Debra Greenfield J.D., Adjunct Assistant Professor

UCLA Center for Society & Genetics

**THE UNENCUMBERED GENE**

**Good Morning. I’d like to thank Fenwick & West partners Michael Shuster and Andrew Sarafini for inviting me to speak to you from the Plaintiff’s perspective. First, a disclaimer, akin to attorney Greg Castanias’s repeated reminders to the Federal court that “he was an English major.” I am also not a scientific expert or even a patent attorney, but an advocate who has worked on legal cases and public policy involving emerging biotechnologies and a professor who researches, writes and teaches about their societal and political implications. Thus my interest and involvement in the case has been influenced by many disciplines outside the law, and suggests that my participation today might reflect or inform based upon these broader contexts. I guess what I’m really saying is that I will not attempt to play ball entirely on your field…and for those of you that listened to the oral arguments; I’ll be addressing further baseball metaphors a little later on.**

**So, the preliminary question: how did this case come into being, what are the underlying issues surrounding the narrow question of subject matter patentability. There have been somewhat dismissive descriptions of the suit, suggestions that the case is, “artificial.” My comments regarding the specifics of the case will come later, but now I’d like you to consider the evolution of the critiques against gene patenting and to focus on the current plaintiffs as being representative of an aggregate of those who have both objected to the practice, and those who have claimed harms and suffered as a result of patented genes: Those who would vehemently dispute the case as being in any way…artificial.**

**\*Insert slide 1**

**Critiques surrounding the patenting of human genes developed from its inception. In 1991 Craig Venter’s attempt to patent 315 Express Sequence Tags, opened the door to calls for a moratorium on the practice of patenting any human genes, and in 1992 the Senate held hearings regarding the ethical issues involved in the practice. Much like today, institutional interests, patent attorneys and biotech representatives warned about a U.S. competitive disadvantage and impediments to research. Testimony urged a separation “between issues of political economy and issues of ethics,” and no action was taken by Congress.**

**Nonetheless, protests continued based upon dignitary concerns, a resistance to the incursion of property and commerce into areas of a human being’s biological make-up. In 1995 180 prominent religious leaders opposed the patenting of genes as a commodification of human processes and in 1996, women’s rights leaders from 69 countries fought against the patenting of the BRCA genes, as it denied them control over the most intimate aspect of their being, their bodies’ genetic blueprint.**

**Around the turn of the century critiques became more economic and consequential, as those involved in biomedical research and clinical practice recognized that the race, the gold rush for patents on a finite resource, the genes responsible for common diseases was producing counterproductive results for both science and health. The ideals of those dependent upon free scientific inquiry were contrasted with monopoly-like restrictions, and resistance to the incursion of patent law into their laboratories developed. Not only scientists, but also patients were beginning to feel the detrimental effects of patenting human genes.**

**Those pictured above represent the human faces at the heart of the growing controversy. Consider the immortal Bella Abzug, a pioneer of women’s rights and a breast cancer survivor, who recognized the need for control over one’s genome. The Greenberg family struggling with a devastating illness; they gathered families, and contributed the source for the identification of the Canavan gene, their deceased children’s tissue only to witness the denial of the test based upon the secretly patented gene.**

**Consider plaintiffs Lisbeth Ceriani, Genae Girard, and Harry Ostrer. After developing breast cancer Ms. Ceriani was advised to test for the BRCA genes looking for an increased risk for ovarian cancer. Myriad Genetics would not accept her insurance and she could not afford to pay the out of pocket costs. Ms. Gerard could not receive a second opinion regarding a positive result for a mutation after her initial diagnosis and BRCA testing. Harry Ostrer, a physician and researcher, who cannot tell his research subjects the results of their BRCA 1 and 2 tests and cannot offer clinical BRCA testing services. He is ready, willing and able to do so should the patents be revoked.**

**Whether or not these plaintiffs have the precise technical grounds upon which to sue, their stories will continue to be illustrative of the harms of exclusionary and restrictive patents on human genes. There are hundreds of stories not pictured: A gene for Long QT syndrome, characterized by irregular heart rhythms and a risk of sudden death, was patented and assigned to the University of Utah Research Foundation. The company with the exclusive license went through corporate upheavals and for two years did not offer diagnostic testing. Other laboratories had the capability and willingness to offer the test but were forbidden to do so by the licensee. A 10 year old girl died from the undiagnosed disease, preventable had testing been available.**

