The Myriad Case (*Assoc. for Molecular Pathology v. USPTO*): Its Implications For Patent Practitioners And The Biotech Industry

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Roadmap

- Myriad's Patents
- District Court
- Federal Circuit
  - Majority-Concurrence-Dissent
- The Amici
- Impact on the Biotech Industry
- Tips for Practitioners
- What is Next
- Unresolved Issues

Myriad's Patent

- Product claims directed to isolated DNA, cDNA, and fragments for BRCA1 and BRCA2 (mutations in the BRCA genes correlate with increased risk of breast / ovarian cancer):

  An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having an amino acid sequence set forth in SEQ ID NO: 2.

Myriad's Patent

- Method claims directed to "analyzing" and "comparing" the isolated genes with those of a patient:
    - Drawn to a method for screening a tumor sample, which comprises comparing a first BRCA1 sequence from a tumor sample with a second BRCA1 sequence from a nontumor sample, wherein the difference in sequence indicates an alteration in the BRCA1 gene in the tumor sample.

Myriad's Patent

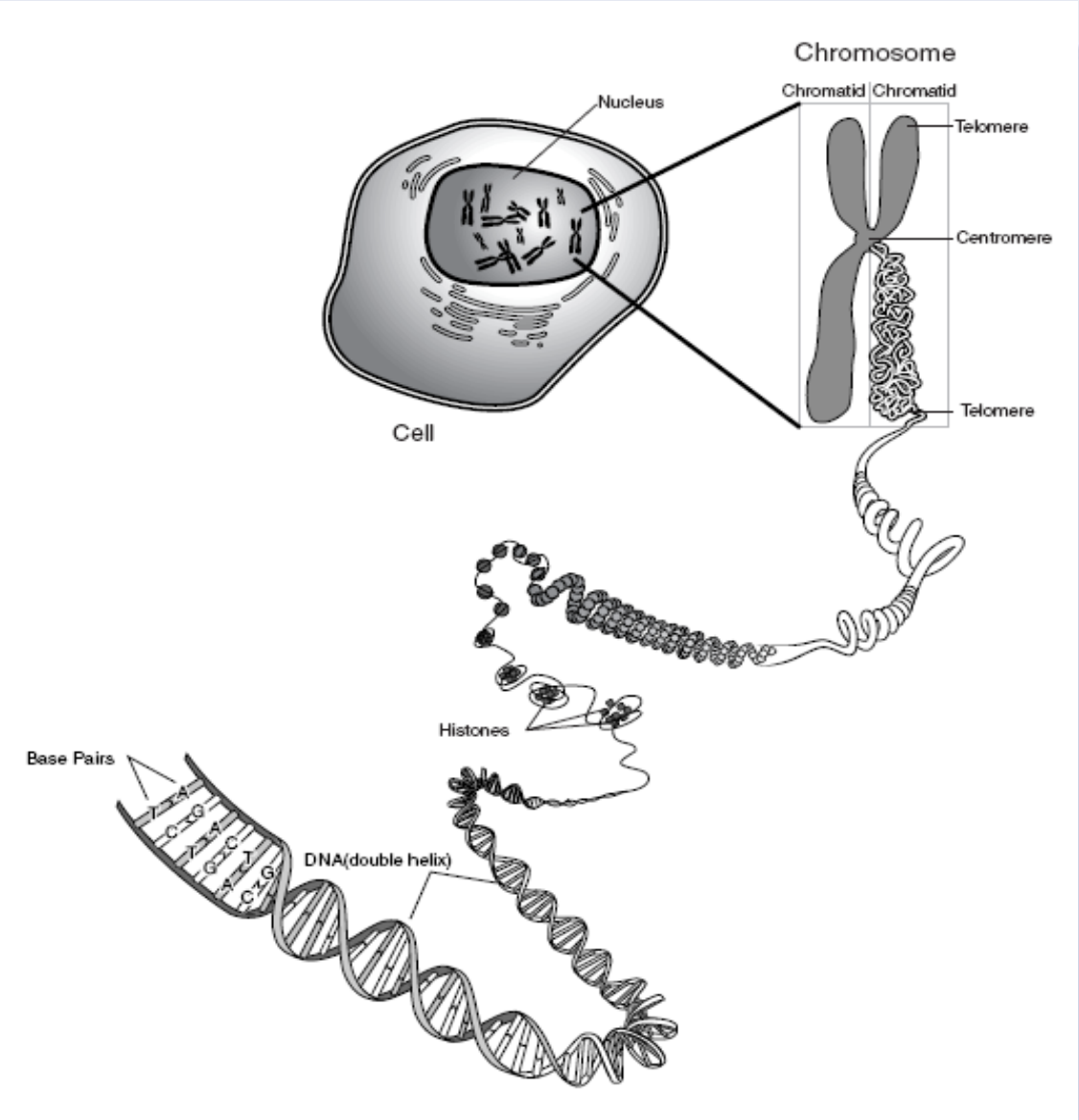
- Method claim directed to screening cancer therapeutics:
  - Drawn to a method for screening potential cancer therapeutics which comprises

