

How and Why Genes are Patentable

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How and Why Genes Are Patentable

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What's a Patent?

- Near-monopoly: prohibition on others making, using, or selling for 20 years
- Infringer's intent irrelevant
a Blackberry Enterprise Server and
- Authority in original Constitution; matter of federal law; no state patents
if so, can you connect to it?
- Economic bargain rationale: government trades monopoly for disclosure, to encourage exploitation of inventions



What Can Be Patented?

- New, useful, nonobvious inventions
- Patentable subject matter: machines, manufactures, compositions of matter, processes; improvements thereon
- *Can't patent: abstract ideas, laws of nature (including pure mathematical algorithms), products of nature—because they're not “inventions”*



Utility

- Usually easy: Does someone have a beneficial use for it?
- Hard cases: chemical intermediates and genes
- Guidelines: specific, substantial, and credible utility



Nonobviousness

- Most subjective test
- Would “person of ordinary skill in the art” have thought it an obvious advance over entirety of “prior art?”
- Supreme Court has just given doctrine a bit more bite



Patent Process

- *Enabling* written description—the disclosure part of patent bargain
- Claims: They define what's patented and what infringes
- Validity of patent can be challenged in litigation—back-end-loading of U.S. system



Patent Applications of DNA Technology

- Patenting genetically engineered organisms
- Patenting isolated and/or “purified” genes
- Patenting gene-related products and applications
- Patenting proteins and cell lines



The Only Supreme Court Genetics Case

- *Diamond v. Chakrabarty*, 447 U.S. 303 (1980)
- Patent on bacterium with new DNA inserted
- Enhanced oil-eating properties
- It *is* patentable subject matter
- Fact that invention is alive is no barrier
- Products of nature versus inventions



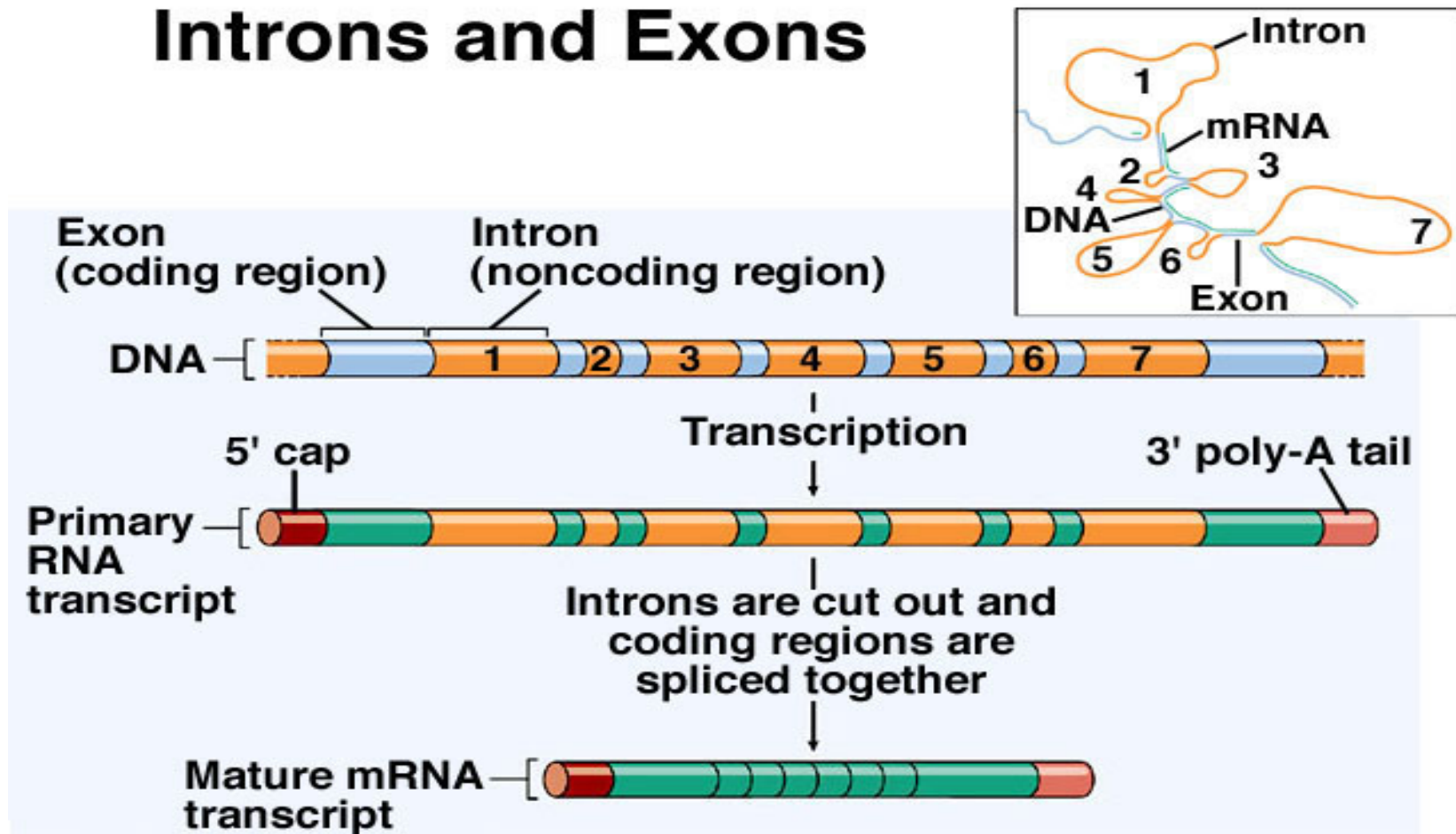
Patenting Genes Themselves: *Amgen v. Chugai* (Fed. Cir. 1991)

