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# Myriad Genetics Case: Patentability of Isolated DNA and Related Methods Under §101

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## Contentions

- Plaintiffs challenged 15 claims in 7 patents
  1. Isolated DNA molecules possessing particular nucleotide sequences from BRCA1/BRCA2
  2. Methods for detecting mutations in BRCA1/BRCA2 genes by analyzing the sequence of DNA, RNA, or cDNA in a human sample
- Various legal challenges
- Primary issue: Patentability under 35 U.S.C. § 101
- USPTO / U.S. Government takes no position on patentability in district court

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## Parties

- Declaratory Judgment Plaintiffs:
  - 4 medical associations, led by AMP
  - 8 physicians
  - 2 advocacy groups
  - 6 patients who seek genetic testing for breast cancer but claim that Myriad's patents or refusal to accept their insurance have impeded it



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## Parties

- Defendants:
  - University of Utah Research Foundation: owner of patents-in-suit
  - Myriad Genetics: exclusive licensee, sole commercial provider of full sequencing of Breast Cancer Susceptibility Genes 1 and 2 (BRCA1/BRCA2) in the U.S.
  - U.S. PTO (constitutional issue only)
- Numerous *Amici* on both sides of the case, including BIO in support of the patentability of isolated DNA molecules





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## District Court Decision

- On Summary Judgment, based on paper record
- “Purification of a naturally occurring substance” is not patentable
- Patentable subject matter must have “markedly different characteristics” from a product of nature
- DNA “carries genetic information” and is “the physical embodiment of laws of nature”
- Utility of isolated DNA comes from its having the same nucleotide sequence as naturally occurring DNA



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## District Court Decision – Other Issues

- Method claims invalid under *Bilski*
- *Prometheus* distinguished
- Constitutional claim against PTO (patents issued in violation of Art. 1, § 8, cl. 8) dismissed without prejudice
- Challenge to Plaintiffs' standing to bring declaratory judgment claim rejected



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## The U.S. Government's Switch In Time

- Significant consultation inside and outside government
- Ultimate position unknown outside government until DOJ filed its *amicus* brief “supporting neither party”
- “Engineered DNA molecules” are patentable (including cDNA)
- “Isolated but otherwise unmodified genomic DNA” is not patentable
- Irony: U.S. Government co-owns four patents-in-suit that it now claims are directed to unpatentable subject matter



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## Federal Circuit Appeal – Questions Presented

- Myriad appealed the district court’s decision on two substantive legal questions:
  1. Whether the district court erred by holding Myriad’s composition claims to isolated DNA molecules, which are compositions of matter, ineligible for patenting under 35 U.S.C. § 101?
  2. Whether the district court erred by holding that Myriad’s claims to diagnostic methods directed to “comparing” and “analyzing” DNA were ineligible for patenting under § 101?



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## Federal Circuit Appeal – BIO/AUTM Position

- BIO and AUTM took a position only on the first question regarding patent eligibility of isolated DNA molecules.
- This issue breaks down into two subsidiary questions as to the patent eligibility of:
  1. Isolated Genomic DNA
  2. Isolated cDNA
- BIO and AUTM argued that each form of isolated DNA is patentable subject matter under § 101.



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## The Breadth of Section 101

- Section 101 provides:

“Whoever invents or discovers any new and useful . . . composition of matter . . . may obtain a patent therefore, subject to the conditions and requirements of this title.”

- “In choosing such expansive terms . . . modified by the comprehensive ‘any,’ Congress plainly contemplated that the patent laws would be given wide scope.” *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980).
- This breadth “ensure[s] that ‘ingenuity should receive a liberal encouragement.’” *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010).



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## Section 101 Eligibility Only a Threshold Test

- Patent eligibility is “only a threshold test”; a claimed invention must be useful, “novel, see §102, nonobvious, see §103, and fully and particularly described, see §112.” *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010).
- Federal Circuit has held invalid patent claims on each ground.
- In human gene context, important to consider that extensive sequencing of genome would render new isolated DNA claims anticipated or obvious.



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## Judicially Created Exceptions to Patentability

- Supreme Court precedent provides three notable exceptions to § 101's broad patent-eligibility principles:
  1. Laws of nature
  2. Physical phenomena
  3. Abstract ideas
- The district court ruled – and plaintiffs on appeal argue – that “products of nature” are categorically excluded from patentable subject matter, and that isolated DNA molecules are such products of nature.
- Plaintiffs thus contend that a fourth, broad exception exists.