**\* Insert slide 2**

**These stories shed light on the ACLU’s participation, unusual in a patent suit. But consider the *Bernstein* case: in an era where object and source code can simultaneously be subjects for copyright and patenting, and where they are protected speech for purposes of the First Amendment, perhaps one can whisper that gene patenting implicates civil rights, even if shouting it out at the Federal Circuit is not a great strategy. Certainly the stories of the plaintiffs can be considered within this context. As noted, “To the degree that American Society comes to understand genetic material as basic to humanity, the production, circulation, and management of that material will implicate our conception of the rights, duties, and interests of our citizens. As genes play an increasingly powerful role in contemporary legal and political culture, individuals are called upon to refer to genetic information as a basis for asserting their rights and duties. In this context, *to know* *your rights, you must first know your genes*….intellectual property in particular, is playing a significant role in this process…” Jonathan Kahn, What’s the Use? Law and Authority in Patenting Human Genetic Material, Stanford Law & Policy Review, Volume 14.2 2003**

**Which brings us to the question at the heart of the case at bar. How do we define the contested subject matter, what is the nature and character of human DNA, even if isolated, purified, extricated or synthesized. Without a mutually shared understanding, questions relating to the composition and methods claims involving the BRCA genes will continue to be spoken of in two separate languages and meaningful resolution of the issues will be difficult to achieve.**

**\*Insert slide 3**

**Plaintiffs, including thousands of scientists and geneticists, their amici, and numerous scholars and commentators, both within and outside the legal discipline, believe the answer is grounded in the realities of the 21st century. They agree with the visionary opinion of Judge Sweet who similarly rests the decision within the challenges of the future. They believe that the denial by Myriad and its amici of an essential fact will perpetuate barriers to true innovation and progress that our infant century so desperately needs. In short, in the age of what has become known as bioinformatics, it has been stated that “…biology is information, and crucially, that information is both material and immaterial.”**

**It completely defies logic to assert that broadly claimed patents on human DNA and genes such as those on BRCA 1 and 2, were and are being sought without regard for their informational content, or that the genes themselves even when isolated, purified, or synthesized do not have a unique functionality based upon their embodied information. As commentator Dan Burk describes, “It’s the three dimensional configuration of the molecule that encodes the information….no one is interested in the strings of human-readable letters, they are instead interested in *what can be done with the structures the letters represent*….and that in turn means that by necessity, they must be interested in building informational structures-the molecules that are the conduit for information transfer. Thus, “it is the information flow that is of interest in biotechnology, and hence of interest in biotechnology patenting….” Dan Burk, *The Problem of Process in Biotechnology*, 43 Hous. L. Rev. 561, 582-87 (2006).**

**Myriad claims that isolated BRCA DNA is a “purified substance,” a chemical composition separate from the information contained in the DNA molecule itself. They compare it to epinephrine, stating that it also, “conveys information.” By, itself, however epinephrine contains no information whatsoever, and everyone’s epinephrine molecules are the exactly the same. One might ask if sunlight contains information because it makes us tan and sweat and synthesize Vitamin D.**

**By characterizing DNA as such Myriad is considering the patented molecules and genes only as the manufactured reagents, ignoring the individual information contained in those genes in situ in the genome, rendered inaccessible by the patents’ broad claims.**

**This disputed characterization informs the legal issue in the case, whether the extracted or isolated or complementary DNA and the BRCA 1 and 2 genes are patentable subject matter, or exceptions to the acceptable categories: physical phenomenon, laws of nature, and abstract ideas, part of the storehouse of knowledge…free to all men and reserved exclusively to none…”**

**forward to refuting this in the discussion of the case as presented in the oral arguments.**

**THE PLAINTIFFS’ THEORY OF THE CASE AND ORAL ARGUMENTS**

**Insert Slide 1**

**Viewing the status of the case through the prism of the oral** **arguments at the Federal Circuit is somewhat of an organizational nightmare. I will attempt to summarize the courts’ discussion regarding the composition and method claims, including the arguments from the United States Solicitor General and then offer arguments the Plaintiffs might have made had time permitted. I will also address the hypothetical offered by Judge Bryson regarding whole genome sequencing.**

