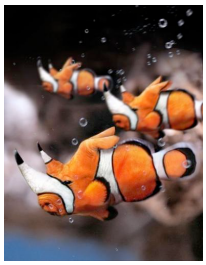


rDNA: Biosafety & Biotech

Phil/Bio 2510
Spring 2009

rDNA Review

- Reading vs. Manipulating DNA
- Recombinant DNA
  - Vectors
- PCR
  - Amplification
- DNA Sequencing

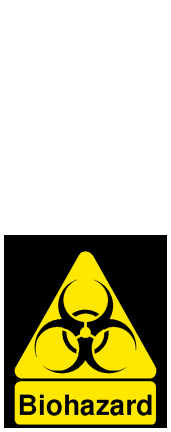
What can we do with rDNA?

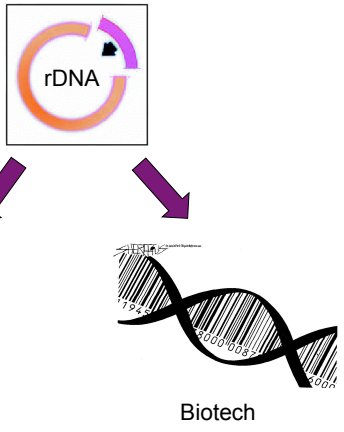
- "Pharming": modify organisms to produce drugs or other usable materials (also xeno-technology)
- Research: designing model organisms
- GM agriculture: modify crops or animals for human consumption
- Gene therapy: modify genetic disease
- "Designer babies": modify offspring
- Bio-weapons: modify biological agents

Should we have public oversight of rDNA science?

- If not, why?
  - Autonomy of science
- If so, what type of oversight?
  - Determine funding
  - Determine research

What is worrisome about rDNA science?





Biotech

rDNA Biohazards

The ability to directly modify organisms at the genetic (molecular) level raises possible safety issues and worries about the proper limits of responsible science.

What are the risks?

- Introduce new genetic combinations with unknown consequences.

  E.g., create a more virulent bacteria or virus that can escape into the "wild".

In the early 1970s Paul Berg was going to introduce a recombination into a simian virus, but decided to stop and think about it…

1974 Asilomar Conference

- Triggering Events
  - Developments in rDNA techniques.
  - Biosafety risks and voluntary moratorium
  - NIH (RAC)
- Results
  - Demonstrated responsible science*(Berg)
  - "Open" process: Diversity of opinion, media, etc.
  - Guidelines for future rDNA research
  - Self-regulation of rDNA science

Criticisms of Asilomar

- Not exactly "open"
  - Controlled by molecular biologists, not epidemiologists, not infectious disease and public health experts, no direct public input, etc.
- Narrow scope of concern
  - Focused only on "biohazard" risk
  - Not other ethical implications considered (e.g., social or commercial implications)
- Actually slowed progress on rDNA science
  - Risks never manifested
  - "Meddling Ethicists" Claim (see Watson)
- Ultimately didn't win public trust
  - Began era of contentious public debate on science policy

What is responsible science?

- Considering risks, putting guidelines in place to protect from risks, while preserving scientific autonomy? (Berg)
- Responsible for future applications of the science/technology?
- Under control of the public -- those who are at most risk from technology?

A conundrum…

It is unreasonable to create restrictive legislation on as-yet unknown technology, especially if it has the potential to benefit society.

But…

Once a new technology is developed and in use it is difficult to create effective and comprehensive policies to protect against risks of that technology.

An objection

Playing God

- Messing with things beyond our control…
- Threat to human dignity…
- Too far, too fast…

Franken-science

- "Mad scientists" not responsive to society…
- "Mob reaction" of superstitious public…
- Pandora's Box…

If we don't play God, who will?

– James Watson

Recall the story of Frankenstein

- Image of science?
  - Hubris of the "mad scientists"
  - Isolated and/or ignores public
- And the angry mob?
  - Emotional response
  - Challenge to accepted values

Arthur Caplan

Director of the Center for Bioethics at the University of Pennsylvania

"The fear of the 'mad' scientist isn't that he or she is mad, it's that he or she is indifferent to the ethics of what they are doing."

Lessons from Frankenstein

- Assumptions about science?
- Assumptions about lay-public?
- Questions about proper relationship between science and public in policy decisions…

Biotech

- The advent of rDNA technology recommended new applications that might be commercialized, and patented.

