Synthetic Biology
Knowledge Sharing, Innovation and Translating Research for the Public Good

Presidential Commission for the Study of Bioethical Issues

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Dr. Ashley J. Stevens
Special Assistant to the VP for Research
Senior Research Associate
Institute for Technology Entrepreneurship and Commercialization
School of Management
Boston University

President
Association of University Technology Managers
Agenda

- Association of University Technology Managers
- Patent System
- Patents and Scientific Research
- Intellectual Property and the Biotechnology Industry
- Impact of Patents on Scientific Research
- Issues with Synthetic Biology
- Technology transfer in the US
Association of University Technology Managers

- The leading association representing technology transfer professionals globally
- 3,500 members in 35 countries
- Primary activities
  - Professional Development
    - Continuing Professional Education Meetings
    - Courses
  - Services to Members
    - Networking
    - Data collection and analysis
  - Advocacy
The Patent System
The Patent System is Always in Flux

1981  Patentability of Software

- *Diamond vs. Diehr* (Supreme Court)

1982  Court of Appeals of the Federal Circuit established

1980-88 Three landmark cases made biotechnology patentable

- *Chakrabarty* (Supreme Court, 1980) – Microorganisms
- *In re. Hibberd* (CAFC, 1985) – Sexually reproduced Plants

1998  State Street Bank decision (CAFC) confirmed patentability of business methods
Recent Supreme Court Decisions

- Integra vs. Merck: Research Exemption
- eBay vs. Merck: Right to an Injunction
- LabCorp vs. Metabolite: Patentable Subject Matter
- KSR vs. Teleflex: Obviousness
- MedImmune vs. Genentech: Right to challenge validity of a licensed patent
- In re Bilsky: Scope of Scope of Subject Matter Patentability
Rochester, Pfizer, Ariad

- Three patents filed ~2000 attempted to claim all downstream drugs that modulated newly discovered biological targets
  - Cox II
  - PDE-V
  - NF-KB
- Claimed “methods of treating”
- All three have been ruled invalid for either enablement or written description
Patents and Scientific Research
US Technology Transfer System

- Established by the Bayh-Dole Act of 1980
- Main components:
  - Universities could elect to retain title to the results of Federally funded research
  - Universities were required to share proceeds with inventors
  - Most restrictions on licensing terms were removed
  - US manufacture required for products to be sold in the US
  - Small business preference
  - Non-exclusive license to US Government for its own use
  - Ability to grant compulsory license in the public interest
The Traditional Scientific Paradigm
The New Scientific Paradigm

- The “Patent-Paper-Pair”
  - Fiona Murray, MIT
  - 50% of papers in *Nature Biotechnology* 1997-1999 had a corresponding patent\(^1\)
  - 33% of biotech papers in *Science* and *Nature* had a corresponding patent\(^2\)

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## Faculty Participation

<table>
<thead>
<tr>
<th>Career Disclosures</th>
<th>%</th>
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<tbody>
<tr>
<td>Never</td>
<td>64.2</td>
</tr>
<tr>
<td>Once</td>
<td>14.8</td>
</tr>
<tr>
<td>Twice</td>
<td>7.6</td>
</tr>
<tr>
<td>Three to five</td>
<td>11.4</td>
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<tr>
<td>Six or more</td>
<td>2.0</td>
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Why Do We Have Patents?

- They are legally sanctioned monopolies to promote the public good by incentivizing inventors to disclose their discoveries to the public so that others can build on them.

- The inventor strikes a deal with the Government:
  - Disclose what you've discovered to the public so that others can build on it.
  - In return, we'll grant you a twenty year monopoly on its use.
  - That way, you can persuade people to invest in developing your invention.
What Does a Patent Let You Do?

- Patents are exclusionary, not permissive
  - They let you build a fence round what you claim
- They don't necessarily allow you to practice your invention
  - There may be broader patents that block you
- They do allow you to stop others from practicing your invention without your permission – a license!
- You are under no obligation to grant a license
  - You can just keep that territory for yourself
- They give you control over the development of the technology
Intellectual Property and the Biotechnology Industry
Intellectual Property in the Biotechnology Industry

- Profoundly different from the traditional pharmaceutical industry
- NCE typically has 2 or 3 three layers of patent protection
  - Composition of matter
  - Methods of treating
  - Formulation
- Biotechnology is characterized: by
  - Many core discoveries being made and patented in academia
  - Platform technologies that translate specific genes/proteins into marketable products
  - Intense licensing activity
  - Products carry substantial royalty burdens
You may need to license other patents to practice yours – i.e., to achieve Freedom-to-Operate
Biotechnology Platform Technologies – University-Owned

- Cohen-Boyer: Recombinant DNA
- Riggs-Itakura: Bacterial production methods for recombinant DNA molecules
- Cabilly: Production methodologies for monoclonal antibodies, Chimerization of monoclonal antibodies
- Axel: Production of glycosylated recombinant proteins in mammalian cells
- Harris: PEGylation techniques to extend the serum half-life of protein drugs
- Thompson: Stem cells
- Tuschl, Mellow-Fire: RNAi methods of gene silencing
Biotechnology Platform Technologies – Company-Owned

- Cabilly: Production methodologies for monoclonal antibodies
  Chimerization of monoclonal antibodies
- Mullis: Polymerase chain reaction
- Queen: Humanization of monoclonal antibodies
- Ladner: Phage display
Licensing Is Highly Nuanced
– Any Degree of Rights Can Be Granted

Degrees of transfer of rights

No transfer -- immunity  
Limited transfer  
Complete transfer

Freedom from Suit  
License  
Assignment

Non-exclusive  
Exclusive by field  
Exclusive by territory  
Exclusive

Degrees of Exclusivity
Why Do People License Their Technologies?