**Although the jurisdictional issues are of considerable interest, consuming a great amount of the court’s time, I believe the court will find a plaintiff with the necessary standing, and has an interest in reaching the substantive merits of the controversy.**

**Insert Slide 2**

**The discussions regarding the composition claims illustrate the aforementioned search for boundaries between the natural and the unnatural, with an abundance of metaphors and analogies used in the exercise to determine whether or not the isolated, purified, and complementary BRCA DNA/Genes are characteristically unique or different enough from those that exist in the human body to render them patentable subject matter, or whether they are products and laws of nature, exceptions to the categories of patentable subject matter.**

**The court seemed to base its questions and answers by examining the exact process involved in the act of isolation. Judge Lourie suggested that a breaking of covalent bonds rendered the gene different enough, a reiteration of Myriad’s basic premise, that the isolated gene is structurally and functionally different from the one found in nature. Myriad’s example was a baseball bat: made from the same material found in a tree, human ingenuity separated the bat and gave it a different function. The Plaintiffs stressed the nature of isolated DNA as not having sufficiently distinct properties in order to be patent-eligible. In response, Judge Bryson noted the different function of isolated DNA and Judge Lourie considered it a different material.**

**Had the ACLU counsel had time, he could have responded more fully to these premises. Myriad’s briefs and experts admit that an “isolated DNA” gene sequence is one that has been removed from its naturally occurring environment, for example from the cell and chromosome where it is found. This contradicts their suggestion of a narrow claim construction, that isolated DNA should be understood as structurally distinct from native DNA.**

**Rather, what is being patented is the structure of the chemical bases that in their ordering direct the synthesis of other molecules in the body, namely proteins. This constitutes both the isolated molecule as well as its linear structure, described as a sequence, the ordering of the chemical bases, As Cs Ts and Gs. Accordingly native DNA inherently contains the claimed isolated compound. The patent claims are broad and encompass both the known natural composition of the native DNA and the claimed isolated naturally occurring compound, thus they are arguably products of nature.**

**Myriad consistently argues that the application of isolated DNA in primers, probes, and diagnostics makes their use distinctive from that of native DNA, and thereby patentable. However the primers, probes and diagnostics rely on their *non-distinctive* natural biological characteristics of DNA sequences to code for a protein and to anneal to its complementary nucleotide sequence. If isolated DNA had a distinctive character or function from native DNA, these applications would not be possible.**

**Solicitor General Katal continued the discussion as to whether isolated DNA was different from that found in nature. He delineated a “magic microscope test,” where, by zeroing in on the gene you could see the exact claim in nature. Under his test the isolated gene such as Claim 1 of patent ‘282 would be found to be a product of nature, while cDNA would not. Although the Plaintiffs did not care to refute the position of the U.S. government, it is arguable that under a magic microscope, one could see the processes of translation and transcription and splicing, the creation of the template mRNA from which cDNA is derived, and thus similarly, a product of nature.**

**\*Insert Slide 3**

**The analogy of the isolated DNA however was to lithium, which is generally not found in its elemental form. Katal argued that even if covalent bonds were broken in order to isolate the element from other minerals, it should not render the element patentable. Myriad disagreed and stated that it was analogous to the question at issue and as such, isolated lithium should be patentable.**

**This statement revealed a void in the discussions regarding the exceptions to patentable subject matter. Although the questioning, the attempted line-drawing and creation of boundaries was extensive there was absolutely no conversation regarding the significant and important rationale undergirding the doctrine: that “manifestations of nature should be free to all men and reserved exclusively to none.” With the suggestion that an element of the periodic table should be privatized and monopolized, that no one else should be privy to its use, perhaps the court was brought back to essential and first principles.**

**Yes perhaps you could patent a wooden bat, but your claim cannot also give you exclusive rights to the wood from which it was made, nor stop anyone else from carving a sculpture or making a table or even making lighter and stronger wooden bats for kids who can’t hold the heavier ones. We want wood to be free, and air to be free and yes, even knowledge regarding the human genome whether or not it is excised from the body to be free, particularly in the Information Age.**