Jonas Salk

On April 12, 1955, after eight years of research and testing, Jonas Salk announced that his polio vaccine was safe, effective, and potent.The 1916 polio outbreak had left six thousand Americans dead and another twenty-seven thousand paralyzed. In the two years following vaccine release, polio cases in the United States dropped by approximately 90 percent. By 1979 no cases of polio from the wild polio virus were reported nationwide… Yet despite its enormous success, the vaccine was not patented. When asked who owned the patent, Salk famously responded: "Well, the people, I would say. There is no patent. Could you patent the sun?"

Josephine Johnston and Angela A. Wasunna, "Patents, Biomedical Research, and Treatments: Examining Concerns, Canvassing Solutions," Special Report, *Hastings Center Report* 37, no. 1 (2007), S2.

Then came the 1980s…

…the birth of Biotech.

Patenting Genetics 1980

- Cohen-Boyer, 1980
  - Patent on 1st genetic engineering and cloning method
  - Insulin producing bacteria
- Chakrabarty, 1980
  - 1st patent on engineered organism
  - "Oil-eating" bacteria
  - Diamond v. Chakrabarty ruling

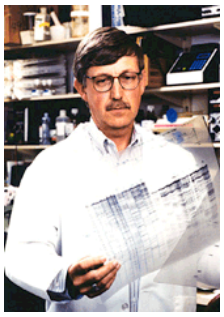
(Also Bayh-Dole Act 1980)

June 26, 2000

President Bill Clinton (and British Prime Minister Tony Blair simultaneously) announced the completion of the rough draft sequence of the entire 3.1 billion base pairs of the human genome. It effectively marked the end of the publicly funded Human Genome Project which started in 1988. Clinton's speech emphasized the promise HGP held for revolutionizing medicine and providing unprecedented insight into human origins, biological function, and our very nature.

Patents and HGP

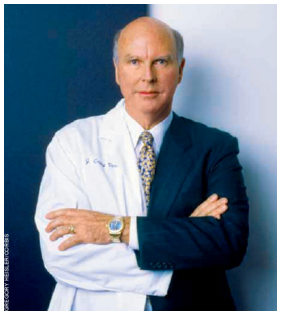
HGP: a publicly funded, international project aimed at sequencing the entire human (and other animal) genomes, primarily for the purposes of potential medical and scientific advances; making the sequence publicly (freely) available so that research in these areas would be enhanced.



Francis Collins (HGP)

Patents and HGP

At the same time commercial interests saw the possibility of developing sequences for profit, licensing or producing exclusively owned products that relate to the use of those DNA sequences. (Including drug targets, PCR, gene chips, bioinformatics, etc.)



Craig Venter (Celera)

Changes in Genetic Patents

- Patents for human DNA sequences tripled from early to late 1980s, and again tripled during the early and late 1990s.
- By the end of HGP, ~ 20%* of the ~23,000 known human genes were the subject of 4,270 US patents.
- Increasing each year, ~ 4,000* new applications for patents on genes or genetic technology are filed at the US patent office.

Genetic Patents

- Patents are the central mechanisms for protecting commercial interests in developing and bring to market inventions (innovations).
- For commercial genetics, this means patenting:
  - the methods of identifying (manipulating) gene sequences;
  - gene products (proteins); and/or
  - particular genes or sequences of DNA*

What is a patent?

- Patenting of inventions under US law: Patent and Trademark Office (PTO) in Department of Commerce.
- Provides a 20 year protection, limited monopoly for use, licensing, or royalties.
- However, cannot patent naturally occurring or raw products of nature (so, genes must be isolated, purified, or modified to produce a unique form not found in nature).

Four Criteria for Patents

1. **Useful**: the invention have an identified use
2. **Novel**: not known or used before the filing
3. **Non-obvious**: not an improvement easily made by someone trained in the relevant area.
4. **Enablement**: invention described in sufficient detail to enable it to be use for stated purpose by someone skilled in the area.

Rationale for Patents

To protect the interests of inventors and society…

- So that inventors will be willing to invest in and develop innovations… for profit;
- And ultimately, society will benefit by the advancement of these innovations; reduces secrecy.

Research and Patents

No one denies the importance of patents for commercial purposes, but some concerns are raised about the impact of patents on (especially medical) research for the public good; some special concerns regarding *genetic* research/patents.

- Patents may unduly limit access to materials and methods, because exclusive use, expensive, deter areas of research (e.g., patient access to drugs, tests, etc.).
- Many inventions derived from *publicly* funded research.
- Genetic sequences may not be properly classified as *inventions*.

