ASSOCIATION OF MOLECULAR PATHOLOGY V. MYRIAD GENETICS :

"GENE PATENTS" AND BEYOND

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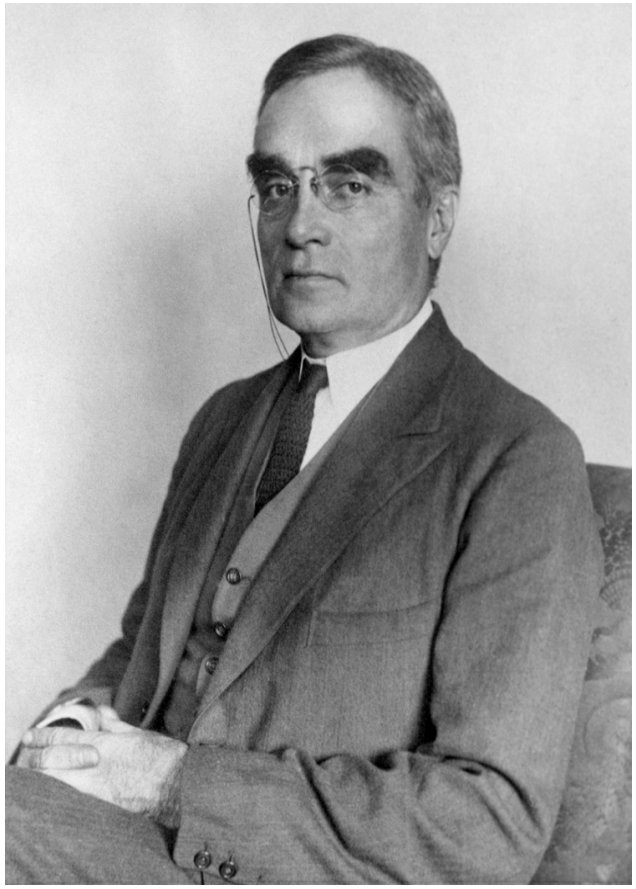
Background: Patents 101 (and Section 101)

- "Any new and useful process, machine, manufacture, or composition or matter"
- Longstanding "common law exceptions"
  - Abstract ideas
  - Laws of nature
  - Products of Nature

"Product of Nature" Doctrine

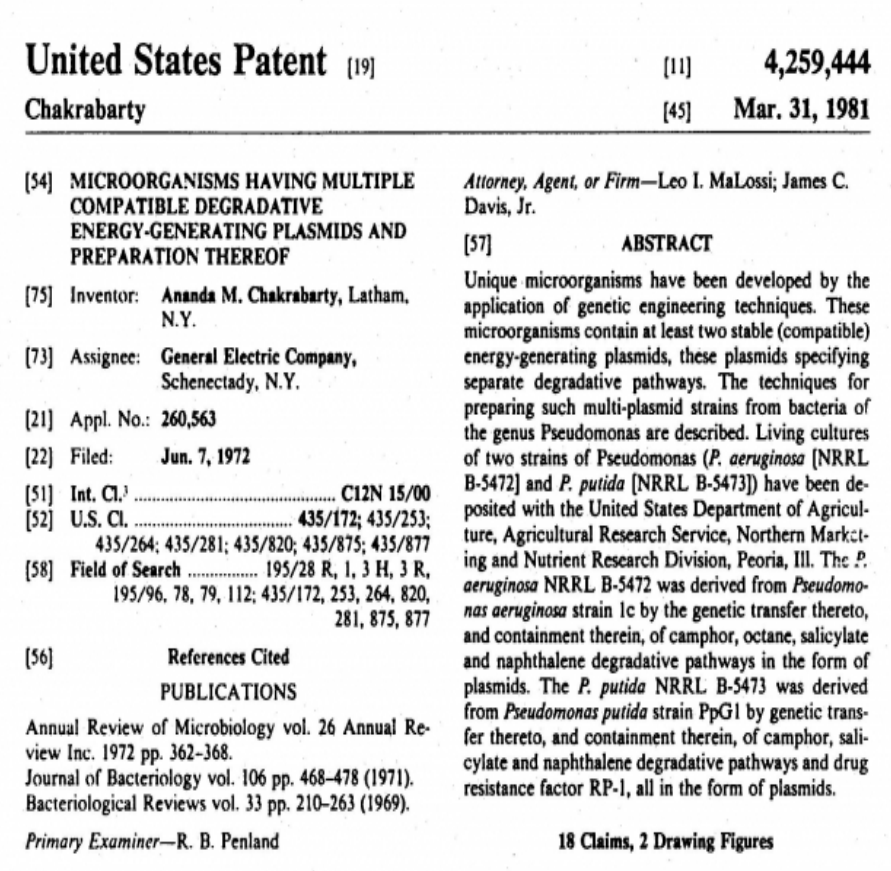
- Judge Learned Hand and *Parke-Davis* (1911)
  - Isolated *and/or* purified adrenaline patent-eligible
  - Not PON if "for every practical purpose a new thing commercially and therapeutically"



