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, 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

 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


 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