    1) ***growing*** host cells transformed with an altered BRCA1 gene in the presence or absence of a potential cancer therapeutic,

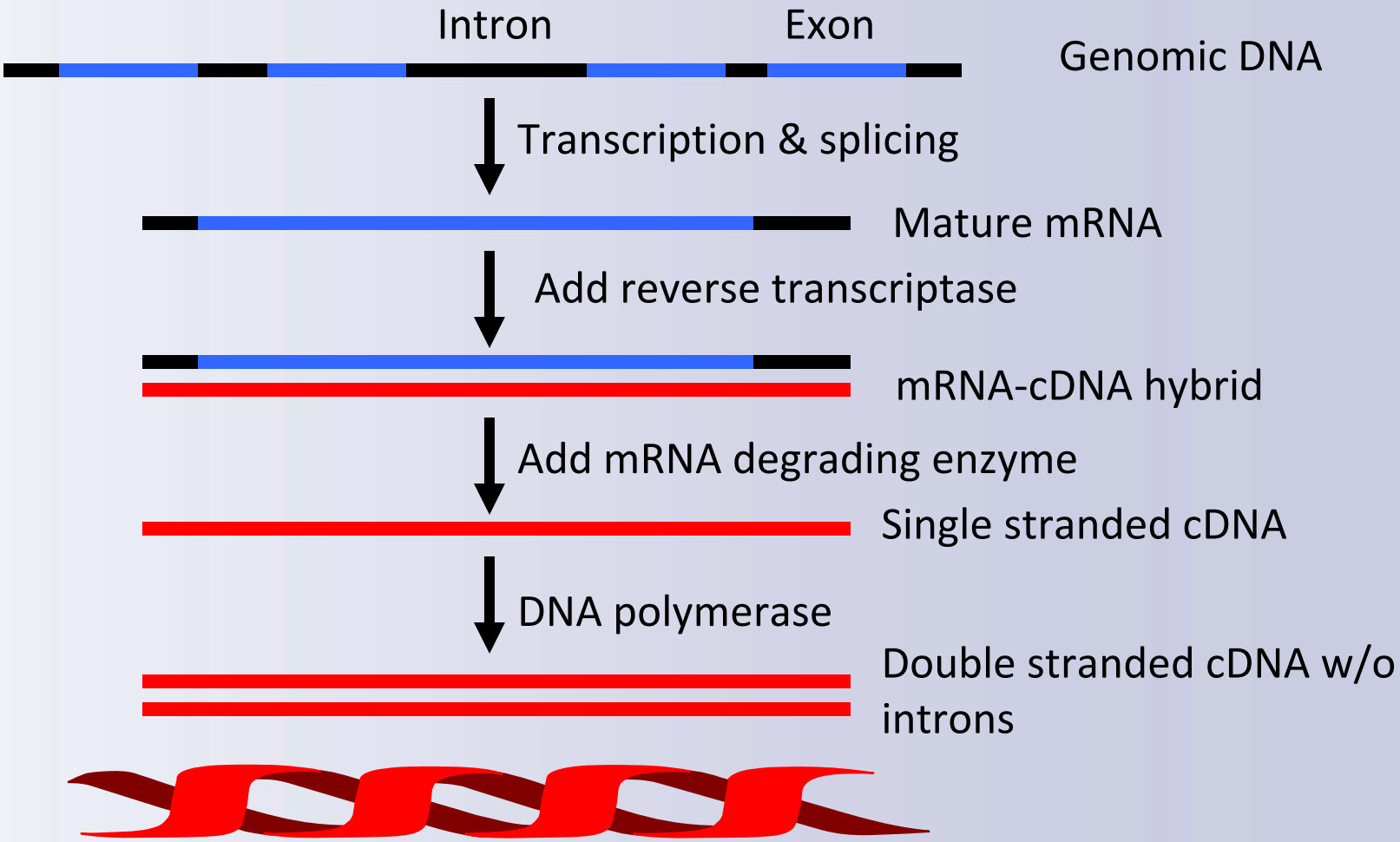
    2) ***determining*** the growth rate of the host cells with or without the potential therapeutic, and

