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In *Athena Diagnostics v. Mayo* (February 6), the Federal Circuit held diagnostic patent claims patent-***in***eligible and provided additional guidance on patent eligibility for claims involving natural laws.

The inventors discovered a link between a cell-membrane protein called MuSK and *myasthenia gravis* ("MG") – specifically that a significant fraction of MG cases involve autoantibodies to MuSK. Based on that discovery, the inventors developed and claimed a diagnostic method that detected the presence of autoantibodies to MuSK. Here is an exemplary claim:

> 1. A method for diagnosing neurotransmission or developmental disorders related to [MuSK] in a mammal comprising the step of detecting in a bodily fluid of said mammal autoantibodies to an epitope of [MuSK].[1]

Alice Step 1: Is the claim directed to a patent ineligible concept?

Answer: **YES**

Identification of the patent-ineligible concept (natural law) at issue.

The district court found the claims directed to the interaction of autoantibodies in the patient's bodily fluid and the corresponding epitope of the MuSK protein, "an interaction that is naturally occurring" and therefore a natural law.[2]

The Federal Circuit agreed that the claims were directed to a natural law, but identified the natural law as "the correlation between the presence of naturally-occurring MuSK autoantibodies in bodily fluid and MuSK-related neurological diseases like MG." The Federal Circuit did not explain the shift from *antibody-antigen interaction* to *correlation of antibody to disease state* as the natural law except to say, in a footnote, that no prior cases had characterized "the binding of two molecules during a sequence of chemical manipulations . . . as a claim to a natural law." The court expressly declined to resolve that issue in this case and instead accepted Mayo's alternative proposal that a correlation of antibody to disease was the natural law at issue.

"Directed to."

Athena argued that its claims were like those found patent-eligible in *CellzDirect*[3] because they "are directed to a new laboratory technique that makes use of man-made molecules" (*i.e.,* ^{125}I-labelled MuSK). The Federal Circuit first distinguished the *CellzDirect* claims as "harness[ing] a natural law to produce a technological improvement that was patent eligible," akin to how improvements in computer-related technology can be patent-eligible,[4] in contrast to the Athena claims which "merely recite observing naturally occurring biological correlations."

The Federal Circuit then explained that "the use of a man-made molecule is not decisive if it amounts to only a routine step in a conventional method for observing a natural law." The court pointed to several

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[1] US Patent No. 7,267,820. Dependent claims added details regarding the method steps (*e.g.,* use of ^{125}I-labelled MuSK, immunoprecipitation, detecting the label).

[2] *Athena Diagnostics v. Mayo,* 275 F.Supp.3d. 306, 310 (D. Mass. 2017).

[3] *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.,* 827 F.3d 1042, 1047–49 (Fed. Cir. 2016);

[4] Citing *Enfish, LLC v. Microsoft Corp.,* 822 F.3d 1327, 1335–39 (Fed. Cir. 2016).

prior cases where the claimed methods used human-made reagents but nevertheless were patent-ineligible – *Mayo* (human-made drug that provided 6-thioguanine to the patient), *Ariosa*[5] (human-made PCR reagents and probes), and *In re BRCA1*[6] (hybridizing a synthetic DNA probe to a DNA strand) – and "reaffirm[ed] that use of a man-made molecule in a method claim employing standard techniques to detect or observe a natural law may still leave the claim directed to a natural law."

Lack of preemption.

Athena argued that its claims were patent eligible because "the specificity of the claimed concrete steps ... leaves open to the public other ways of interrogating the correlation between MuSK autoantibodies and MuSK-related disorders." The Federal Circuit agreed in principle, but explained that "[p]reemption is sufficient to render a claim ineligible under § 101, but it is not necessary." The court concluded that routine steps being "set forth with some specificity" and thereby avoiding preemption is not enough to change the conclusion that the claims are directed to a natural law.

***Alice* Step 2: Is there an inventive concept to ensure the patent in practice amounts to significantly more than a patent on the ineligible concept itself?**

Answer: **NO**

Claim steps besides the natural law.

The Federal Circuit found that the steps of the claimed methods that were recited in addition to the natural law – *e.g.,* use of ^{125}I-labelled MuSK, immunoprecipitation, detecting the label[7] – "only apply conventional techniques to detect that natural law." The specification worked against the patentee, Athena, by (i) emphasizing the importance of the discovery of the natural law,[8] and (ii) characterizing the other claim steps as well-known in the art.[9] The Federal Circuit concluded that the "patent thus describes the claimed invention principally as a discovery of a natural law, not as an improvement in the underlying immunoassay technology" and as "only requir[ing] standard techniques to be applied in a standard way."