Pro	**Con**
• Spur innovation, benefit society.	• Limit or stall important research, increase cost.
• Designed to decrease secrecy in research.	• Increases secrecy in research.
• Genes are inventions: DNA are isolated, purified sequences.	• Genes not inventions: merely identifying sequences not enough to be invention.
• Many pharmaceuticals are patented for use even though part of human heritage.	• Genes are common biological heritage of all humans, not for private ownership.
• Most inventions are built on previous work, often publicly funded (Cf. Bayh-Dole Act, 1980)	• HGP funded by public (NIH, NSF, DoE, etc.)

Pro Quotes

- "A patent serves a purpose in society. The goal of patenting a gene is not to make anyone rich, but to force disclosure of secret information." (Craig Venter pointing to example of Genentech's patent on human insulin gene)
- "When you isolate something as it appears in its natural state you change it, even if the only change is the isolation. You have left behind the natural product and created something artificial. No isolated gene sequence occurs in nature." (Harold Edgar)

Con Quotes

- "DNA is considered to be so intimately related to species identity that no parts of it should be contoled by corporate interests. In the case of human beings, human DNA is unique because it is human, and therefore possessing intrinsic value of a sacred kind. As one critic puts it, DNA bears the image of God." (Mark Hanson, director of religion and biotechnology policy at the Hastings Center)
- "The plants, animals, and microorganisms comprising life on Earth are part of the natural world into which we are all born. The conversion of these species, their molecules, or parts into corporate property through patent monopolies is counter to the interests of the peoples of this country and of the world. No individual, institution, or corporation… should be able to hold patents on organs, cells, genes, or proteins, whether naturally occurring, genetically altered, or otherwise modified." (Council for Responsible Genetics, statement on biotech patents.)

Example: Cohen-Boyer and Stanford

- Considered a successful model for **"enabling technologies"** that are fundamental to carrying out necessary research and development.
- Generally available (free) to non-profits and universities, but charge a reasonable fee for commercial use.

BRCA Example

BRCA1 and BRCA 2 genes account for 5-10% of breast cancer cases. BRCA 2 was patented by British Patent Office (Nov. 27, 1997) to Institute of Cancer Research in London and Duke University. Oncormed, Inc. (Gaithersburg, MD.) obtained exclusive worldwide license to the gene patent.

Worry: test for breast cancer could be done for $1,000, but now costs $3,000. Also research involving BRCA 2 may be limited or avoided because of patent enforcement.

Michael Crichton, Patenting Life, Op-ed, New York Times, Feb. 13, 2007. Accessed Feb. 26, 2007. www.nytimes.com/2007/02/13/opinion/13crichton.html

Onco-mouse Example

In 1988 an (US) patent was granted for the "onco-mouse" – a mouse genetically engineered to be susceptible to cancer – to Harvard (Phil Leder) and owned by Du Pont. Patent was not limited to the specific mouse, but to *all cancer prone transgenic animals*.

Worry: Companies and researchers interested in developing new forms of cancer-prone mice, or use transgenic cancer-prone animals, must pay Du Pont licensing, royalties, or other fees.

James Watson, *DNA: The Secret of Life*, page 123-24.
See also Of Transgenic Mice and Men, by Peter Shorett online at Council for Responsible Genetics.

Rifkin Example

Anti-biotechnology activist Jeremy Rifkin and Dr. Stuart A. Newman applied for a patent on chimera research techniques, including ones that would combine human and monkey or ape cells into a single "humanzee" embryo. In another, human and mouse cells would form a "humouse" embryo. Their goal was to challenge biotechnology efforts that would produce these chimeras.

If the patent was denied, then a precedent would be established limiting the type of human-animal crosses that would be allowable under patenting law, with the extended effect of influencing other regulations concerned with human-animal chimeras and transgenic animals. (Recently US patent office denied patent, citing thirteenth amendment concerns…)

If the patent was granted, Rifkin and Stuart would enforce the patent by not allowing anyone to use or develop their technology, at least for 20 years.

Worry: patents can be used for commercial and non-commerical purposes, such as these. In effect it could shut down an entire area of research or technology that promises to provide advances in genetic (medical) research.

http://www.bioethics.umn.edu/resources/topics/chimeras.html

Another Troubling Example?

Venter's Sargasso Sea…

- Is this biopiracy?
- Commercializing rDNA science makes biology a resource that can be exploited, but who owns that biological resource?

With great power,
comes great responsibility.

– Uncle Ben to Peter Parker
in *Spider-Man*

Key Concepts

- Biohazards of rDNA
- Asilomar Conference (1974)
- Playing God and Franken-science
- Biotech and rDNA
- Genetic Patents