    3) comparing the growth rate of the host cells.

Myriad's Patent



Isolated genomic DNA & cDNA



The Parties

Plaintiffs	Defendants
• Association of Molecular Pathology & various not-for-profit organizations involved in genetic testing and research and individual researchers • Three (3) doctors who received a cease and desist letter from Myriad many years ago • Patients → Represented by the ACLU	• Myriad Genetics, Inc. • USPTO

The District Court
Southern District of New York, March 2010

- Plaintiffs have standing under DJ action to challenge Myriad's patents (relying on *MedImmune*)
- Product Claims not patent eligible under § 101

  → isolated DNA falls under "product of nature" exception because isolated BRCA DNA not "markedly different" from naturally existing BRCA1/2 (relying on *Chakrabarty*) → encoded information is the same in both.
- Method Claims not patent eligible under § 101

  → claims directed to "analyzing" and "comparing" invalid under "machine-or-transformation" test (*Bilski*) – mental processes independent of physical transformations.

  → claim directed to "comparing" cell growth rates → "arguably recites certain transformative steps" but transformative steps are "nothing more than preparatory, data gathering steps to obtain growth rate information"

669 F. Supp. 2d 365; 702 F. Supp. 2d 228-237

Issues on Appeal

Issue 1 – threshold matter - whether the plaintiffs had standing to bring the suit

Issue 2 – merits – whether "isolated" DNA and Myriad's claimed methods are patent eligible subject matter

35 U.S.C. § 101 – Inventions Patentable

- "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."
- Construed broadly, but excludes laws of nature, physical phenomena, or abstract ideas.

Federal Circuit – score board

- **Reversed** District Court (2-1) – claims to "isolated" DNA are patent eligible
- **Reversed** District Court (3-0) – complementary DNA (cDNA) patent eligible
- **Reversed** District Court (3-0) – method claim to screening cancer therapeutics through changes in cell growth rate are patent eligible
- **Affirmed** District Court (3-0) – method claims "comparing" and "analyzing" are not patent eligible
- **Affirmed** District Court (3-0) – one plaintiff has standing

Standing

→ Court applied *MedImmune*'s "all-the-circumstances test" - to establish an injury in fact traceable to the patentee,

a DJ plaintiff must allege both:

(1) an affirmative act by the patentee related to the enforcement of his patent rights, and

(2) meaningful preparation to conduct potentially infringing activity.

Myriad Slip Op. at 26

Standing – affirmed but limited

- Only three Plaintiffs (the doctors) survived application of first prong because they had received C&D letters from Myriad constituting the required "affirmative act" (. . . about a decade ago)
- Only Dr. Ostrer had standing, surviving the second prong because he, having resources and skill, sought to "immediately begin" BRCA diagnostic testing (versus "considering" resuming . . .).