Diamond v. Chakrabarty (1980)

- "Bacterium for the genus *Pseudomonas* containing therein at least two stable energy-generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway . . ."

- Not PON because "markedly different" from anything found in nature



United States Patent [19]

Chakrabarty

[11] **4,259,444**

[45] **Mar. 31, 1981**

[54] **MICROORGANISMS HAVING MULTIPLE COMPATIBLE DEGRADATIVE ENERGY-GENERATING PLASMIDS AND PREPARATION THEREOF**

[75] Inventor: **Ananda M. Chakrabarty**, Latham, N.Y.

[73] Assignee: **General Electric Company**, Schenectady, N.Y.

[21] Appl. No.: **260,563**

[22] Filed: **Jun. 7, 1972**

[51] **Int. Cl.**[3] **C12N 15/00**

[52] **U.S. Cl.** **435/172**; 435/253; 435/264; 435/281; 435/820; 435/875; 435/877

[58] **Field of Search** ..... 195/28 R, 1, 3 H, 3 R, 195/96, 78, 79, 112; 435/172, 253, 264, 820, 281, 875, 877

[56] **References Cited**

PUBLICATIONS

Annual Review of Microbiology vol. 26 Annual Review Inc. 1972 pp. 362–368.
Journal of Bacteriology vol. 106 pp. 468–478 (1971).
Bacteriological Reviews vol. 33 pp. 210–263 (1969).

Primary Examiner—R. B. Penland

Attorney, Agent, or Firm—Leo I. MaLossi; James C. Davis, Jr.

[57] **ABSTRACT**

Unique microorganisms have been developed by the application of genetic engineering techniques. These microorganisms contain at least two stable (compatible) energy-generating plasmids, these plasmids specifying separate degradative pathways. The techniques for preparing such multi-plasmid strains from bacteria of the genus Pseudomonas are described. Living cultures of two strains of Pseudomonas (*P. aeruginosa* [NRRL B-5472] and *P. putida* [NRRL B-5473]) have been deposited with the United States Department of Agriculture, Agricultural Research Service, Northern Marketing and Nutrient Research Division, Peoria, Ill. The *P. aeruginosa* NRRL B-5472 was derived from *Pseudomonas aeruginosa* strain 1c by the genetic transfer thereto, and containment therein, of camphor, octane, salicylate and naphthalene degradative pathways in the form of plasmids. The *P. putida* NRRL B-5473 was derived from *Pseudomonas putida* strain PpG1 by genetic transfer thereto, and containment therein, of camphor, salicylate and naphthalene degradative pathways and drug resistance factor RP-1, all in the form of plasmids.

