The Clones War: Chapter Two – Myriad Files Their Brief on Appeal

By – Mark J. Nuell, Ph.D. – Partner at Birch, Stewart, Kolasch & Birch, LLP, San Diego, CA

Abstract

Myriad Genetics has filed their brief in their appeal of the decision in *Assoc. of Med. Pathology et al. v. Myriad Genetics et al.* This case is one having effect on patent-eligibility of claims directed to purified natural products and to sequence-based diagnostic methods. Myriad's brief is a paper of advocacy, and it is persuasive of an asserted lack of jurisdiction. Thus, the Federal Circuit might not even reach the questions of patentability of isolated DNA and of nucleic acid (sequence)-based diagnostic methods. But, should the Federal Circuit choose to consider those questions, it appears that claims to "isolated DNA" meet the standard for patent-eligibility. Despite their arguments to the contrary, some of Myriad's diagnostic method claims are likely to fail to meet the standard, as falling within the scope of abstract ideas or laws of nature. The other method claims that are challenged, although they can be interpreted to include a "transformative" step and so include a strong clue in favor of patent-eligibility under *Bilski v. Kappos*, might be deemed ineligible for patent protection because the "transformative" steps represent mere data-gathering steps.

Introduction

On March 29, 2010, in a district court far, far away (from Utah, anyway), Judge Sweet's decision, by summary judgment, in the Declaratory Judgment action *Assoc. of Med. Pathology et al. v. Myriad Genetics et al.*[1] upset settled expectations that "isolated DNA" and the like were subject matter eligible for claiming in a U.S. Patent. His decision that diagnostic methods that rely upon comparison of "sequences" of nucleotides to reach a conclusion about the likelihood or prognosis of a disease are also not eligible to be claimed in a U.S. Patent came after a decision (now vacated and remanded) the other way on a similar question presented by *Prometheus Laboratories v. Mayo Collaborative Services*.[2]

Plaintiffs had selected only a few claims from among seven different patents[3], and it is plain that they chose their targeted claims carefully, because the claims that were not challenged did not meet the facts they asserted in support of their position. The Defendants' claims that were not challenged appear to sufficiently cover their commercialized embodiments of the invention, and so even if Judge Sweet's decisions are left standing, Defendant Myriad Genetics will be left with enforceable, commercially valuable patent claims.

Nonetheless, Myriad has appealed Judge Sweet's decisions, and their principle brief in support of their appeal was filed on October 22. Their opening salvo presents three issues for consideration by the Court of Appeals for the Federal Circuit; standing, are composition claims directed to isolated DNA molecules ineligible for patenting under 35

USC § 101 and are diagnostic methods based upon analysis of nucleic acid sequences ineligible for patenting under 35 USC § 101?[4]

Justiciability

Standing is a threshold issue that must be established for the Court to have jurisdiction. 28 U.S.C. 2201(a) - the Declaratory Judgment Act – provides that the rights and other legal relations of parties to an "actual controvery" may be decided by a Federal Court.[5] Myriad points to *Medimmune, Inc. v. Genentech, Inc.*[6] as their articulation of the standard for a justiciable "actual controversy".

> All the circumstances … [must] show that there is a substantial controversy, *between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.*

All of the attorneys in the audience will recall at least one case they read in law school where the judge reached a result that was at odds with the case law on the subject, and the unsurprising lesson that judges sometimes make decisions they feel are right, as in the interests of justice, and then stretch and pull and piece together the rules to justify their opinions. Myriad asserts that is how standing was acknowledged by Judge Sweet.

In essence Myriad asserts that his primary error was to truncate the rule from *Medimmune* at "controversy"and then this was compounded by his supposition that "all of the circumstances" can include a desire to see a public policy that is at least mildly controversial be considered by the judicial system. Even though it is not likely that the Federal Circuit will support him, this is an at least understandable reason on the part of Judge Sweet to find justiciability.

Myriad then supposes the entire *Medimmune* rule and points out that Plaintiffs' evidence of any assertion of their patent claims by Myriad and the University of Utah was at least ten years old. They make the quite persuasive point that, had Myriad actually sued any of the Plaintiffs at the date of filing of the Declaratory Judgment complaint, said Plaintiff would likely have succeeded with a defense of laches, and so Plaintiffs were hardly in a position to assert "sufficient immediacy … to warrant the issuance of a declaratory judgment."

Myriad also denies the "reality" of the adversity of legal interests of the parties, asserting that none of the parties Plaintiff had ever been communicated with in a manner that could credibly be understood to be a threat of a suit for infringement. In fact, some of the parties Plaintiff had not been communicated with at all. Indeed, Myriad somewhat suggests that Plaintiffs are "reverse trolls"; having no products or services on the market, they nonetheless sue for invalidity of a patent claim.

