Effects of gene patents and licenses on clinical genetic testing

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Background

- Patents are seen as necessary to enhance an inventor's ability to recoup the substantial investments necessary to bring a new drug or device to market.
- Are patents an effective incentive for the development of new clinical genetic tests?

Concerns about IP

- Concerns about restrictive IP
  - decreased access to testing services
  - increased test costs
  - decreased quality of testing
  - decreased ability to conduct R&D
- Concerns about insufficient IP
  - lack of incentive for development of genetic tests

Empirical studies

- Effects of gene patents and licenses on the provision of clinical genetic testing services
  - Mildred K. Cho, Samantha Illangasekare, Meredith A. Weaver, Debra G. B. Leonard, Jon F. Merz (2003) **Effects of gene patents and licenses on the provision of clinical genetic testing services.** *J. Mol. Diagnosis* 5:3-8.

Empirical studies

- Case study of hereditary hemochromatosis
  - Jon F. Merz, Antigone G. Kriss, Debra G. B. Leonard and Mildred K. Cho (2002) **Diagnostic testing fails the test: the pitfalls of patents are illustrated by the case of hemochromatosis.** *Nature* 415:577-579.

Empirical studies

- Licensing study - interviews
  - Henry, MR, Cho, MK, Weaver, MA and Merz, JF (2002) **DNA patenting and licensing.** *Science* 297:1279.
  - Henry MR, Cho MK, Weaver MA, Merz JF. (2003) **A pilot survey on the licensing of DNA inventions.** *Journal of Law, Medicine & Ethics.* 31(3):442-9.

Survey methods

- Sample: all laboratories in the US conducting genetic tests
  - GeneTests
  - Association for Molecular Pathology
- Telephone survey

Results: Study 1

- 132 respondents of 211 labs contacted (63%)
- 122 included who conducted genetic tests
- 121/122 conduct testing for clinical purposes

Results: Study 1

- 79 (65%) had been contacted by a patent- or license holder
- 30 (25%) said that patent/license holder had prevented lab from continuing a test service
  - 17 for one test, 12 for more than one test
  - Companies more likely to report being prevented than university labs (P=0.001)

Results: Study 1

- 11 tests stopped being performed
  - Apo E
  - BRCA1/BRCA2
  - DMD/BMD
  - HFE
  - Myotonic dystrophy
  - Canavan disease
  - SCA1,2,3,6
  - APC
  - CMT1A/CMTX
  - FraX
  - APC

Results: Study 1

- All 11 tests performed by 11 labs or more in June, 2001
  - 67 tests performed by 11 labs or more
  - 394 tests performed by 10 labs or fewer
- 14 patents in USPTO db relevant to 11 tests
  - 10 held by universities
  - 4 held by for-profit companies
  - 7 from research funded by US government

Results: Study 1

- 64 (53%) decided not to develop or perform a clinical genetic test because of a patent
  - No significant difference between companies and university labs (P=0.28)

Results: Study 1

- Opinions about effects of patents

Effect	neg	0	pos
Access	107	10	3
Cost	115	4	1
Quality	53	61	5
Development	105	10	1
Information sharing	98	16	1
Ability to do research	79	35	4

Conclusions: Study 1

- Patents and licenses have had some negative impacts on ability of labs to conduct and develop genetic tests
- Patents and licenses have affected tests that are most commonly performed

Conclusions: Study 1

- Patented tests often result from government funded research performed at universities
- Laboratory directors in the US believe that patents and licenses have had negative impacts on access, cost, and quality of testing, and on information sharing between researchers

HFE Patent history

- **Mercator Genetics** spent approximately US$10 million developing its method of positional cloning and discovering the association between HFE mutations and hemochromatosis
- **US patents** (numbers 5,712,098; 5,753,438; and 5,705,343) **issued to Mercator Genetics** in early 1998 for genetic testing of two variants, C282Y and H63D
- **Mercator went out of business**, Progenitor merged with Mercator and was assigned its pending and issued patents