Myriad Slip Op. at 27-28

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Standing – another twist

- Dr. Ostrer (the one with standing) left NYU and moved to Albert Einstein College of Medicine (which Myriad argued is not qualified to offer BCRA testing)
- It is currently unknown whether Dr. Ostrer will be able to maintain his pledge to "immediately begin" testing
- → Federal Circuit could vacate and reconsider standing based on this new development

Federal Circuit – isolated DNA

- Reversed District Court (2-1) – claims to "isolated" DNA are patent eligible – but three opinions
- Turns on the interpretation of "**markedly different**"

→ Structure (Lourie)

→ Structure & Function/Utility (Moore)

→ Structural differences not controlling – focused on similarities rather than marked differences (Bryson)

Federal Circuit – isolated DNA (Lourie)

- Supreme Court decisions in *Chakrabarty* and *Funk Brothers* set out framework for deciding patent eligibility of isolated DNA
- Distinction "between a product of nature and a human-made invention for purposes of § 101 turns on a change in the claimed composition's identity compared with what exists in nature"
- Challenged claims patent eligible "because the claims cover molecules that are markedly different —have a distinctive chemical identity and nature—from molecules that exist in nature"

Myriad Slip Op. at 39-41 (emphasis added)

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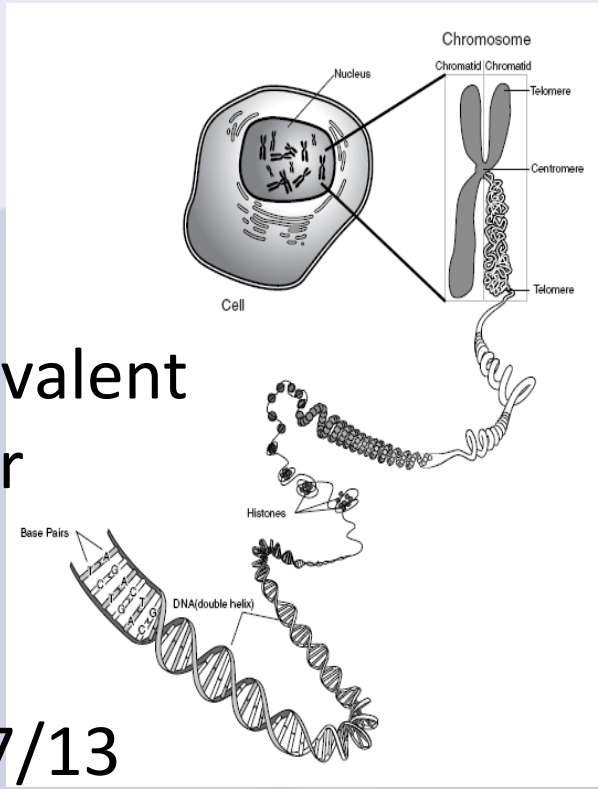
Federal Circuit – isolated DNA



- Why is isolated DNA "markedly different"?
- "Isolated DNA has been cleaved (*i.e.,* had covalent bonds in its backbone chemically severed) or synthesized to consist of just a fraction of a naturally occurring DNA molecule"
- Native BRCA1/2 resides on chromosomes 17/13 part of millions of nucleotides
- Isolated BRCA1/2 – exons only covering as few as 15 to about 10000 nucleotides → not found in nature
- → Focus is on **structure**

Myriad Slip Op. at 42

Federal Circuit – isolated DNA ≠ purified DNA

- "Purification makes pure what was the same material, but was previously impure"
- Not the case here because "claimed isolated DNA molecules do not exist as in nature within a physical mixture to be purified" – rather need to be "chemically cleaved [i.e. covalent bond broken] from their chemical combination with other genetic materials"
- "Thus, when cleaved, an isolated DNA molecule is not a purified form of a natural material, but a distinct chemical entity."
- "[D]istinctive nature of DNA molecules" determines patent eligibility rather than similarity of information content.

Myriad Slip Op. at 42-44

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Federal Circuit – in line with longstanding PTO practice

- PTO has issued patents directed to isolated DNA molecules for almost thirty years

  → first human gene patents granted in the early 1980s

- If the law were to be changed contrary to the expectations of the inventing community, it must be done by Congress not the courts

Myriad Slip Op. at 47-48

Moore's Concurrence – isolated DNA

- For isolated cDNA sequences agreed with majority
- Concurred with respect to the remaining sequences
  - → focus: Structure imparting New Utility
  - →"markedly different . . . with the potential for significant utility"
  - →"The ability to use isolated DNA molecules as the basis for diagnostic genetic testing is clearly an 'enlargement of the range of ... utility' as compared to nature."
- Short strands - an alteration of the natural product with the potential for significant utility.
- Long strands - no clear new utility compared to nature
  - → No upset of expectations
  - → Up to Congress to resolve