Any associate charged with writing a "soft" cease-and-desist letter would do well to read these sections of the brief (esp. pp. 20-21).

If Myriad's characterization of the facts is found correct, then it is quite possible that the Federal Circuit will never reach the more interesting issues.

Patent-eligibility of isolated DNA

But, let's suppose they can't resist…

> Whoever 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 essence of Judge Sweet's opinion on patent-eligibility of isolated DNA as a composition stems from an interpretation of 35 U.S.C. § 101 that it includes an element above and beyond "new and useful", i.e. that a patent-eligible composition is one that is "markedly different" in its characteristics and use from "native DNA" that is the natural product comprising the claimed isolated DNA.

So, a threshold question is, "Is patent-eligibility of subject matter a question separate from (or perhaps in addition to) novelty and utility, or merely limited to these two considerations?

Myriad argues in part that either way it is not reasonable to interpret 35 U.S.C. § 101 as including a requirement that "isolated DNA" (that is, the claimed "product of nature") have a "markedly different" characteristic from "native DNA" as found in the natural state. They assert that such a standard is too subjective as to what would constitute a "marked" difference.

Myriad then argues a textualist interpretation of the statute, *i.e.* new and useful are the criteria. They assert that the case law to date on the question of patent-eligibility is consistent with this interpretation in that claims to products purified from organisms have been upheld as novel over the natural occurrences of the product, and that in such instances, the concentration of the product made it useful in a new way or more conveniently for an old purpose. One might say that the product is placed into the hands of the technologists by the purification, thus achieving the goal of improving the public good underlying the grant of patent rights.

Myriad also points out that the exceptions to patent-eligibility – abstract ideas, laws of nature and physical phenomena – are judge-made, then argues that a sweeping "products of nature" exception is too broad, contrary to USPTO policy (which is entitled to great deference) and would deprive society of many useful innovations. This could be thin ice; it seems to invite the Court to consider that if three judge-made exceptions are a good thing, four might be better. But, Myriad asserts, rewriting statutes is the job of the legislature.

If you can't win on the facts, pound on the law...

Myriad also argues that Judge Sweet misinterpreted Supreme Court case law. They tell an eloquent story relating his misinterpretation of *Chakrabarty*[7] and *Funk Bros.*[8]. The tale includes an argument showing how reliance on opinion text, without consideration of the statutory context of the opinion, can lead to an incorrect interpretation of the language of present day statutes. This is excellent strategy, as Judge Sweet had expressly cautioned such a possible failure of his reliance on old cases.[9]

Myriad makes a further argument in support of their composition claims. Taking the approach of the *Bilski* Justices, they point out the existence of 35 U.S.C. § 103(b), which relates to obviousness of biotechnology-related inventions and provides an exception to the inventive step requirements for inventions residing in biotechnological methods that utilize or produce a novel and unobvious composition of matter, including "nucleotide sequences" (35 U.S.C. § 103(b)(A)(i)) .[10]

If you can't win on the law, pound on policy…

Myriad makes their plea that the biotechnology industry has been good for America, all kinds of wonderful therapeutic products have been purified from natural sources to the great benefit of mankind, all kinds of wonderful research has been conducted as a result of the discoveries claimed in their patents, and there is a well-established and settled expectation that isolated DNA is patent-eligible subject matter. The more succinct argument is presented at page 46,

> These inventors' work yielded a new composition of matter with substantial societal benefit, which added to the body of human knowledge. That is enough to demonstrate that these compositions of matter are patent-eligible under § 101.

"The crux of the biscuit."[11] Case closed.

If you can't pound on policy, pound on the table!

Finally, Myriad argues procedure. The assertion is essentially that, given Judge Sweet's legal standard for determining patent-eligibility, it is erroneous to grant summary judgment on a question having an element, the marked difference between the claimed subject matter and the naturally occurring subject matter, that is one of fact and is in dispute. And furthermore, Judge Sweet erroneously ignored facts that did not fit his argument.

If the appeal is not thrown out for lack of jurisdiction at the outset, then it appears likely Judge Sweet's decision that isolated DNA is not patent-eligible will be overturned. Even if the Federal Circuit agrees with him on the legal standard to be applied, it seems that the case must then be returned to him to reconsider the facts of the matter.

Patent-eligibility of nucleic acid (sequence)-based diagnostic methods

The fate of Defendants' claims directed to diagnostic methods is much harder to predict.