HFE patent history

- **Progenitor licensed the patents exclusively** for clinical testing to SmithKline Beecham Clinical Laboratories (SBCL) for an up-front payment and guaranteed continuing fees worth around $3 million
- SBCL's exclusivity and payment guarantees continued until a kit became available for use by clinical laboratories

HFE Patent enforcement

- **Summer 1998: SBCL began enforcing patent rights.** Sublicenses for $25,000 from academic laboratories, 5 to 10 times more than this from commercial laboratories, plus royalties of up to $20 per test.
- **Fall 1999: Sale of SBCL to Quest Diagnostics completed.** During and after the sale, SBCL and Quest curtailed active enforcement of the patents

HFE Patent enforcement

- **April 1999: Bio-Rad Laboratories acquired patent portfolio from Progenitor**, subject to the exclusive clinical-testing license held by SBCL.
- **2001: Bio-Rad began offering a test kit for C282Y and H63D**, and was offering to license laboratories to perform testing without its kits — but at a cost that makes its kit more economically attractive than the laboratories' own tests, with up-front payments inversely proportional to the testing volume of the laboratory, plus a per test fee of about $20.

Results: Study 2

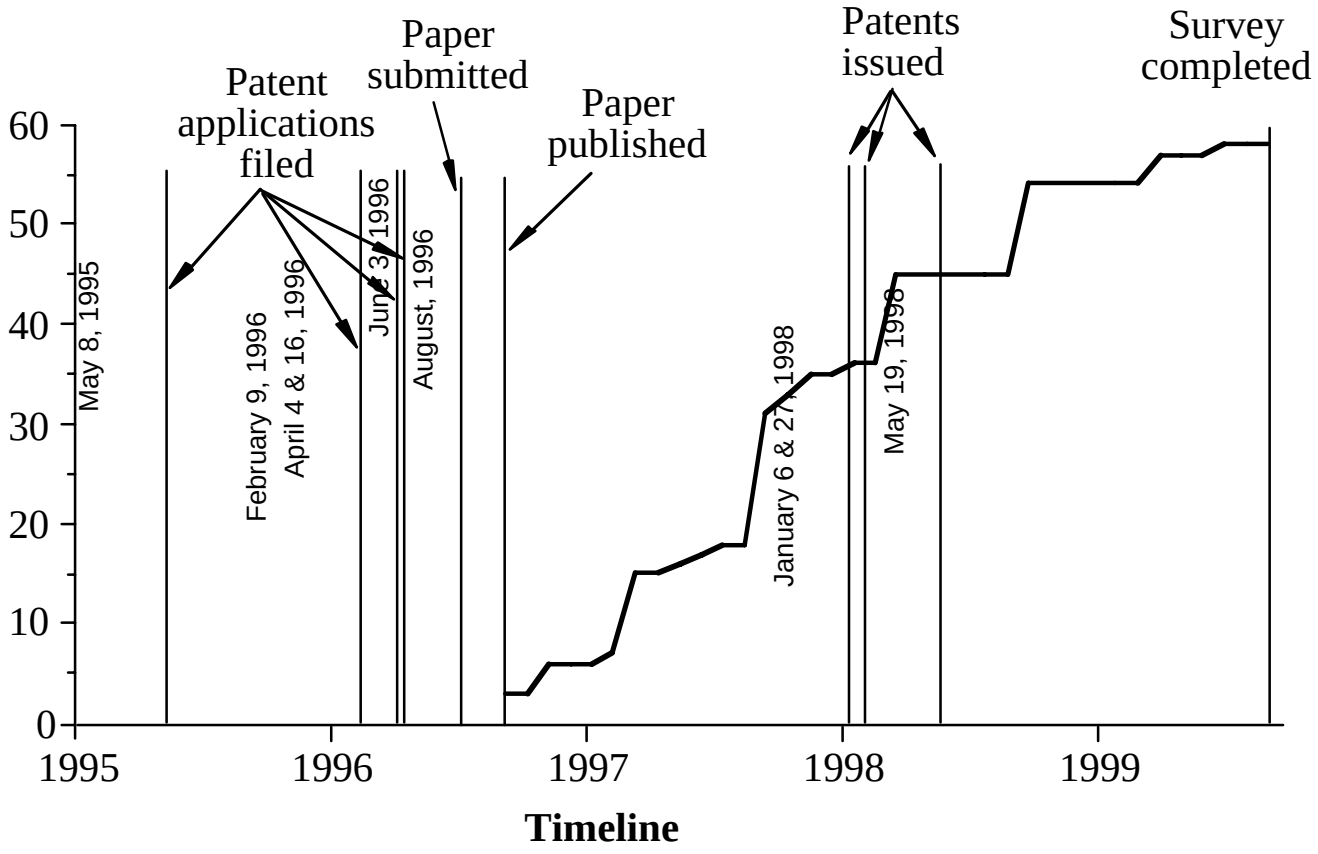
- 119/128 respondents of labs that conduct hemochromatosis (HFE) testing in US (93%)
- 58 labs were performing HFE testing
- 54 labs had received a letter from SBCL