Routine, conventional steps in "novel" context.

Athena also argued that the claimed method steps were "were unconventional because they had not been applied to detect MuSK autoantibodies prior to Athena's discovery of the correlation between MuSK autoantibodies and MG." Accepting that as true, the Federal Circuit nevertheless explained that "we cannot hold that performing standard techniques in a standard way to observe a newly discovered natural law provides an inventive concept."

Use of human-made molecule in claimed method.

Athena argued that there was an inventive concept because the claims made use of a human-made molecule, ^{125}I-labelled MuSK. The Federal Circuit explained that "the method claims at issue here are unlike the claims held eligible in *Myriad*, which recited a new composition of matter that was not a

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[5] *Ariosa Diagnostics, Inc. v. Sequenom, Inc.,* 788 F.3d 1371, 1376 (Fed. Cir. 2015).

[6] *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 764 n.4 (Fed. Cir. 2014).

[7] In dependent claims.

[8] *E.g.,* "[t]he present inventors surprisingly found that many of the 20% of MG patients [who] do not exhibit any autoantibodies to [the acetylcholine receptor], instead have . . . antibodies directed against the extracellular [amino]-terminal domains of MuSK." '820 Patent, 1:54-57.

[9] *E.g.,* "[t]he actual steps of detecting autoantibodies in a sample of bodily fluids may be performed in accordance with immunological assay techniques known per se in the art," including radioimmunoassays and ELISA" and identifying "[i]odination and immunoprecipitation" as "standard techniques in the art." '820 Patent, 3:33-37, 4:10-12.

natural product" (*i.e.,* cDNA) and held that "appending labeling techniques to a natural law does not provide an inventive concept where, as here, the specification describes ^{125}I labeling as a standard practice in a well-known assay."

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A few closing thoughts and practice tips:

- The Federal Circuit drew a clear distinction between patent-eligible therapeutic claims that apply a natural law or phenomenon to treat disease and patent-ineligible diagnostic claims that merely use conventional techniques to observe or detect a natural law or phenomenon.
- The Federal Circuit also drew a clear distinction between patent-eligible claims to human-made (*i.e.,* non-naturally occurring) compositions of matter and patent-ineligible claims to methods employing standard or conventional human-made reagents. The court did, however, leave open the possibility that the use of a non-standard or unconventional human-made reagent in a method claim could tip the balance in favor of patent eligibility.
- Underlying reasons for the shift from *antibody-antigen interaction* (the natural law at the district court) to *correlation of antibody to disease state* (the natural law at the Federal Circuit) might include the following:
    - Relying on correlation of an antibody to a disease state as the natural law more closely aligns with the express claim language (*e.g.,* "diagnosing neurotransmission or developmental disorders related to [MuSK]" by "detecting ... autoantibodies" to MuSK).
    - Relying on the correlation of an antibody to a disease state provides a closer analogy to *Mayo v. Prometheus*,[10] which involved a correlation between metabolite levels and drug dosage efficacy and toxicity.[11]
    - Setting aside the antibody-antigen interaction as the putative natural law helps avoid the patentee's argument that the antibody-antigen interaction at issue in its claims is not naturally-occurring because it involves a human-made labeled antigen (^{125}I-labelled MuSK).
    - Treating antibody-antigen binding broadly as the relevant ineligible natural law could encourage over-simplification of claims reciting antibody-antigen binding (or other well-known physical and chemical interactions) to deem them "directed to" a natural law, allowing a recited application of or reliance on a natural law or phenomenon in a method to serve as a tail to wag an otherwise patent-eligible dog.
- Application in a novel context does not necessarily convert a set of routine, conventional method steps into a patent-eligible inventive concept. However, a combination of otherwise routine, conventional method steps that yields a new result or an improvement to prior art technology supports patent-eligibility.
- There was also a procedural issue decided under First Circuit law that highlighted the potential benefits of laying out patent-eligibility fact issues in the complaint (*e.g.,* assertions regarding lack of preemption, how certain method steps are not routine or conventional, how a new result is achieved, how a prior art technology is improved, etc.).

[10] 566 U.S. 66 (2012).

[11] In contrast, if *Mayo* had cited the naturally-occurring enzymatic breakdown of a drug to its metabolites as the natural law, then the antibody-antigen interaction might be a closer analogy.