- Claim: “A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin”
- Subject matter status taken for granted—
why not a product of nature?



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Introns and Exons





Amgen Patent Revisited

- *Isolated*: Outside the body
- *Purified*: Non-coding regions [introns] removed
- *cDNA*: Not found naturally in *exactly* this form: structure v. function v. information
- N.B.: The *gene* is what's patented, not the process for making it; additional patents on products and applications are also possible



Skolnick BRCA1 Patent

- “An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID No. 2”
- And Turley hyaluronan receptor protein patent:
- “An isolated protein comprising the amino acid sequence of Fig. 2”



Wisconsin (WARF) Stem Cell Patents

“A purified preparation of primate embryonic stem cells which (i) is capable of proliferation in an in vitro culture for over one year, (ii) maintains a karyotype in which all the chromosomes characteristic of the primate species are present and not noticeably altered through prolonged culture, (iii) maintains the potential to differentiate into derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) will not differentiate when cultured on a fibroblast feeder layer.”



WARF patents were reexamined, reportedly were being revoked for obviousness, but were reaffirmed in spring of 2008.



Supreme Court's Near Miss on Patentable Subject Matter: *Laboratory Corp. v. Metabolite Labs (2006)*

- Invention: Process for diagnosing vitamin deficiencies
- Covers using any test to measure the level of homocysteine in a body fluid and then noticing whether its level is elevated above the norm
- S. Ct. takes case and asks for briefs on whether invention violates products/laws of nature prohibition



Laboratory Corp. v. Metabolite Labs

- Might patent claim “monopoly over a basic scientific relationship”? (law of nature); could a doctor infringe through routine tests and calculations?
- S. Ct. then dismisses over strong Breyer/ Stevens/Souter dissent—so three votes for putting some brakes on biotech patents?
- “At most, [the patentees] have simply described the natural law at issue in the abstract language of a ‘process.’”



In Re Fisher (Fed. Cir. 2005): ESTs Not Patentable

- Expressed Sequence Tags: Short cDNA sequences, useful for fishing for genes in DNA libraries
- What gene they come from, what that gene does not usually known
- Federal Circuit (2005): Doesn't meet standard of *specific and substantial utility*



SmithKline Beecham Corp. v. Apotex Corp. (Fed. Cir. 2005)

- Did Apotex’s generic drug compound PHC anhydrate (subject of an earlier, expired patent) infringe SmithKline’s patent on PHC hemihydrate?
- PHC anhydrate tablets convert naturally into PHC hemihydrate—including upon ingestion by the patient
- Is this “making” the patented compound ?
- Patent invalid: PHC anhydrate “inherently anticipated” hemihydrate under section 102(b)



SmithKline, cont'd

- Judge Gajarsa's concurrence: claim encompassed *unpatentable subject matter*
- SmithKline claimed *all* “crystallized PHC”—including PHC resulting from “a natural physical process”
- “A synthetic compound, created by humans in a laboratory, never before existing in nature, that is nevertheless capable of ‘reproducing’ itself through a natural process.”



SmithKline, cont'd

- Invention falling into both the “nonnaturally-occurring” and “found in nature” categories is not patentable
- “Merely limiting the claim to ‘synthetic PHC hemihydrate’ would have solved the problem. But SmithKline Beecham did not.” So any implications for gene patents?



