GENOMIC PATENTS

John H. Barton
Stanford Law School (emeritus)
And (2004-05) Visiting Scholar,
NIH Department of Clinical Bioethics
(My comments are in my individual capacity – I am not speaking for Stanford or for NIH)

OUTLINE

- The key issues relating to genomic patents (based on recent reports)
- Some realities on diagnostic genomic patents (based in part on unpublished work carried out at NIH)
- Evaluation of recent Supreme Court decisions as achieving the reforms sought

GENOMIC PATENTS

- Typical claims are to
  - A particular sequence
  - Various constructs embodying that sequence
  - Proteins coded for by the sequence
  - Sometimes research use of the sequence (e.g. as an assay)
- Novelty depends on fact that the sequence and perhaps the protein has been isolated from that found in nature
- Utility depends on understanding about the function of the sequence

THE REPORTS

- Nuffield Council on Bioethics, *The ethics of patenting DNA* (July 2002)
- Royal Society Working Group on Intellectual Property, *Keeping Science Open: The Effects of Intellectual Property on the Conduct of Science* (April 2003)
- National Research Council, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* (2006)

KEY POLICY ISSUES

- Protect the patentability of therapeutic protein based on a natural protein
- Avoid restriction of scientific use of gene sequence (receptors, pharmacogenomics etc.) and limit impact on science. (Split between biotech industry and science/pharmaceutical industry)
- Question on patentability of diagnostic test and impact on diagnostic testing. (Split between diagnostic industry and science/patient communities)

THE NUFFIELD REPORT

- Apply legal principles, e.g., non-obviousness to restrict problems associated with genomic patents
- As an implicit theme, to extent possible, distinguish the sequence as information (kept unpatentable) from the embodied sequence as a chemical (which would be patentable). This would permit patenting of therapeutics, but restricts use of patent to bar future research or to control diagnostic test
- If those approaches don't work, define various restrictions/licenses to achieve the same result with respect to scientific research and diagnostics

OTHER REPORTS

- Stronger on concerns about impeding scientific research (although the Walsh-Cohen-Arora (2003) study sees only limited problems)
- Not as strong on diagnostic tests – concerned about incentives for invention as opposed to costs to consumers

EVALUATING PATENTS AS INCENTIVES IN DIAGNOSTIC CONTEXT

- Need an unbiased sample of tests, rather than a sample designed to show problem cases (e.g. Cho et al, 2003)
- Need a sense of role of patents (e.g. by industry or by government grantees)

THE TEST SAMPLE

- GeneTest website
- Chose ten tests most commonly chosen for a lab directory search
- Plus ten most common gene review access choices
- Based on inquiry to GeneTest
- Because of overlaps, etc., 17 tests were used

PATENT SEARCH

- NOT RANDOM!
- Based on secondary literature, on searches on disease name, on searches on author names from key scientific articles
- Found
  - Patents on technological methods
  - Patents on relevant proteins
  - Patents on gene mutations
  - Patents on consensus sequences

THE NUMBERS

DISEASE	PRIVATE	PUBLIC	UNKNOWN
Amyotrophic lateral scleroris	1	3	
Anophthalmia/Microsphthalmia	1		
BRCA1 and BRCA2	6	1	
CFTR related disorders		3	
Congenital central hypoventilation syndrome			1
Duchenne/Becker Muscular Dystropy		3	
Factor V Leiden thrombophilia		1	
Fanconi anemia		2	
Fragile X syndrome			3
Hereditary non-polyposis colon cancer		1	
HFE associated hereditary hemochromatosis	5	3	
Homosystinurea		1	
21 hydroxylase deficiencye		1	
Marfan syndrome			
Neurofibromatosis 1		1	1
Prader-Will syndrome			
Spinal muscular atrophy	3		
TOTALS	16	20	5

IMPLICATIONS

- Patents *are* incentives and *do* encourage private investment in genomics
- But this effect has been limited to the most common genetic diseases
- Note that, where the phenotype/genotype relationship has been identified with public funds, there may be no need for patents, depending on possible changes in FDA regulation of genomic tests

EMERGING PHARMACOGENETIC ISSUES

- **IP on the drug v. IP on associated genetic tests (Herceptin example)**
- **IP on relevant metabolic agents (P450)**
- **IP on correlations deriving from pharmacogenetic studies**
- **Arrays**

HAS THE LAW CHANGED SINCE 2005?

- *Merck v. Integra* – (2005) "Bolar amendment" – opened up research possibilities by a pharmaceutical firm
- *Laboratory Corporation of America v. Metabolite* (2006) – Patent on correlation questioned on subject matter grounds – Court reached out for case, and then retreated over dissent by three justices – would have struck down sequence-based diagnostic patents
- *eBay v. MercExchange* (2006) – Reinstated traditional equity test for injunction – may well restrict ability to enforce a patent on scientific research tool. (But interpreted narrowly in *CSIRO v. Buffalo Technology* (ED Texas 2007)).
- *KSR International v. Teleflex* (2007) – Raised obviousness standard – may well be basis for striking down some genomic patents

EVALUATION

- Diagnostic patents are now uncertain as a result of *Metabolite*, and perhaps of *KSR* and enforceability may be weakened by *Merck* and *eBay*.
- Obvious question about incentives to litigate, and possibility of living with ambiguous situation for a long time.
- The US has effectively accepted *some* of the positions of the reports from earlier in the decade.

THANK YOU

jbarton@stanford.edu