Concurrence at 2, 16-18, 31

Bryson's Dissent– isolated DNA

- cDNA patent eligible but isolated DNA is not
- Disagrees with bond-breaking / part of larger structure reasoning
- While bonds must necessarily be broken to isolate "the genetic coding sequence that is the subject of each of the BRCA gene claims remains the same whether the gene is in the body or isolated"
- Myriad's claimed sequences – unlike *Chakrabarty*'s are directed to genetic coding material – are structurally and functionally the same.

Dissent at 7, 8

Federal Circuit – diagnostic methods

- Myriad's claims to "comparing" or "analyzing" two sequences fall outside of § 101 because only abstract mental processes
- Rather than claiming a comparison step as part of a process – comparing is the entire process → not patent eligible.
- Myriad argued that the steps of "comparing" or "analyzing" were necessarily preceded by extracting and sequencing DNA molecules from a human sample - satisfying the machine-or-transformation test as applied in *Prometheus* – but those steps not in the claims
- Court found Myriad's claims distinguishable from *Prometheus* which included steps of "administering" and "determining"

Myriad Slip Op. at 49, 50-52

"Comparing" ≠ "Determining"

- In *Prometheus,* the court concluded that a/the "determining" step was transformative – because metabolite levels could not be determined by mere inspection, transformation was required
- Myriad's claims do not include, e.g., a sequence "determining" step (by isolating / sequencing) and the comparison of the two sequences (lists of Gs, As, Ts, and Cs) can be accomplished by mere inspection
- Fail the machine-or-transformation test (see *Bilski*).

Myriad Slip Op. at 52

Federal Circuit – screening therapeutics

- Myriad's method claim directed to screening –

  patent-eligible because method recites steps of:

  (1) "**growing**" transformed host cells in presence/absence of cancer therapeutic,

  (2) "**determining**" the growth rate, and

  (3) comparing the growth rates.

- "Starting with the machine-or-transformation test, we conclude that the claim includes transformative steps, an "important clue" that it is drawn to a patent-eligible process." (citing *Bilski*) **.**

Myriad Slip Op. at 53

Moore's concurrence

- "Diagnostic testing, however, is not a natural utility—the body does not naturally engage in this type of testing, and certainly does not do so with the shorter (non-naturally occurring) isolated DNA used by man. As such, the claimed DNA does not 'serve the ends nature originally provided.'"

Concurrence at 16

Federal Circuit – more on methods / §101

Classen Immunotherapies v. Biogen (Fed. Cir., Aug. 31, 2011)

- Claims directed to methods of immunizing and methods of determining whether immunization schedule affects occurrence/severity of chronic-immune-mediated disorders.
- Majority (Newman, Rader) found claims of 2/3 patents directed to patent-eligible subject matter because of "immunizing" step – i.e., a "specific, tangible application."
- Dissent (Moore) found this case "not even close" – all claims are directed to patent-ineligible discovery of a principle / correlation.
- Rader's additional views - expresses frustration with the increased number of challenges under §101.

Supreme Court - even more on methods . . . soon

- On June 20, 2011, Supreme Court granted Mayo's cert. petition in *Prometheus v. Mayo* – the case heavily relied upon by the Myriad panel in determining patent eligibility of Myriad's method claims.
- Question presented: "Whether 35 U.S.C. § 101 is satisfied by a patent claim that covers observed correlations between blood test results and patient health, so that the claim effectively preempts all uses of the naturally occurring correlations, simply because well-known methods used to administer prescription drugs and test blood may involve "transformations" of body chemistry."
- → Can ask a very similar question in *Classen.*

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Third Party Interest – 30 Amici in *Myriad*

Support for Appellees and /or Affirmance:

