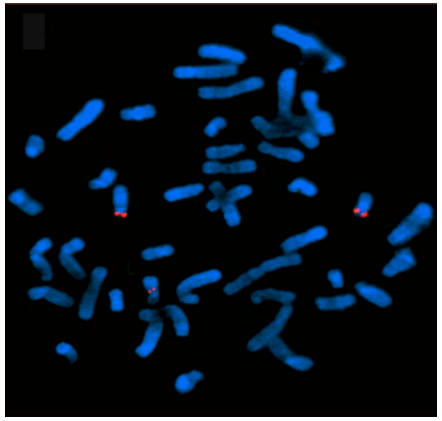

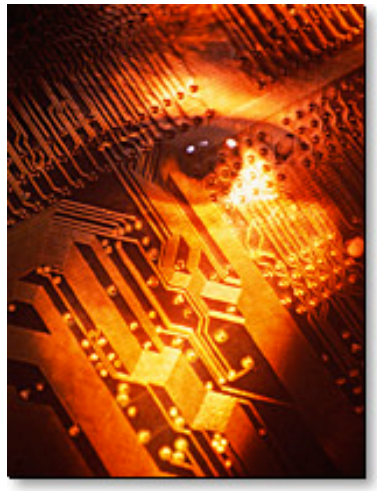

Intellectual Property, Genetics, and Medicine

Vineeta Agarwala
Final Project, BIO118Q
Professor Brutlag
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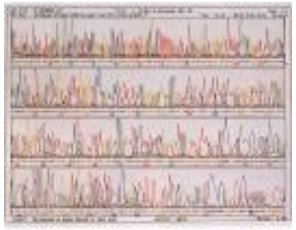
? Patentable or Not ?

- Genetically modified bacteria?

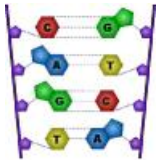
- A DNA sequence? Sequence with identified function?



- Discovery of a protein and its function in a disease?

- A gene sequence whose function is determined by computational comparison to known sequences rather than by traditional laboratory methods?

- A process that can be used to manipulate genetic information?



- A drug that can potentially save millions of lives in the developing world?

The Major Questions

As outlined recently by the WHO, there are two primary pressing questions that scientists and scholars must work to answer:

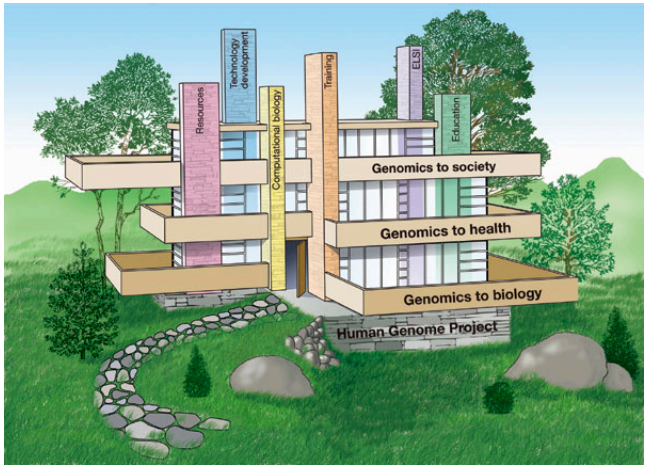
(1) “a general worry surrounding the appropriateness of intellectual property (IP) regimes for developing countries juxtaposed by an impetus toward increased global harmonization of patent policy”