18 Claims, 2 Drawing Figures

Early "Gene Patents"

- Generally claimed cDNA (DNA with introns excised)
- Intended to cover therapeutics
- Began to issue in early 1980s
- *E.g.* Patent No. 4,703,008: issued to Amgen in 1987
  - "DNA Sequences Encoding Erythropoeitin"
  - Claim 1: "A purified and isolated DNA sequence encoding erythropoeitin, said DNA sequence selected from the group consisting of the DNA sequences set out in Figs. 5 and 6 or their complementary strands . . ."

Controversies over patents covering diagnostics

- Increase cost, restrict access
- LDTs not FDA-regulated, so patents less necessary as incentives than for therapeutics
- Federal funding involved

http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf

nih.gov

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Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests

Report of the
Secretary's Advisory Committee on Genetics, Health, and Society


MYRIAD
GENE PATENT LITIGATION

Patent law and access

AMP v. Myriad at the Federal Circuit

Judge Lourie: *[T]his appeal is not about . . . whether individuals suspected of having an increased risk of developing breast cancer are entitled to a second opinion . . .*

Other judges also focused on innovation

- Bryson's dissent (drawing distinction between cDNA, gDNA for purposes of WGS)
  - cites SACGHS

- DOJ's distinction between cDNA/gDNA motivated by follow-on innovation concern
  - Long history of OSTP/NIH concern about follow-on innovation (utility and WD guidelines, 1999-2001)
  - Rai, *Duke Law Journal* (2012)

Supreme Court decision

- 9 “composition of matter”/product claims at issue
- Court adopts cDNA vs. gDNA distinction (Bryson, SG, Lander)
  - says that cDNA *not* “naturally occurring” (though not clear why it thinks gDNA at issue *is* naturally occurring)
    - Lander brief on naturally occurring gDNA?
- “information” vs. “chemical”
  - but thinks that both cDNA and gDNA claims cover “information”
  - fails to “connect dots” as to why cDNA information more problematic than gDNA information
  - implicit reliance on SG, Lander briefs discussing differential impact of claims on downstream research? (Rai and Cook-Deegan, *Science*. 341:137-38 (2013))

Immediate Aftermath

- June 13, 2013
  - Ambry Genetics, Gene Dx, DNATraits, Quest Diagnostics, Pathway Genomics, others state they will begin testing for BRCA1, BRCA2 mutations
  - Ambry → $2,280 (vs. Myriad's $4,040)
- July 9, 2013: Myriad sues Ambry; July 10, 2013: Myriad sues Gene-by-Gene
  - Both suits in Utah district court
  - 10 patents, dozens of claims
  - Claims generally unaffected by prior suit (except claim 6 of 5,747,282)

Assessing the Suits

- Claims for sequence amplification, sequencing, then comparison with wild type; primers plus PCR claims
  - *Myriad* plus *Mayo v. Prometheus* (2012)
    - Is inventive activity *beyond* law or product of nature always required?
- Ambry counterclaims, arguing antitrust violations, invalidity and noninfringement
  - Basis for antitrust violations (Section 2, Sherman Act) unclear
  - Notes secret data Myriad has but doesn't link to antitrust
  - Data arguably more important than (soon-to-expire) patents

The Data Issue

Myriad

- Says that public databases have 25-30% VUS rate

Publicly Available Data

- Myriad stopped contributing to Breast Cancer Information Core in 2005
- Free the Data! (SCRP)

Larger Impacts

- Graff et al., *Nature Biotechnology*. 31:404-410 (2013)
  - ~8700 U.S. “gene patents” with “naturally occurring sequences” still in force
    - 41% human
  - unfortunately, Graff def’n of “naturally occurring” doesn’t map to cDNA/gDNA distinction
  - Percentage of “natural” (vs. synthetic) began to decline circa 2000
- Implications of *Myriad/Mayo* for claims to “purified” large and small molecules?
- Patent bar most concerned about claims to proteins, antibodies

Questions?

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