- Because they can’t or won’t develop a technology
  - University Not part of the mission
  - Small company Inadequate resources to take to market
  - Invention may not be sufficient to market a product
    - Platform technology, needs additional inventions to productize
- Do a deal whereby someone else bears the majority of the risk and receives the majority of the return
  - The inventor/licensor receives a small part of the return
In other words

- 5% (or 10% or 25%) of a **big** pie is worth more than 100% of a **small** pie
Licensing Platform Technologies has Been Highly Profitable

- Genentech – $250 million from Cabilly in 2007
- Protein Design Labs – $250 million Queen antibody humanization patents in 2008
- Cohen-Boyer – $254 million lifetime
- City of Hope – $500 million jury award against Genentech for Riggs-Itakura;
- Axel patents – $790 million lifetime
Do Patents Inhibit Research?

- *Madey vs. Duke* established that universities are in the business of doing research” and that patents must be respected.
- Infringement suits are expensive
  - Rarely sufficient economic value in basic research to justify enforcement actions
- Only issued patents can be enforced
  - Cutting edge research builds on prior work before patents can be issued
- Robust material transfer systems in place
  - UBMTA has over 300 signatories
- Academic institutions license their patents with explicit disclaimers concerning blocking patents
  - Ensuring freedom-to-operate is left to the licensee
Over-Reaching Use of Patents

- There have been attempts to use patents on research tools overly broadly
  - Reach through to claim rights to discoveries made using these tools
    - Harvard mouse
    - CRE-LOX
  - These were all made by companies, not academic institutions
Do Patents Encourage Secrecy?

- Patents require complete disclosure of the best known way of practicing the art as of the date of filing
  - “Best mode”
  - Another form of publication
  - US patent applications published after 18 months since 2001
- Scientists are secretive about the interim results of their research until they reach a publishable conclusion
- Availability of provisional patent applications since 1995 has facilitated patenting without delaying publication
Intellectual Property and Synthetic Biology

- Is there anything fundamentally different about intellectual property aspects of synthetic biology?
- Some is being developed in the private sector
  - e.g., Venter Institute
- Some is being developed in academia
  - E.g., University of Wisconsin
- The scope of what is patentable subject matter will be determined by the patent office and the courts
- The intellectual property regime is sufficiently robust to handle the challenges
Data Pertaining to US Technology Transfer
US Technology Transfer Activity in 2008

- 20,115 invention disclosures
- 18,949 patent applications filed
- 3,156 patents issued
- 5,132 new options/licenses executed
- 32,405 licenses/options active
- 15,498 yielding some sort of income
- 7,917 yielding running royalties
Licenses Granted

- 50% small companies
- 35% large companies
- 15% start-up companies
- 56% non-exclusive
- 44% exclusive
Invention Disclosures Received

Source: AUTM 2008 Licensing Activity Survey unless otherwise noted
The Positive Impact of Academic Innovations on Quality of Life
Impact of Academic Research in Healthcare

- 154 FDA approved drugs, biologics, vaccines and \textit{in vivo} diagnostics
  - 13.3\% of global sales
  - $103 billion worldwide sales in 2008
  - 9\% of all NDA’s approved by the FDA 1990-2008
  - 22\% of most innovative NDA’s approved

The Internet

CERN

University of Illinois Urbana-Champaign

University of Illinois Urbana-Champaign

(Stanford)

Carnegie-Mellon

MIT

Stanford
Major Products in Different Sectors

- V-chip
- Hollow optical fibers
- PSA test
- Honeycrisp apple
- Cochlear implant
- Lightning detection technology
- Cell phone technologies

AUTM Better World Report
Innovations from Academic Research That Positively Impact Global Health
Knowledge Sharing, Innovation and Translating Research for the Public Good

Start-Ups Formed

Year

Number of Start-Ups Formed


- 100 200 300 400 500 600 700 800 900
Start-Up Companies

- 6,652 formed 1980-2008
  - 72% located in same state as institution
    - Every state except Alaska
      - 12.3% from California institutions
      - 11.8% from Massachusetts institutions
      - 363 by MIT
      - 349 by University of California System
      - 175 by University of Utah
  - 52% still active in 2008
## Financial Performance

<table>
<thead>
<tr>
<th>Financial Contribution</th>
<th>Number</th>
<th>%</th>
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<tbody>
<tr>
<td>Loss making</td>
<td>68</td>
<td>52.3%</td>
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<tr>
<td>Gross profitable</td>
<td>27</td>
<td>20.8%</td>
</tr>
<tr>
<td>Net profitable</td>
<td>14</td>
<td>10.8%</td>
</tr>
<tr>
<td>Self sustaining</td>
<td>21</td>
<td>16.2%</td>
</tr>
<tr>
<td>Total</td>
<td>130</td>
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Why Such a Difficult Business Model?

- Income is distributed very unevenly
  - A business of a few “big hits”
  - $3.4 billion income in 2008
    - 24.1% Northwestern
      - Lyrica monetization
    - 12.0% City of Hope
      - Cabilly
    - 16.1% MSK, CHOP and U. of California System
    - 47.9% remaining 180
  - Only 198 licenses generated over $1 million
    - 1.3% of 15,498 generating any income

- Distribute 70-100% of what is generate
  - Inventors
  - Labs, Departments, Colleges