- Universities Allied for Essential Medicines
- International Center of Technology Assessment, The Indigenous Peoples Council on Biocolonialism, Greenpeace, Inc., Friends of the Earth, and the Council for Responsible Genetics
- Canavan Foundation, Claire Altman Heine Foundation, March of Dimes Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, National Tay-Sachs and Allied Diseases Association
- AARP
- Southern Baptist Convention
- National Women's Health Network, the Asian Communities for Reproductive Justice, the Center for Genetics and Society, Generations Ahead, the Pro-Choice Alliance for Responsible Research and Alliance for Humane Biotechnology
- Professor Andrew Chin
- Professor Eileen M. Kane
- E. Richard Gold, James P. Evans, and Tania Bubela
- American Medical Association, American Society of Human Genetics, American College of Obstetricians and Gynecologists, American College of Embryology, and the Medical Society of the State of New York
- Cancer Council Australia and Luigi Palombi
- Erika R. George and Kali N. Murray

Third Party Interest – 30 Amici in *Myriad*

Support for Appellants:

- Gilead Sciences, Inc., Biogenerator and Elan Pharmaceuticals, Inc.
- Alnylam Pharmaceuticals, Inc.
- University of New Hampshire School of Law
- Animal Health Institute & Merial Limited
- Kane Biotech Inc.
- Curiae Rosetta Genomics, Ltd., Rosetta Genetics, Inc., and George Mason University
- Boston Patent Law Association
- Genomic Health, Inc., Celera Corporation, XDx, Inc., Target Discovery, Inc., The Coalition for 21st Century Medicine, and Burrill & Company
- Pharmaceutical Research and Manufacturers of America

Third Party Interest – 30 Amici in *Myriad*

Support for Neither Party:

- United States DOJ (cDNA patent eligible, isolated DNA not)
- American Intellectual Property Law Association (AIPLA) (support of reversal)
- Genetic Alliance (support of reversal)
- Federation Internationale Des Conseils En Propriete Industrielle (support of reversal)
- Croplife International (support of reversal)
- International Christopher M. Holman and Robert Cook-Deegan (support of reversal)
- Intellectual Property Owners Association (IPO) (no standing, isolated DNA patent eligible)

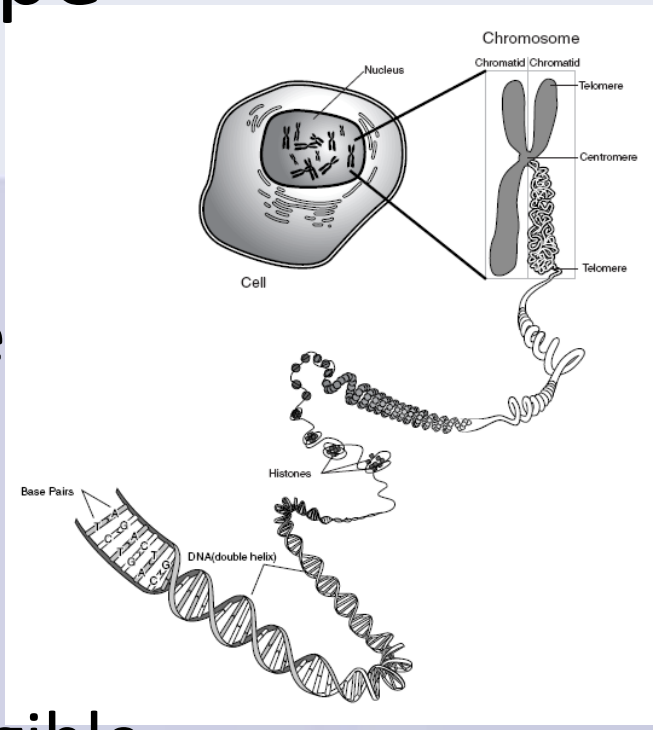
Briefs – Myriad's supporters

- Arguments on legal merits
- Arguments based on treaties with the WTO and TRIPS
- Policy grounded arguments that patents to isolated DNA promote innovation and benefit public → consistent with policy of the patent laws to promote useful arts and benefit society

Briefs – plaintiff's supporters

- Policy grounded arguments that "gene patents" raise costs and limit availability of genetic testing
- E.g., Univ. Allied for Essential Medicines argued that gene patents block process b/c researchers have to stop research based on blocking gene patents
- EU prohibits patent blocking research

Briefs – DOJ's "Magic Microscope"



- cDNA patent eligible but isolated and unmodified genomic DNA not, because sequence exists in humans based on evolution not made by man
- DOJ did not defend PTO's longstanding position that isolated DNA is patent eligible
- DOJ's "magic microscope" (oral argument) could focus on the claimed BRCA sequences as they exist in the human body but could not *in vivo* focus on cDNA → therefore only cDNA is patent eligible

Briefs – DOJ's real reason?

