Lecture 20
Recombinant DNA and the Limits of Science?

Case: Mousepox dilemma

- **Engineered Mousepox Virus I**
- **New research, St. Louis University**
- **Justification**
- **Objections**

The limits of science?

- **criticisms of the late 1960s**
- **new criticism, early 1970s:**
- **Some research is not ethical, should not be undertaken**

Limits of inquiry?

- **Bible - tree of knowledge**
- **Middle Ages, earth-centered universe**
- **Galileo, Copernican system**
- **Faust legend**
- **19th C, evolution**

20th C

- **nuclear energy and the Bomb**
- **chemical and biological weapons**
- **race and IQ**
- **Recombinant DNA research**

History

- **1953, Francis Crick & James Watson , structure of the DNA molecule.**
- **1958, Matthew Meselson & Frank Stahl , prove the semiconservative replication of DNA.**
- **1958, Arthur Kornberg , Purified DNA polymerase I from E. coli.**
- **1962, "restriction enzyme" discovered**
  - ☑ break DNA at specific points
  - ☑ ...GAATTC... ...CTTAAG...
- **1966 , Marshall Nirenberg & H. Gobind Khorana , triplet mRNA codons specify each of the twenty amino acids**

- ☑ Three base-pair combinations that produce all proteins

History continued

- ☛ **1970 , Hamilton Smith & Kent Wilcox , isolated the first restriction enzyme that could cut DNA molecules.**
- ☛ **1972 , Paul Berg & Herb Boyer , produced first recombinant DNA molecules.**

Cohen & Boyer

- ☛ **November, 1972, meeting in Hawaii**
  - ☑ US-Japan joint meeting on bacterial plasmids
- ☛ **Stanley Cohen, Stanford, working on restriction enzymes**
- ☛ **Herbert Boyer, University of California, SF, working on plasmids**
- ☛ **cut plasmids, inserting genes, insert into bacteria**

March 1973, succeed

- ☛ **antibiotic resistance gene from Staphylococcus inserted in the E. coli**
  - ☑ tested by growing on antibiotics
  - ☑ RDNA comes of age
- ☛ **Technology quickly applied**
  - ☑ plasmids used to deliver genetic material
  - ☑ Escherichia coli used
- ☛ **1973, Joseph Sambrook , refined DNA electro-phoresis using agarose gel & ethidium bromide.**
- ☛ **1973, Annie Chang & Stanley Cohen , maintained a recombinant DNA molecule in E. coli.**
- ☛ **1975, International meeting at Asilomar, California.**

Applications

- ☛ **medically useful proteins**
  - ☑ insulin
  - ☑ growth hormone (somatistatin)
  - ☑ interferon
- ☛ **Other applications**
  - ☑ environment, bacteria that would eat oil spills
  - ☑ agriculture, nitrogen fixing property in all plants
  - ☑ energy, increase the production of alcohol, oil, etc.
  - ☑ repair genetic damage or defective genes
- ☛ **1971, James Watson letter to House**

- **1973, Gordon Conference on Nucleic Acids**
  - ☑ Maxine Singer, Heinrich Soll, letter to NAS
  - ☑ NAS committee established, headed by Paul Berg
- **1974, RDNA Committee issued three letters**
  - ☑ first called for moratorium on some experiments
  - ☑ second asked NIH to step in
  - ☑ third asked for an international conference
- **February 1975, Asilomar Conference, CA**
- **1975, NIH RDNA Advisory Committee (RAC)**

Analysis of the guidelines:

- **classified experiments as to level of danger, P1-P4**
- **recognized two types of containment**
  - ☑ physical
  - ☑ biological
- **Properly controlled, rDNA technology was safe**
- **Ethical issues not explored**

Public response

- **Boston, City Council adopted a resolution banning RDNA research in City limits**
  - ☑ effected Harvard and MIT
- **numerous law suits,**
  - ☑ Jeremy Rifkin, Ice-minus bacteria
- **University of Michigan, elaborate debate**
  - ☑ the delay caused some of our best researchers to leave

Recombinant DNA debate at UM

- **1974 UM sets up 3 committees**
  - ☑ Committee A, Social and Ethical
  - ☑ Committee B, Scientific
  - ☑ Committee C, Implementation
- **temporary moratorium**
- **similar debate nationally**
  - ☑ Asilomar Conference, CA
- **a few researchers leave**
  - ☑ do not want to slow research
  - ☑ no limitations in industry

Resolution

- **"safe" *E. coli* bacterium developed**

- ☑ cannot live outside laboratory

- ☛ **Committee A votes to proceed**
  - ☑ two no votes
- ☛ **installed P-3 labs**
- ☛ **by 1978, doing research**
  - ☑ lost valuable time
- ☛ **Questions**
  - ☑ should we have questioned research
  - ☑ what about academic freedom

RDNA research advanced rapidly

- ☛ **NIH issues guidelines, not policies**
  - ☑ Affect only publicly funded research
- ☛ **private corporations quickly set up for research and development**
- ☛ **by late 1970s, first genetically engineered products were coming on the market**
- ☛ **the moral issues never were solved and remain a problem today**

Stanford, Cohen-Boyer patent, Neils Reimer

- ☛ **April 1974, *New York Times* story**
- ☛ **Reimer called Cohen, inquired about patenting**
- ☛ **deal with UCSF**
  - ☑ split profits 50/50
  - ☑ Stanford 15% up front for administration
  - ☑ NSF, NIH, and American Cancer Society agreed to let Stanford administer for public benefit
- ☛ **November 4, 1974, Stanford took out the Cohen-Boyer patent**

Cohen-Boyer patent, continued

- ☛ **1975, Asilomar**
- ☛ **May 1976, Stanford internal meeting**
- ☛ **June 1976, press coverage**
- ☛ **July 1976, Senate hearings,**
- ☛ **March, 1978 NIH, Stanford can patent and license**
- ☛ **June 16, 1980, Supreme Court agreed that new bacterium could be patented**
- ☛ **December 1980, Stanford granted patent**
- ☛ **Genentech goes public**

Human genome project

- **1987, began the Human Genome Project:**
- **Goal, to fund the development of a comprehensive map of the human genome**
- **human genome consists of 50,000-100,000 genes**
- **genes are further divided roughly 3 billion base pairs**

Explanation:

- **23 pairs of chromosomes, have all characteristics, blueprint for life**
- **chromosomes made up of phosphate group, sugar (deoxyribose), and a base**
- **expressed DNA regions = genes, only part of total chromosome**
- **can only identify if regions vary producing varied characteristics (polymorphic markers)**

Mapping varies in resolution:

- **chromosomal map, made by microscopic observation and ways of marking**
- **more detailed maps made by cutting, duplicating, and characterizing**
- **2001 announced successful sequencing**
- **Number of genes still uncertain**
    - ☑ Ca. 30,000