**These same principles did not arise in any conversations regarding the method claims. Judge Lourie asked whether the steps of comparing and analyzing were merely thought processes. Myriad responded that the claims were analogous to those in *Prometheus*, in that the process necessarily included a transformation when the gene was sequenced. The ACLU responded that unlike *Prometheus* the claims only recited the mental step of comparing and that the process of isolation does not produce a transformation.**

**Myriad’s method claims are not limited to any steps other than comparing or analyzing genetic sequence information, no matter how the information is obtained. These claims cover the use of any and all techniques for determining the presence of mutations from the “normal” *BRCA 1* & 2 genes. These claims prohibit the use of the very information that was disclosed as a requirement of obtaining the patents.**

**As such these claims to correlations are synonymous with laws of nature exemplified by the Supreme Court. They reveal “a relationship that has always existed.” They are scientific principles, ideas and abstract concepts, “the necessary basis for scientific and technological work.” Like the hedging process of *Bilski*, these method claims create “monopolies over procedures that others would discover by independent creative application of general principles.”**

**In *Prometheus* chemical and physical changes in the level of metabolites in the blood were determined after the administration of specific drugs. No drugs are involved in these claims, rather it is only the naturally occurring molecule which embodies the nucleotide information, referenced as a sequence that is compared and analyzed. Despite isolation and sequencing they are not transformed by the processes involved. Had those sequences been transformed it is arguable that the utility and efficacy of the diagnostics would be in question.**

**\*Insert Slide 4**

**Which brings us to the Judge Bryson’s hypothetical: whether whole genome sequencing would necessarily infringe Myriad’s patents. When first asked, Myriad counsel replied that “I’m not sure my client has formed a view on that…” When pressed, he stated that Myriad did not claim the entire genome, and that without an isolating procedure directed to finding BRCA mutations, he concluded that whole genome sequencing would not infringe Myriad’s patents.**

**This labored analysis necessarily illustrates that counsel was relying on Myriad’s construction that the isolated DNA is a purified chemical compound separate from the information contained within native DNA, and thus considers the isolated BRCA genes only as manufactured reagents. This despite the broad claims which cover large stretches of the BRCA genes, including as noted by the Solicitor General, “…an ordinary BRCA gene isolated from a tissue sample taken from a woman in a hospital.”**

**Myriad’s counsel was also vague regarding the definition of isolation. According to Robert Cook Deegan, this gives those wishing to conduct whole genome sequencing little guidance. He asked, “How do you do DNA sequencing without some purification step? Even nanopore or scanning-tunneling [electro machining] means isolating some piece of DNA. That’s an isolated molecule you’re measuring. It’s a meaningless distinction.”**

**( Turna Ray, “At Appeals Hearing, Myriad Outlines Stance on BRCA IP Rights for Whole-Genome Sequencing,” Pharmacogenomics Reporter (April 4, 2011), available at available at** [**http://www.genomeweb.com/dxpgx/appeals-hearing-myriad-outlines-stance-brca-ip-rights-whole-genome-sequencing?page=show**](http://www.genomeweb.com/dxpgx/appeals-hearing-myriad-outlines-stance-brca-ip-rights-whole-genome-sequencing?page=show)**, last visited April 11, 2011.)**

**Hansen of the ACLU noted that the broadness of Myriad’s patents leave open the possibility that the company may take action against doctors and researchers who are identifying their patients’ BRCA mutations via whole-genome sequencing techniques. Even if the sequencing did not violate the composition claims, if doctors used the technique, studied the BRCA sequences and reported the results to the patient, the use of the information could still violate Myriad’s patents.**

**George Church has observed that as whole genome sequencing will be used in the approaching field of personalized medicine, “Myriad is losing the bigger battle.” He notes that “the entire industry will be reformatted” and gene association patents as they exist today, “won’t really matter.”**

**Until that time, they matter. They matter to women who want high quality, affordable and accessible testing. They matter to researchers, chilled by the threats of infringement litigation. They matter to physicians, unsure of the implications of using modern technologies for their patients’ health. Until the Federal Circuit 3-judge or full panel or the Supreme Court decides that these patents should be invalidated, the practice will continue to produce concrete harms. Isolated and even synthesized BRCA genes and human DNA are not man-made; they are not “artificial.” Neither is the case brought by the Plaintiffs and argued by the ACLU.**