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## Standards Articulated by the Supreme Court

- In 1931, the Supreme Court in *American Fruit Growers* indicated that a preexisting product that undergoes a “transformation” to produce a “new and different article” with “a distinctive name, character, or use” is patent eligible.
- More recently in 1980 in *Chakrabarty*, the high court applied that standard to find that a new bacterium with “markedly different characteristics from any found in nature” with “the potential for significant utility” was eligible.



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## BIO: Isolated DNA Molecules Are Patent Eligible

- Isolated DNA molecules are freestanding chemical compounds that do NOT occur in nature, but rather are new compositions that are patent eligible under § 101 and long-standing precedent.
- Even if considered to be “naturally occurring,” isolated, purified DNA molecules are so transformed in that process that they take on a distinctive character and use from chromosomal DNA.

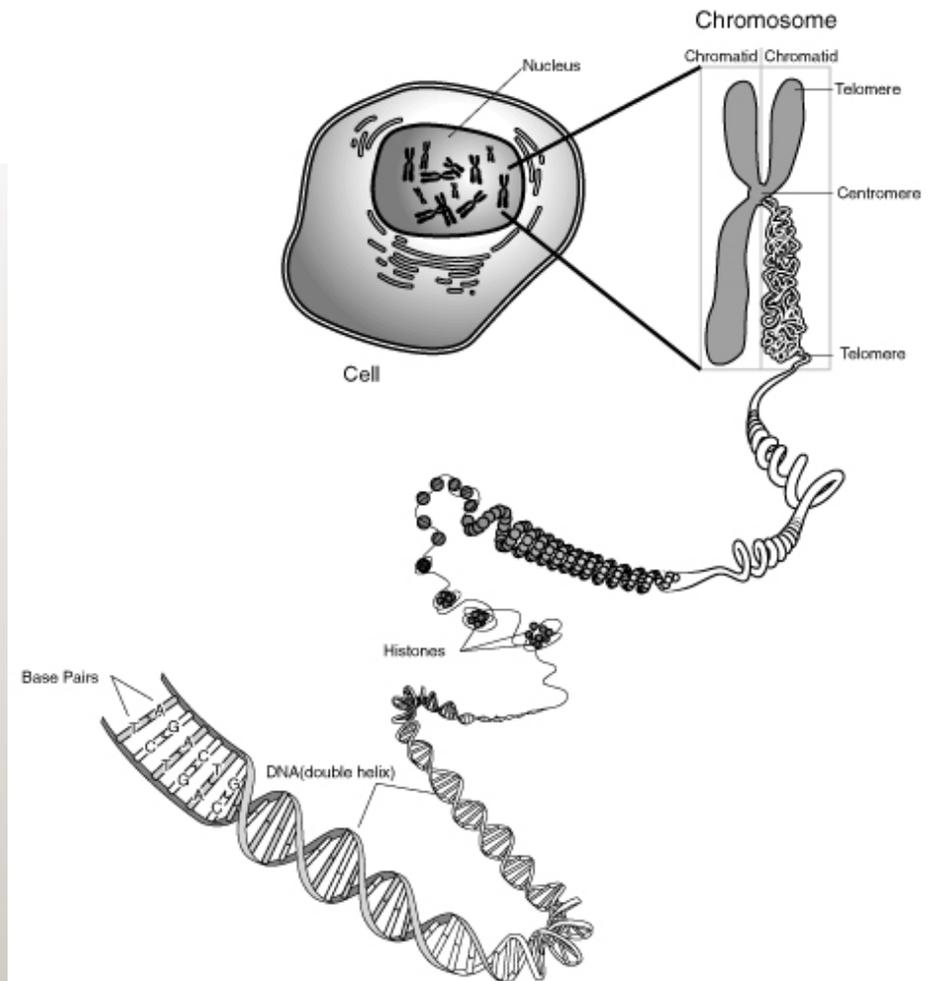
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## Isolated DNAs Are New Compositions

- Human DNA in its “native” form exists within chromosomes – complex, stable structures of DNA bound together with numerous proteins.
- Covalent chemical bonds must be broken to “isolate” new DNA molecules from within the chromosome, forming new chemical compositions.





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## Isolated DNAs Do Not Exist Naturally

- At no point in an organism's natural life are genes excised or uncoupled from the rest of the chromosome.
- But for human ingenuity and innovation, genes or other smaller DNA molecules that are contained within the chromosome would not exist as stand-alone molecules or separate chemical compounds.
- These facts are critical under applicable Supreme Court precedent.