Results: Study 2

- 31 labs (26%) had not developed and were not performing the HFE test
- 5 (4%) had stopped performing the test

Results: Study 2

- 35 labs (60% of 58 performing HFE test) introduced clinical test before first patent issued in Jan. 1998, and after critical paper published in Aug. 1996
- mean time from publication to adoption = 14 mo.


Patent applications filed
Paper submitted
Paper published
Patents issued
Survey completed
May 8, 1995
February 9, 1996
April 4 & 16, 1996
June 3, 1996
August, 1996
January 6 & 27, 1998
May 19, 1998
60
50
40
30
20
10
0
1995
1996
1997
1998
1999
Timeline

Conclusions

- Patents and licenses have a significant effect on provision of clinical genetic testing services in the US
- We do not know whether the total volume of tests has decreased
- Laboratory directors feel that impacts on cost, quality, access and research are negative for patients

Conclusions

- Labs do not appear to require patents as incentive to develop findings into clinical practice
- Still, patents may provide incentives to conduct research necessary to identify genes associated with disease

Study 3: Licensing

- Identified all institutions holding patents in class 435/6 (molecular biology, nucleic acid) with “Seq. ID” assigned 3 or more patents
  - 62 non-profits
  - 48 for-profits

Study 3: Licensing

- Telephone interviews
  - 27/32 non-profits + NIH (82%)
  - 19/32 for-profits (59%)

Results: Study 3

- Average # of disclosures and patents filed:
  - 24/163 (15%) disclosures filed by non-profits
  - 32/37 (86%) disclosures filed by for-profits

- Exclusive licensing reported by:
  - 68% of non-profits
  - 27% of for-profits

Results: Study 3

- No agreement about “research tools” vs. “targets”
  - “a drug target or a disease diagnostic is not generally considered a research tool”
  - “genes that are drug targets are viewed by large companies as research tools, but small companies feel that they are not research tools”

Conclusions: Study 3

- Most DNA-based inventions may not be controlled by a patent and an exclusive license
- However, clinically-important patents on diagnostics may be more likely to be subject to patents

Discussion: Study 3

- Kyle Jensen & Fiona Murray (2005) **Intellectual Property Landscape of the Human Genome.** *Science* 310:239-240.

- Nearly 20% of human genes are claimed as US intellectual property

Discussion: Study 3

- 4270 patents held by 1156 assignees
- 63% by private firms
- 28% held by public entities
- Uneven distribution
  - Of 291 cancer genes, 131 patented
  - BRCA1 (breast cancer), PIK3R5 (diabetes), LEPR (obesity)