directed to MuSK . . . [i]nstead, the claims recite using a man-made chemically-modified version of MuSK to form a specific complex that does not occur in nature," and are therefore patent eligible. Id. at 5.

The patent describes a method in which ^{125}I-MuSK is put into a sample of bodily fluid, and then the bodily fluid is filtered so that autoantibodies attached to the ^{125}I-MuSK are detected. '820 Patent col. 3 l. 66-67, col. 4 l. 1-9. The presence of the ^{125}I-MuSK autoantibodies indicates the person suffers from Myasthenia Gravis. Id. The relevant portion of the patent states:

> The invention claimed is:
>
> **1.** A method for diagnosing neurotransmission or developmental disorders related to muscle specific tyrosine kinase (MuSK) in a mammal comprising the step of detecting in a bodily fluid of said mammal autoantibodies to an epitope of muscle specific tyrosine kinase (MuSK).
>
> **2.** A method according to claim 1 wherein said method comprises the steps of:
>
> a) contacting said bodily fluid with muscle specific tyrosine kinase (MuSK) or an antigenic determinant thereof: and
>
> b) detecting any antibody-antigen complexes formed between said receptor tyrosine kinase or an antigenic fragment thereof and antibodies present in said bodily fluid, wherein the presence of said complexes is indicative of said mammal suffering from said neurotransmission or development disorders.
>
> **3.** A method according to Claim 2 wherein said antibody-antigen complex is detected using an anti-IgG antibody tagged or labeled with a reporter molecule.
>
> . . .
>
> **6.** A method according to claim 3 whereby the intensity of the signal from the anti-human IgG antibody is indicative of the relative amount of the anti-MuSK autoantibody in the bodily fluid when compared to a positive and negative control reading.
>
> **7.** A method according to claim 1, comprising contacting MuSK or an epitope or antigenic determinant thereof having a suitable label thereon, with said bodily fluid, immunoprecipitating any antibody/MuSK complex or antibody/MuSK epitope or antigenic determinant complex from said bodily fluid and monitoring for said label on any of said antibody/MuSK complex or antibody/MuSK epitope or antigen determinant complex, wherein the presence of said label is indicative of said mammal is suffering from said neurotransmission or developmental disorder related to muscle specific tyrosine kinase (MuSK).
>
> **8.** A method according to claim 7 wherein said label is a radioactive label.
>
> **9.** A method according to claim 8 wherein said label is 125I.

‘820 Patent Claims 1-9. Plaintiffs argue that because ^{125}I-MuSK is not naturally occurring, the claim is patent eligible under § 101. Pls.’ Mem. Opp’n Defs.’ Mot. Dismiss. 11 [#37] (“Those antibody/MuSK complexes are created in the laboratory and result from the use of a non-naturally-occurring laboratory-created molecule, ^{125}I-MuSK, and therefore, the antibody/MuSK complexes formed and detected by claim 9 are not found in nature.”).

While ^{125}I-MuSK and the antibody/MuSK complexes are not found in nature, this does not transform the patent at issue here to a patent eligible concept. Contrary to Plaintiffs’ argument, the ‘820 patent is not a composition patent directed at the creation of the ^{125}I-MuSK auto-antibody complex. Rather, the patent is directed at a method for the diagnosis of a disease. ‘820 Patent col. 1 l. 9-11 (“The present invention is concerned with neurotransmission disorders and, in particular, with a method of diagnosing such disorders in mammals.”). Although the patented method uses man-made ^{125}I-MuSK, the use of a man-made complex does not transform the subject matter of the patent. The focus of the claims of the invention is the interaction of the ^{125}I-MuSK and the bodily fluid, an interaction which is naturally occurring. The purpose of the patent is to detect whether any antibody-antigen complexes are formed between the ^{125}I-MuSK receptor and the antibodies “present in said bodily fluid.” Id. Claim 2. Counter to Plaintiffs’ argument, because the patent focuses on this natural occurrence, it is directed to a patent-ineligible concept. See Elec. Power Grp., LLC v. Alstom S.A., 830 F.3d. 1350, 1353 (Fed. Cir. 2016) (quoting Enfish, LLC v. Microsoft Corp., 822 F.3d 1327, 1335-36 (Fed. Cir. 2016)) (“[W]e have described the first-stage inquiry as looking at the ‘focus’ of the claims, their ‘character as a whole.’”).