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## Isolated Genomic DNA Differs from Chromosomal DNA

- In the case of genomic DNA molecules, DNA is excised from the chromosome by unbundling the chromosomal DNA from structural proteins and breaking covalent chemical bonds.
- The excised DNA molecule must typically be “amplified” and physically separated from other genomic DNA.
- This resulting process yields an isolated, new and separate genomic DNA molecule.



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## cDNA Differs Even More Greatly

- With cDNA molecules, the nucleotide sequence differs from that of chromosomal DNA in that intron regions have been spliced out.
- cDNA sequences do not occur naturally even within the chromosome and are therefore a degree further removed from what “naturally occurs.”
- Notably, the United States takes the position that cDNA molecules are patent eligible as they do not naturally occur.



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## Distinctive Character and Use of Isolated DNA

- Even if isolated DNA molecules are products of nature, isolated genomic DNA and cDNA molecules are man-made and exhibit new and distinctive “character” and “uses.”
- In natural form, human genes are inaccessible and under the control of the physiology of the organism.
- Isolated DNA allows for mass production of therapeutic proteins or replacement of missing, mutated, cancer-inducing, or otherwise malfunctioning genes.



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## DNA As “Information”

- District court concluded:

“DNA’s existence in an ‘isolated’ form alters neither [its physical embodiment of biological information] as it exists in the body nor the information it encodes.”

- The court often employed the metaphor of DNA as “information” in that the sequence of a gene can be said to “tell” which protein is produced.



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## DNA Is Not Merely Information

- “Informational” metaphors used in nomenclature of processes associated with DNA – transcription, translation, editing, codes – are just metaphors.
- Isolated DNA and cDNA molecules are chemical compounds with characteristics distinct from their natural counterparts.
- Patent statute does not provide for a one-off exception for isolated DNA molecules merely because DNA can be metaphorically described as “information.”



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## Invalidating Isolated DNA Patents Would Discourage Innovation

- Plaintiffs argue that gene patents discourage innovation and impede medical progress.
- BIO has argued that the opposite is true, citing as specific examples:
  - Amgen's patent on isolated DNA that codes for erythropoietin supported development of Epogen®.
  - Chiron's patent covering isolated DNA of hepatitis C supported development of screening blood banks.
- In each instance, these isolated DNA patent positions provided critical protection allowing for development of these important products.



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## Invalidating Isolated DNA Patents Would Discourage Innovation

- Isolated DNA patents are critical to research and development in a number of areas:
  - Therapeutic Proteins
  - Gene Therapy
  - Vaccination
  - Genetic Testing
  - Agriculture
  - Food Safety
  - Industrial and Environmental Biotechnology



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## Invalidating Isolated DNA Patents Would Have Far-Reaching Negative Consequences

- The biotechnology industry depends heavily on patent protection to encourage the investment of time and capital necessary to develop inventions into real-life products.
- Biotechnological investment is substantial: over \$30 billion in biotech-related R&D was invested in the United States alone in 2008.
- In light of high risk/difficulty, patents are critical to reassuring investors that they will earn a reasonable financial return.



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## Isolated DNA Patents Do Not Impede Research or Harm Patients

- AMP argues isolated DNA patents stifle basic research, but this claim is unsupported.
- As the National Research Council recently concluded: “[I]t appears that access to patents or information inputs into biomedical research rarely imposes a significant burden for academic biomedical researchers....”
- A 2005 survey of biomedical scientists found that “patenting does not seem to limit research activity significantly, particularly among those doing basic research.”



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## Isolated DNA Patents Do Not Impede Research or Harm Patients

- Abolishing patents on isolated DNA molecules is misdirected and shortsighted, mistaking problems in insurance market for problems in patent system.
- Without patent protection for isolated DNA molecules, many companies would be unable to see projects through to completion.
- Numerous life-saving therapeutics and diagnostics would die in the pipeline, and their absence would be acutely felt by patients.