Myriad opens their case here with a plea for expansive interpretation of the law and generous findings on the facts. Biotechnology is an emerging technology, and so poses "questions of such intricacy and refinement that they risk obscuring the larger object of securing patents for valuable inventions without transgressing the public domain."[12] Be that as it may, the value of some of the method claims challenged is highly questionable, and the Court has no social obligation to deem one step of a laboratory protocol an invention just because it is performed in a biotechnology laboratory.

Again, it is important to remember that only a part of Defendants' claims are challenged. Those claims not at issue are quite adequate to protect Myriad's commercial embodiments. But, claim 1 of 6,033,857 is among the claims challenged:

> 1. A method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence, wherein a difference between the suspected mutant and the wild-type sequences identifies a mutant BRCA2 nucleotide sequence**.**

A skilled molecular biologist understands that the definition of a "mutant allele" is one that has a sequence change in comparison with a wild-type allele. This claim is a tautology, not a "valuable invention".

Claim 2 comes much closer to the criterion of a valuable invention, and indeed recites the essence of the portfolio:

> 2. A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a predisposition to said cancer.

The question for the Court here will be whether or not the relationship stated in '857 claim 2 is a law of nature within the judge-made exceptions to patent-eligible subject matter. It certainly looks like one; mutation = cancer looks a lot like $E = mc^2$.

Myriad completely ignores this question, and seeks instead to rely upon the rule from *Bilski* that a method that transforms the form of matter is likely patent-eligible. (Myriad seems to believe a transformative method is *per se* patent eligible – contrary to repeated caution by the Supreme Court that there are no *per se* rules for determining patent-

eligibility.[13]) They depart from the textualist approach they adopt for statutory interpretation and go to the "legislative history" (i.e. the prosecution history) to argue that a "sequence" is not purely information, but is actually a molecule.[14] Here they point out the specification from the US 5,709,999[15] recites that, "the target nucleic acid sequence is amplified with polymerases" and "if the sequence is double-stranded, the sequence will probably need to be denatured." Then, so the argument goes, a "sequence" of letters of the alphabet cannot be amplified or denatured, but a nucleic acid, being an actual molecule, can be.

On this argument, "comparing a sequence" includes all the steps implied in obtaining the data of the sequences to be compared, which steps are transformative under the (now vacated) holding of *Prometheus.*

Supposing that Myriad's challenged claims are found to indeed recite transformative steps, there is then the second question of whether those steps are "central to the claimed process" or merely ancillary "data gathering". Of course, Myriad takes a position that these steps are central to the claimed method, being required to collect the data to be used in the comparison step. So, yes the transformative steps are central to the data gathering steps.

It seems that reasonable minds can differ on patent-eligibility of those of Myriad's claims that do not expressly recite any step of changing matter from one form into another, but likely that the Federal Circuit will invalidate one or more of Myriad's broadest claims to diagnostic methods as ineligible for patent protection.

Conclusion

Myriad tells a good story. The Federal Circuit could very well decide that AMP's pleading is a tempest in a teapot. If they so decide, they might not even reach the questions of patentability of isolated DNA and of nucleic acid (sequence)-based diagnostic methods. But, should the Federal Circuit choose to consider those questions, it appears that claims to "isolated DNA" meet the standard for patent-eligibility. On the other hand, some of Myriad's diagnostic method claims are likely to fail to meet the standard, as falling within the scope of abstract ideas or laws of nature. The other method claims that are challenged, although they can be interpreted to include a "transformative" step and so include a strong clue in favor of patent-eligibility under *Bilski v. Kappos*, might be deemed ineligible for patent protection because the "transformative" steps represent mere data-gathering steps.

Amicus briefs are pouring in. Perhaps of interest, the Department of Justice has filed a brief against the USPTO position that isolated DNA is patent-eligible![16]

---

[1] *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, 94 U.S.P.Q.2d (BNA) 1683, ____ F. Supp. 2d ___, 2010 WL 1233416, No. 09 Civ. 4515, (SDNY March 29, 2010).

[2] *Prometheus Laboratories v. Mayo Collaborative Services*, 581 F.3d 1336 (Fed. Cir. 2009), *certiorari granted, judgment vacated and remanded*, 130 S.Ct. 3543 (2010).