Athena’s patent is similar to the patent invalidated by the Supreme Court in Mayo. In Mayo, the Supreme Court invalidated the patent of a diagnostic test which measured how well a

person metabolized thiopurine drugs. 566 U.S. at 74. The patent claimed a method in which the drug 6-thioguanine was given to a person, after which the level of 6-thioguanine in the person's blood stream was measured. Id. The Court held that the patent method was directed to observing a law of nature. "'Prometheus' patents set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of thiopurine drug will prove ineffective or cause harm." Id. at 77. While the Court acknowledged that it took human action (the administration of a thiopurine drug) to trigger the desired reaction, the reaction itself happened apart from any human action. Id. at 78. The Court found the claim invalid because the method sought to measure how well a person metabolizes the drug, which the Court described as "entirely natural processes." Id. at 77. Likewise, Plaintiffs' method seeks to measure autoantibodies that have attached to a receptor protein, an interaction which is a similarly natural process. In Mayo, a man-made substance was administered to a person, and the by-product of the metabolization of that man-made substance was observed. Id.; see also Genetic Techs. Ltd. v. Merial LLC, 818 F.3d 1369, 1376 (Fed. Cir. 2016) (finding that when the patent claim focuses on a newly discovered fact about human biology, the claim is directed to unpatentable subject matter). Here, a man-made substance (^{125}I-MuSK) is administered to a sample of bodily fluid, and the by-product (^{125}I-MuSK autoantibodies) is observed.

Further support can be found in Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1372 (Fed. Cir. 2015). That case involved the patent for a method using fetal DNA for the diagnosis of certain conditions. The inventors discovered that cell-free fetal DNA ("cffDNA") was present in maternal plasma and serum. By implementing a method for detecting the small fraction of paternal cffDNA in the maternal plasma or serum, the inventors were able to determine certain inherited characteristics. Id. at 1373. The patent method isolated and amplified

cffDNA, allowing for greater efficiency in diagnosis of genetic defects. As the court noted, "[t]he only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum . . ." Id. at 1377. Likewise, what is new and useful here is the discovery that some patients with Myasthenia Gravis have MuSK autoantibodies in their bodily fluid.

Relying on CellzDirect, 827 F.3d at 1042, Plaintiffs seek to distinguish the '820 patent from Ariosa and Mayo by arguing that the '820 patent is focused on the steps required by the claimed method, rather than on the outcome of the diagnostic test. In CellzDirect, patent inventors discovered that hepatocytes, special liver cells that are used for testing, diagnostic, and treatment purposes, could be refrozen. Id. at 1045. Refreezing of hepatocytes was a breakthrough because the cells naturally have a short life span, and can only be harvested from a limited number of people. Id. Prior to the discovery, hepatocytes could only be frozen one time, which limited their utility. Id. The patented method importantly allowed for multi-donor hepatocyte pools, a useful research tool that allows the study of a drug's impact on a representative population. Id. The Federal Circuit found the "end result of the '929 patent claims is not simply an observation or detection of the ability of hepatocytes to survive multiple freeze thaw cycles. Rather, the claims are directed to a new and useful method of preserving hepatocyte cells." Id. at 1048. The court found that the process' "desired outcome" was a method to produce something useful, and therefore was not directed at a patent ineligible concept. Id. at 1048-49. The method allowed for refrozen hepatocyte cells to be used in a myriad of ways. Conversely, the desired outcome of the Plaintiffs' method is the detection of MuSK autoantibodies. It does not produce something useful beyond that diagnosis.

Plaintiffs' argument that the patent is transformed by the use of a man-made molecule is

unavailing. The stated purpose of the patent is to diagnose Myasthenia Gravis, and the method is directed to a patent ineligible law of nature under § 101.

C. Step Two: Does the Inventiveness of the Claim make it Patent Eligible?

While the patent is directed to a patent ineligible concept under § 101, the patent can still be upheld if the method contains an "inventive concept." See Alice, 134 S. Ct. at 2355; Genetic Techs. Ltd., 818 F.3d at 1376 ("[T]he application must provide something inventive beyond mere 'well-understood, routine, conventional activity.'"). The Supreme Court has "described step two 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.'" Alice, 134 S. Ct. at 2355 (quoting Mayo, 566 U.S. at 72-73). At step two the claims are examined "in light of the written description," Amdocs (Israel) Ltd. V. Openet Telecom, Inc., 841 F.3d 1288, 1299 (Fed. Cir. 2016), and "more is required than well-understood, routine, conventional activity already engaged in by the scientific community." CellzDirect, 827 F.3d at 1047 (internal quotations omitted).