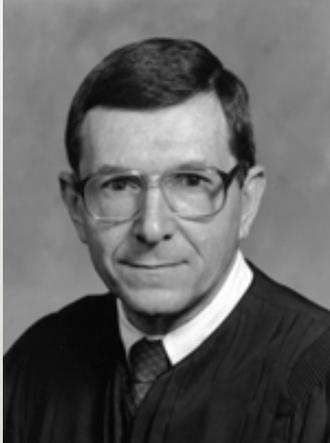
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## Oral Argument: April 4, 2011

- Panel



Judge Lourie



Judge Bryson



Judge Moore

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## Oral Argument: April 4, 2011

- Arguing counsel



Greg Castanias  
Myriad Genetics



Chris Hansen  
AMP



Neal Katyal  
United States



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## Threshold Question: Standing

- Are these plaintiffs entitled to sue?
- District court decision indicated that any patient who might potentially seek genetic testing would have standing.
- Panel asked detailed questions about adequacy of affidavits used to establish standing.



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## Threshold Question: Standing

- AMP: “If the 150,000 physicians I represent started sequencing tomorrow, is there any doubt in the world that Myriad would start suing someone?”
- Judge Moore: “But do you not recognize the profound impact that would have on our patent system if anyone who was ready, willing, and able to compete tomorrow could bring a [declaratory judgment] action against the patentee in any forum of their choosing without any affirmative act directed at all towards them by the patentee?”



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## Isolated DNA as “Information”

- Judge Lourie: “The trial court said that the claimed materials are simply conveyors of information. That may be true, but the claims don’t read a method of conveying information. They claim substances, and whether they convey information or not, they are still substances, correct?” . . . .
- US: “Absolutely, Judge Lourie. We’re not here trying to defend the district court’s judgment about information. I think the contours of that are very uncertain, and I think the district court’s opinion wouldn’t be a wise course to go down.”



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## Argument Dominated By Hypotheticals

- Numerous questions and arguments about mining in light of Supreme Court's statement in *Diamond v. Chakrabarty* that "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter."
- AMP: "If a surgeon cuts me open and slices out my kidney and takes it out and holds it in his hand, it's an isolated kidney. But it's still a kidney. It's not an invention."
- Myriad: A baseball bat is patentable subject matter even though it is, in a sense, always in the tree and merely isolated from the other wood.



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## Magic Microscope

- US: “There is a cardinal distinction for § 101 purposes between products of nature on the one hand and human-made invention on the other, and the mere act of isolating a substance doesn’t mean that it is a human-made invention.”
- US: “Our test is ... if you had almost a magic microscope that allowed you to zero in on the gene and ... if you could see the exact claim to which the patent is being sought in nature ... that itself is something that is a product of nature.”
- Judge Moore labeled magic microscope test “kitschy.”



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## Isolating a Composition from Nature

- Judge Lourie: In their natural state, genes are covalently bonded with other genetic material.
- Judge Bryson: “There are lots of complex molecules which can be changed by lopping off some portion of the complex molecule and creating another molecule which was in a sense embedded in the first molecule. . . . Why isn’t that at least analogous to this setting where . . . you’re not cutting in the sense of getting a pair of tweezers or scissors . . . but you’re cutting by a chemical process that alters the chemical identity of the object that’s being extracted?”

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## US Response

- US: Lithium “exists in natural form in salts . . . . [N]obody would think that the third element of the periodic table is patentable simply because . . . [the] bonds of lithium attach to other substances.”

A standard periodic table of elements. The top row is labeled 'Group' and numbered 1 through 18. The left side is labeled 'Period' and numbered 1 through 7. The elements are arranged in a grid, with colors used to distinguish groups: Group 1 (green), Group 2 (yellow), Groups 13-18 (various shades of green, yellow, and blue), and the Lanthanides and Actinides (pink).

Group	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	1 H																	2 He
2	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5	37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6	55 Cs	56 Ba		72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
7	87 Fr	88 Ra		104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Uub	113 Uut	114 Uuq	115 Uup	116 Uuh	117 Uus	118 Uuo
Lanthanides	57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu			
Actinides	89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr			



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## Line Drawing: Different Function

- What is the function of isolated DNA?
- How does it differ from the function of chromosomal DNA?
- If having a different function were sufficient to support patent protection, would coal and gold be patentable?



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## Line Drawing: Rewarding Inventiveness

- Myriad argued that patents on isolated DNA molecules are necessary to reward inventiveness.
- US: “If someone discovers that the pollen of a certain flower cures cancer, that person has discovered the cure for cancer. They haven’t discovered the pollen.”
- Judge Moore: “Why isn’t the ingenuity the process, as opposed to the resultant DNA which is in your body? Why isn’t the ingenuity the process of extracting it, the process of figuring out what it is useful for?”