Obviousness

- *KSR International Co. v. Teleflex (2007)*: S. Ct. rejects “rigid” Teaching-Suggestion-Motivation test for combinations
- Now, “a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ”
- So easier to show obviousness and defeat patent



Obviousness, cont'd

- *PharmaStem Therapeutics Inc. v. ViaCel* (2007): Fed. Cir. applies *KSR* to biotech
- Patents on the collection, preservation, and use of stem cells from umbilical cord blood held invalid for obviousness
- “it was reasonable for the inventors of the patent, like the authors of the prior art references, to infer the presence of high concentrations of stem cells in cord blood, even though the prior art studies did not offer conclusive proof”



***KSR* and Biotech: *In re Kubin*, 561 F. 3d 1351 (Fed. Cir. 2009)**

- *KSR*: “The fact that a combination was obvious to try might show that it was obvious”
- Kubin claimed polynucleotides encoding natural killer cell activation proteins; NK cells help fight infections and cancer
- Fed. Cir. affirms BPAI’s § 103 rejection: would have been obvious to try to isolate these sequences in light of knowledge of proteins and sequencing methods



In re Kubin, cont'd

- *Deuel* (1995) had rejected “obvious to try” objection to comparable gene patent —”discredited” by *KSR*
- No exception for “unpredictable art” of biotechnology
- Obvious to try requires only “a reasonable expectation of success”



More Trouble for Gene Patents: *Ariad v. Eli Lilly*, 560 F.3d 1366 (Fed. Cir. 2009)(aff'd en banc 3/22/10)

- Ariad is licensee of Harvard patent on method to treat disease by reducing activity of “messenger” protein that regulates gene expression in cells
- \$65 million infringement verdict against two Lilly drugs
- Reversed: method fails § 112 written description requirement
- § 112 contains both *possession* and *enablement* requirements—not always co-extensive in biotech
- Strong message on “vast scope of generic claims”
- Nibbling around the edges of gene patents



In re Bilski, 543 F. 3d 943 (Fed. Cir. 2009)(en banc)(pending in S. Ct.)

- BPAI and Fed. Cir. reject business methods claims (commodities hedging) under § 101; 100+ pp. of fractured opinions
- Primary claim on “method for managing the consumption risks of a commodity sold by a commodity provider at a fixed price”
- Q: Does claim recite abstract idea/fixed principle, and, if so, does it preempt uses?



In re Bilski, cont'd

- ***Test:*** (1) is method tied to particular machine or apparatus, or (2) does it transform particular article into different state or thing?
- ***This claim fails:*** would preempt mathematical forms of hedging, no machine or transformation
- Court rejects *State Street's* “useful, concrete, and tangible result” test—***no longer relied on***
- **S. Ct. decision forthcoming**—how broad will it be?



Prometheus v. Mayo, 581 F.3d 1336 (Fed. Cir. 2009)

- Claim 1: “a method of optimizing therapeutic efficiency for treatment of an immune-mediated gastrointestinal disorder”
- Comprises “administering” a specified drug to a patient and then “determining” the level of the drug in the patient
- Specifies threshold levels of drug’s metabolites in patient’s blood below which dose should be increased (because of lack of efficacy) and above which it should be decreased (because of potential toxicity)



Prometheus and Bilski test

- Both “administering” and “determining” steps brought about sufficient transformations
- “The transformation is of the human body following administration of a drug and the various chemical and physical changes of the drug’s metabolites.”
- Determining levels of drug metabolites in the body “necessarily involves a transformation, for those levels cannot be determined by mere inspection”



Prometheus and Bilski test

- Transformative methods might include high-pressure liquid chromatography or the extraction of metabolites from the body
- “The asserted claims are in effect claims to methods of treatment, which are always transformative when a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition.”



And Now a Frontal Attack: *Assoc. for Molecular Pathology et al. v. USPTO, Myriad Genetics, et al.*

- Plaintiffs include ACLU, patients, universities, researchers, scientific organizations
- Suit seeks to invalidate BRCA1-2 and other patents—could affect gene patents generally
- Challenges BRCA patents as “claims on natural human genes”—same function and information
- “Product of nature” patents violate Constitution’s patent clause, patentable subject matter statute
- Patents on screening methods preempt “thought,” violate First Amendment
- Court has denied motions to dismiss—USPTO and standing
- Cross-motions for summary judgment heard 2/4/10
- Legitimate shot or publicity stunt?
- Subtext: Who pays for expensive tests?



And This Just In: Myriad Loses (3/29/10)

- District Court grants summary judgment invalidating all Myriad patents
- Product and process patents both invalidated: products of nature and abstract mental processes
- Information function of DNA versus chemical structure—the most radical part of opinion
- Where does the case go now?
- What will be the practical effects?



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- Much more on *Myriad* at Genomics Law Report, genomicslawreport.com