Defendants argue that Plaintiffs' patent fails step two of § 101 analysis because it uses well-known techniques for identifying the presence of autoantibodies to MuSK and therefore does not contain an "inventive concept." Defs.' Mem. Supp. Mot. Dismiss 14 [#26] ("[P]rocess steps that recite techniques scientists would have already known to use in conjunction with the newfound natural law cannot supply the inventive concept."). Defendants cite to the patent specification which states that "[i]ondination and immunoprecipitation are standard techniques in the art, the details of which can be found in references (4 and 6)." Id. at 10; '820 Patent col. 4 l. 9-12. Defendants note that the two publications referenced in the specification date from 1976 and 1985, and according to Defendants the publications "describe (1) the introduction of a ^{125}I-

labeled antigen (AChR) into a bodily fluid sample, (2) immunoprecipitation, and (3) detecting the radioactive label." Defs.' Mem. Supp. Mot. Dismiss 10 [#26]. Defendants argue that the publications show that the methods described in the patent are commonly used by researchers in the field, and thus the claims do not pass step two of the analysis under § 101.

Plaintiffs argue that at the time the invention was made, the step of "detecting" autoantibodies was neither well understood nor routine, and that the step of contacting MuSK or a MuSK epitope with a suitable label was novel. Pls.' Memo. Opp'n Defs.' Renew Mot. Dismiss 8 [#136]. Plaintiffs admit that the specification states "[i]odination and immunoprecipitation are standard techniques in the art," but Plaintiffs argue that none of those steps are routine when applied to proteins. According to Plaintiffs, proteins are complex, and getting known iodination methods to work with proteins is not routine. Id. at 11.

Plaintiffs' argument is unavailing. Patent applications are required to provide the precise description of the manner and process of making the invention. 35 U.S.C. § 112(a) ("The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention."); see also In re TLI Commc'ns LLC Patent Litig., 823 F.3d 607, 613-614 (Fed. Cir. 2016) ("[W]e must be mindful of extraneous fact finding outside the record, particularly at the motion to dismiss stage, here we need to only look to the specification . . . ."). None of the complexity to which Plaintiffs cite is described or claimed in the patent. While Plaintiffs argue that "Production of 'MuSK or an epitope or antigenic determinant thereof having a suitable label thereon' required several steps that were neither well-known, not standard, nor

conventional for MuSK," Pls.' Mem. Opp'n Defs.' Renewed Mot. Dismiss 15 [#136], this statement directly contradicts the language in the specification. In the specification, the inventors simply state that the "suitable label" is ^{125}I or the like, and that iodination of the label is a standard technique in the art. '820 Patent col. 4 l. 9-12. Furthermore, complexity alone does not make their method patentable. See Myriad, 133 S. Ct. at 2117 ("Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry.").

Plaintiff also argues that the use of a man-made molecule necessarily makes the claims patent eligible. Plaintiffs' claim that "[a] process that requires the use of a novel non-naturally-occurring patent-eligible element is necessarily a patent-eligible process." Pls.' Mem. Law. Opp'n Defs.'s Renewed Mot. Dismiss 8 [#136]. However, the patent specification itself states that the "present invention is concerned with neurotransmission disorders and, in particular with a method of diagnosing such disorders in mammals." '820 Patent col.1 l.9-11. The patent claims it is "for diagnosing neurotransimission or developmental disorders related to muscle specific tyrosine kinase (MuSK) in a mammal compromising the step of detecting in a bodily fluid of said mammal autoantibodies to an epitope of muscle specific tyrosine kinase (MuSK)." Id. Claim 1. On its face, the patent claims a process for detecting autoantibodies, not a process for creating the ^{125}I-MuSK. See Myriad, 133 S. Ct. at 2119 ("Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could have possibly sought a method patent.").

III. Conclusion

For the foregoing reasons, Defendants' Renewed Motion to Dismiss [#131] is GRANTED.

Date: August 4, 2017

/s/ Indira Talwani
United States District Court