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## Concerns about Breadth of AMP's Challenge

- Panel appeared to assume that cDNA would be patentable.
- Judge Moore: “What about antibodies?”
- Limits on judicial competence to draw a bright line without a record on other inventions that might be affected.



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## Whole Genome Sequencing

- Judge Bryson worried that thousands of licenses would be required to sequence a patient's entire genome.
- Myriad: Client does not have a view, but whole genome sequencing probably does not infringe isolated DNA patents.
- AMP: Whole genome sequencing would infringe isolated DNA patents.



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## Split in the Government

- Judge Moore: “The PTO guidelines conclude that the very thing you are arguing now is not patentable subject matter is patentable subject matter....While you’re here representing the government, I’m not sure what that really means, since it seems that we have a split in the government.”
- Judge Moore: “You say that this isn’t a dramatic theory that undoes things, but the PTO has been allowing these patents for 35 years. I think this is a pretty dramatic theory that would undo a lot of existing patents.”



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## Reliance Interests

- Judge Moore: “Congress has never spoken to this. [Section] 101 is broad. To the extent there are exceptions, they are judicially created, and I get a little nervous expanding the umbrella in light of 35 years of industry development, in light of the fact that there is clearly a split within the Executive on this point....Why isn't *stare decisis* a concern? Why shouldn't Congress figure this out, not us?”



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## Options for Further Review

- Petition for rehearing en banc
  - Case would be reheard by all active judges on the Federal Circuit
  - Majority of judges must vote to rehear case
- Supreme Court
  - Four Justices must vote to hear case
- Congress

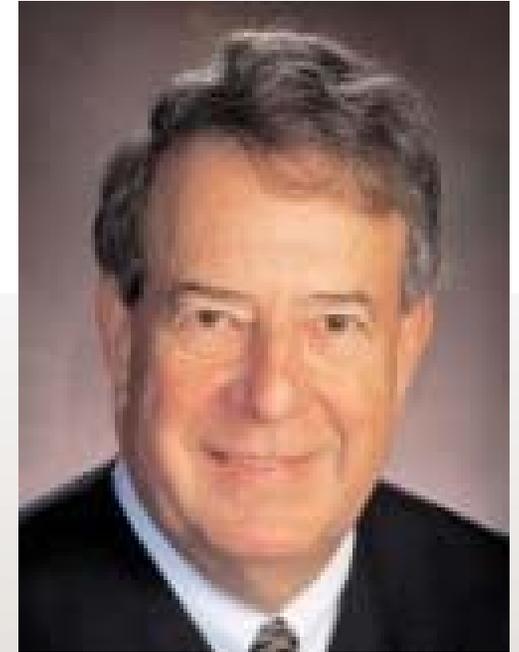
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## Judge Dyk

- Wrote separately in *Intervet, Inc. v. Merial, Ltd.*, 617 F.3d 1282 (Fed. Cir. 2010).
- Argued that a claim to an isolated DNA molecule “raises substantial issues of patentable subject matter under 35 U.S.C. § 101.”
- “It is far from clear that an ‘isolated’ DNA sequence is qualitatively different from the product occurring in nature . . . . It would be difficult to argue, for instance, that one could patent the leaves of a plant merely because the leaves do not occur in nature in their isolated form.”



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## Other Judges

- Judge Lourie replaced Judge O'Malley only on the *Myriad* panel, prompting speculation that Judge O'Malley had recused herself because her husband's firm filed an amicus brief.
- AMP requested that Chief Judge Rader recuse himself because he had participated as a panelist in a session entitled "Patenting Genes: In Search of Calmer Waters" at the 2010 BIO International Convention in Chicago. Consideration of the motion was deferred because Chief Judge Rader was not assigned to the *Myriad* panel.



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# Supreme Court





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## Congress

- America Invents Act, H.R. 1249
  - Draft Managers Amendment included provision exempting “confirming genetic diagnostic test activity” from infringement liability where “an independent confirmation of the prior test is not available from another test provider under a license from the patent owner.”
  - Originally proposed by Rep. Debbie Wasserman Schultz (D-FL).
  - ACLU opposed amendment on the ground that it “risks allowing gene patent holders to argue that Congress implicitly endorses the validity of such patents.” (<http://patentdocs.typepad.com/files/aclu-letter.pdf>)
  - Amendment not included in version of bill that passed the House on June 23, 2011.

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Questions?