[3] The challenged claims are:

PATENT NO.	LIST OF CLAIMS
5,747,282	1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2. 2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1. 5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1. 6. An isolated DNA having at least 15 nucleotides of the DNA of claim 2. 7. An isolated DNA selected from the group consisting of: (a) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having T at nucleotide position 4056; (b) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having an extra C at nucleotide position 5385; (c) a DNA having the nucleotide sequence set forth in SEQ ID NO: 1 having G at nucleotide position 5443; and, (d) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having 11 base pairs at nucleotide positions 189-199 deleted. 20. A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.
5,837,492	1. An isolated DNA molecule coding for a BRCA2 polypeptide, said DNA molecule comprising a nucleic acid sequence encoding the amino acid sequence set forth in SEQ ID NO:2. 6. An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer. 7. The isolated DNA molecule of claim 6, wherein the DNA molecule comprises a mutated nucleotide sequence set forth in SEQ ID NO:1.
5,693,473	1. An isolated DNA comprising an altered BRCA1 DNA having at least one of the alterations set forth in Tables 12A, 14, 18 or 19 with the proviso that the alteration is not a deletion of four nucleotides corresponding to base numbers 4184-4187 in SEQ. ID. NO:1.
5,709,999	1. A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1.
5,710,001	1. A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises gene comparing a first sequence selected form the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample.

5,753,441	1. A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject.
6,033,857	1. A method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence, wherein a difference between the suspected mutant and the wild-type sequences identifies a mutant BRCA2 nucleotide sequence. 2. A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a predisposition to said cancer.

[4] *Myriad brief,* p. 1.

[5] **28 U.S.C. § 2201(a) -** In a case of actual controversy within its jurisdiction, except with respect to Federal taxes other than actions brought under section 7428 of the Internal Revenue Code of 1986, a proceeding under section 505 or 1146 of title **11**, or in any civil action involving an antidumping or countervailing duty proceeding regarding a class or kind of merchandise of a free trade area country (as defined in section 516A(f)(10) of the Tariff Act of 1930), as determined by the administering authority, any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such declaration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.

[6] *Medimmune, Inc. v. Genentech, Inc.*, 549 U.S. 118 (2007).

[7] *Diamond v. Chakrabarty,* 447 U.S. 303, 100 S. Ct. 2204, 65 L. Ed 2d 144, 206 U.S.P.Q. (BNA) 193 (1980).

[8] *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130, 76 U.S.P.Q. 280 (1948*).*

[9] *Association for Molecular Pathology v. U.S. Patent and Trademark Office,* 94 U.S.P.Q.2d at 1712 (slip. op. at p. 101).

[10] **35 USC § 103(b)**:

(1) Notwithstanding subsection (a), and upon timely election by the applicant for patent to proceed under this subsection, a biotechnological process using or resulting in a composition of matter that is novel under section 102 and nonobvious under subsection (a) of this section shall be considered nonobvious if-
(A) claims to the process and the composition of matter are contained in either the same application for patent or in separate applications having the same effective filing date; and
(B) the composition of matter, and the process at the time it was invented, were owned by the same person or subject to an obligation of assignment to the same person.
(2) A patent issued on a process under paragraph (1)-
(A) shall also contain the claims to the composition of matter used in or made by that process, or
(B) shall, if such composition of matter is claimed in another patent, be set to expire on the same date as such other patent, notwithstanding section 154.
(3) For purposes of paragraph (1), the term "biotechnological process" means-
(A) a process of genetically altering or otherwise inducing a single- or multi-celled organism to-
(i) express an exogenous nucleotide sequence,
(ii) inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or
(iii) express a specific physiological characteristic not naturally associated with said organism;
(B) cell fusion procedures yielding a cell line that expresses a specific protein, such as a monoclonal antibody; and
(C) a method of using a product produced by a process defined by subparagraph (A) or (B), or a combination of subparagraphs (A) and (B).

[11] Frank Zappa, “Apostrophe/Overnite Sensation”, p. 1973, 1974 Pumpko Industries, Ltd., c. 1986 RYKODISC.
[12] Myriad brief at p. 53, quoting *Bilski v. Kappos*, 561 U.S. ____ (2010), 130 S.Ct. 3218, 3227 (2010).
[13] *See, e.g. Bilski v. Kappos*, 561 U.S. ____ (2010), 130 S.Ct. _____ (2010). (slip. op. at p. 8, quoting *J.E.M Ag Supply v. Pioneer Hi-Bred Int’l, Inc.*, 534 U.S. 124, 135 (2001); and *Bilski v. Kappos*, slip. Op. p. 10 (“Section 101’s terms suggest that new technologies may call for new inquiries.”); and *id.*, J. Stevens, concurring, ("[T]he machine or transformation test is not the sole test for what constitutes a patentable process; rather it is a critical clue.”) at slip. op. p. 2..
[14] Myriad brief at p. 59.
[15] A different patent family from ‘857! But the term “sequence” is used in relation to “amplifying” in the ‘857 patent as well.
[16] http://www.patentlyo.com/patent/2010/10/us-government-argues-in-court-that-isolated-genes-are-unpatentable.html