- Commentators question whether DOJ's real reason is one of public interest? →

  cost of genetic assays & health care as a whole?

Briefs – IP law organizations

- IPO → Court did not have jurisdiction b/c Myriad made no contemporary threats to enforce patents & Plaintiffs had no plans to engage in infringing conduct
- AIPLA → "consumer" plaintiffs no standing
- Both organizations agreed – isolated and cDNA patent eligible, and warned that contrary decision could impact other therapeutics and expectations of patent owners & inventors

Impact on the biotech industry

- Analysts agree – **impact will be minimal** – at least for now.
- Relatively favorable to Biotech industry.
- Decision provides certainty for industry's existing patents & research endeavors.
- No upset of PTO's longstanding practice issuing patents for isolated DNA sequences.
- Even dissent acknowledges that practical applications of isolated DNA patentable even if the DNA is not.

Tips for Practitioners - methods – include "transformative" step

- Isolating / extracting gene, DNA or substance
- Determining sequence or sequencing
- Administering a drug or, e.g., "immunizing"
- Measurement beyond mere inspection
- Determining growth rate of cells / physical manipulation of cells
- Growing transformed cells
- Manipulation of cells in growth medium
- Information gathering – plus – treatment

Tips for Practitioner – products - be creative & forward thinking

- Claim “isolated” not “purified” products
- Include claims to cDNA if possible
- Identify structural / chemical differences and point out differences from product (DNA) in nature
- Identify and describe “potential for significant utility” of new product
- Add claims to systems using / including gene (e.g., vectors and promoters w/ additional structural features, kits, assays, DNA chips, buffers)
- Cover your commercial embodiment.

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Tips for Practitioner – eye on litigation

- Revisit existing patents, especially for method claims (wait until fully resolved).
- Consider reissue before seeking to enforce patent if patent eligibility is questionable (wait until fully resolved).
- Revisit pending / new applications.
- Draft claims likely to be infringed by a single entity, not jointly by several entities.

  → Single entity issue awaiting *en banc* decision in *Akamai Tech., Inc. v. Limelight Networks, Inc.*

Next Steps

- **What are the options?**
- Panel rehearing
  - Plaintiffs-Appellees filed Aug. 25, 2011 – denied Sept. 13, 2011
  - Myriad filed Aug. 29, 2011
- Rehearing en banc not available (Fed. Cir. R. 35(d))
- Petition for Writ of Certiorari: 90 days from date of denial of rehearing or, if rehearing is granted, from subsequent entry of judgment (Sup. Ct. R. 13)
- (Good companion case to *Prometheus*)

Next Steps → (same) panel rehearing?!

- Plaintiffs-Appellees (ACLU) on Aug. 25, 2011
- Alleges legal & factual errors →

  (1) claims define function not structure of the patented genes;

  (2) short gene fragments can be found in nature.

- Alleges Court erred not finding that two additional plaintiffs have standing (for example – Dr. Ellen Matloff)
- Petition denied Sept. 13, 2011

Next Steps → (same) panel rehearing?!

- Myriad on Aug. 29, 2011
- Panel review makes more sense here because Myriad essentially won the case
- Focuses on standing → Dr. Ostrer's job change extinguished DJ jurisdiction
- Motion should be dismissed as moot

  without vacatur of the panel decision

Unresolved issues & questions

- Are claims to only a purified product patent eligible?
- If reconsider patent eligibility of isolated DNA / cDNA –
  - How to differentiate?
  - Where to draw the line?
  - What will be the standard?
- Structure only? Structure & enhanced utility?
- Or will Bryson prevail in the end on isolated DNA?

Thank You

- Many thanks to Claudia Schultze for help with research and slide preparation.
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