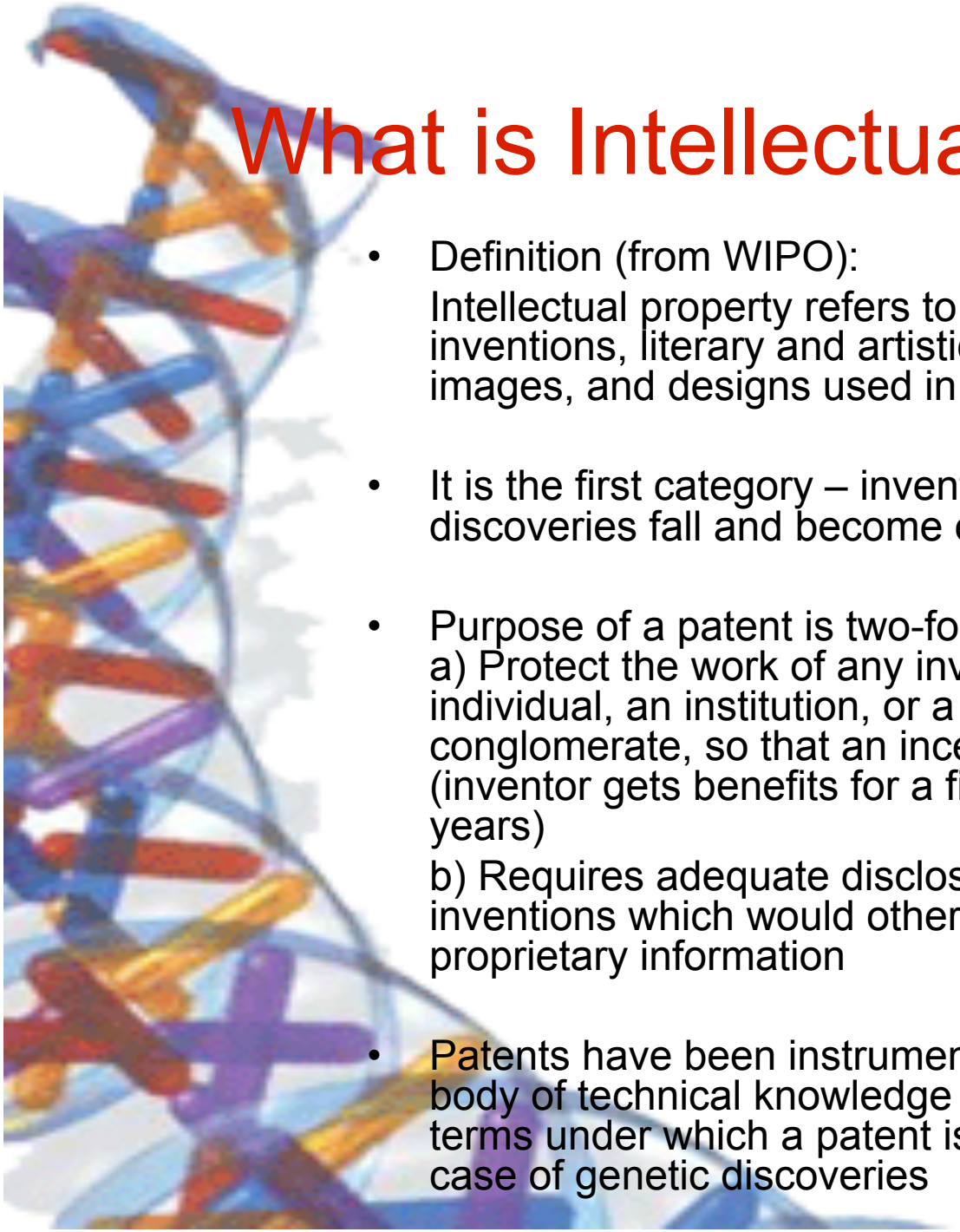
(2) “more specific to genomics, a concern around the adequacy and appropriateness of current national patent regimes to address questions of DNA patenting and commercialization of the human genome in both developing and developed countries”

The Challenge: Genomic IP

- NHGRI (National Human Genome Research Institute) has identified addressing intellectual property issues as one of the “Grand Challenges” for the future of genomics.

- In 2003, in a document entitled “A Vision for the Future of Genomics Research,” the Institute called for “the development of policy options in the area of intellectual property that will facilitate the widespread use of genetic and genomic information in both research and clinical settings.”





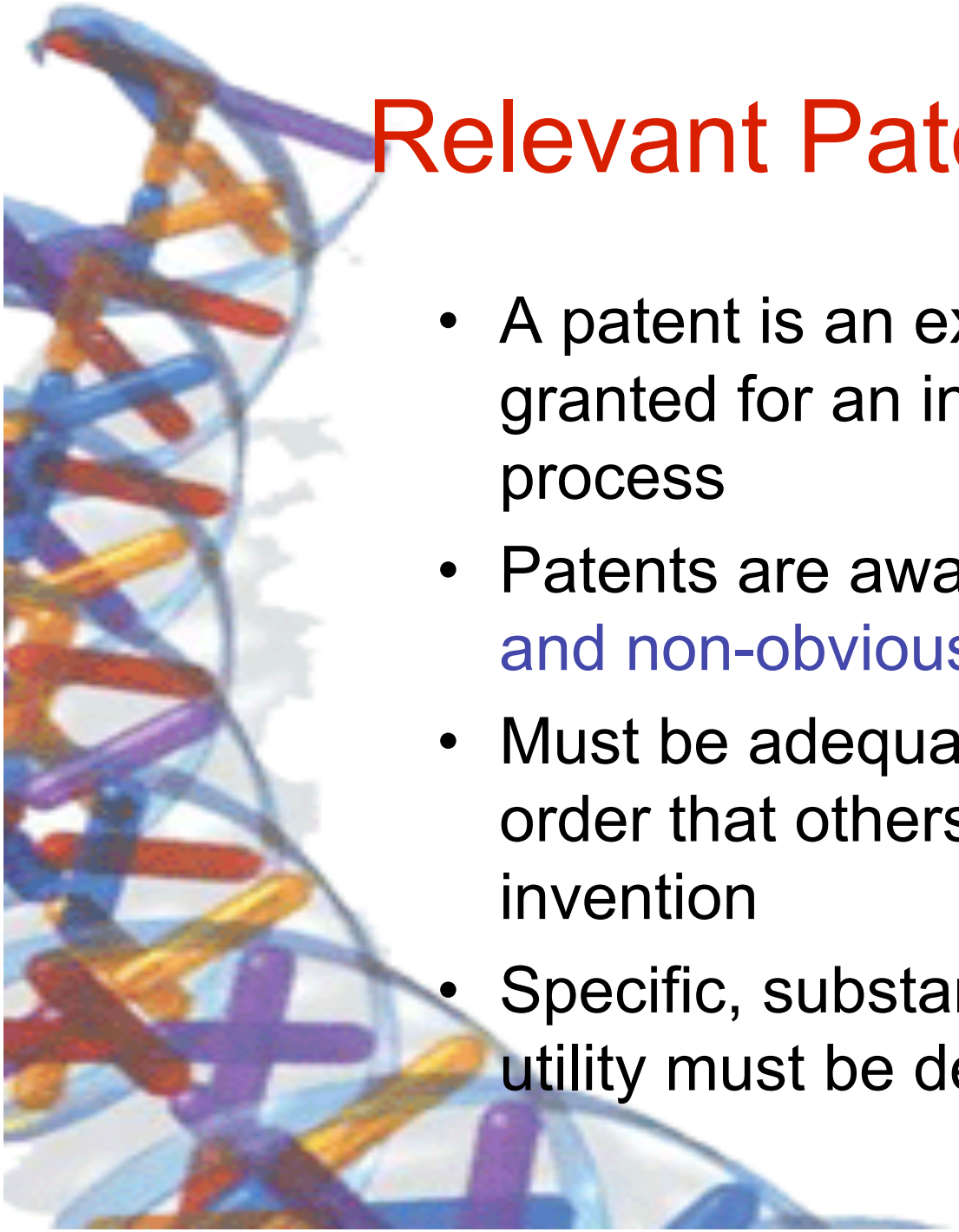
What is Intellectual Property (IP)?

- Definition (from WIPO):
  Intellectual property refers to creations of the mind: inventions, literary and artistic works, and symbols, names, images, and designs used in commerce.

- It is the first category – inventions – under which genetic discoveries fall and become eligible for patent protection

- Purpose of a patent is two-fold:
  a) Protect the work of any inventor, whether it is an individual, an institution, or a multinational business conglomerate, so that an incentive structure is in place (inventor gets benefits for a fixed period of time – about 20 years)
  b) Requires adequate disclosure of information about new inventions which would otherwise remain secret as proprietary information

- Patents have been instrumental in increasing the general body of technical knowledge in the world, but some of the terms under which a patent is granted become unclear in the case of genetic discoveries

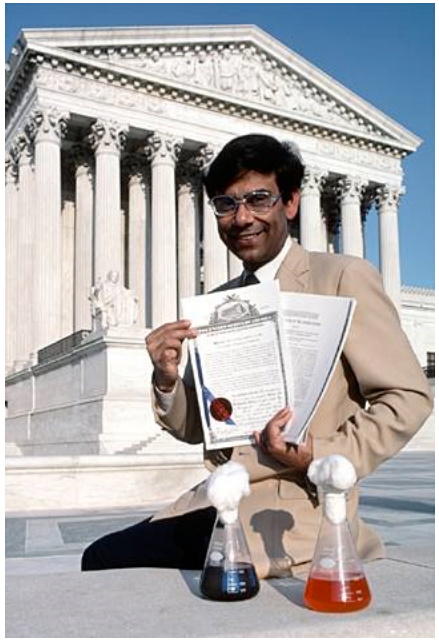


Relevant Patent Law

- A patent is an exclusive right granted for an inventive product OR process
- Patents are awarded for new, useful and non-obvious inventions
- Must be adequately described in order that others can use the invention
- Specific, substantial, and credible utility must be demonstrated

Legal Precedents

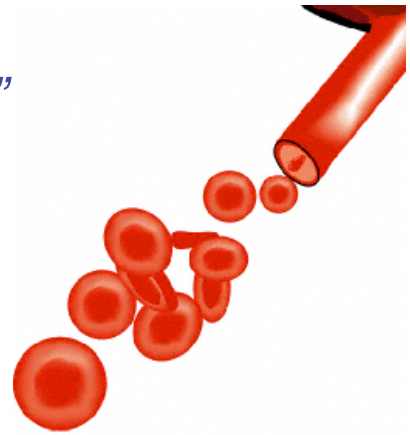
- 1966 – Chemical compounds must have real world utility in order to be patentable.
- *1980 - Diamond v. Chakrabarty* – Genetically engineered bacteria used to clear oil spills were patented. Court emphasized that patents could be awarded to "anything under the sun made by man."
- 1988 – First transgenic animal patented: the "Harvard OncoMouse" developed with increased susceptibility to tumors
- *1991 – Amgen v. Chugai* – DNA encoding erythropoietin (red blood cell production stimulant) is treated as a chemical compound that is patentable and distinguishable from other chemical compounds. The judge ruled that genetic material had never existed in nature in its inventive form until it was "removed, isolated, purified, and understood by man."
- However, the nucleotide sequence is required in addition to knowledge of the polypeptide which the gene encodes.

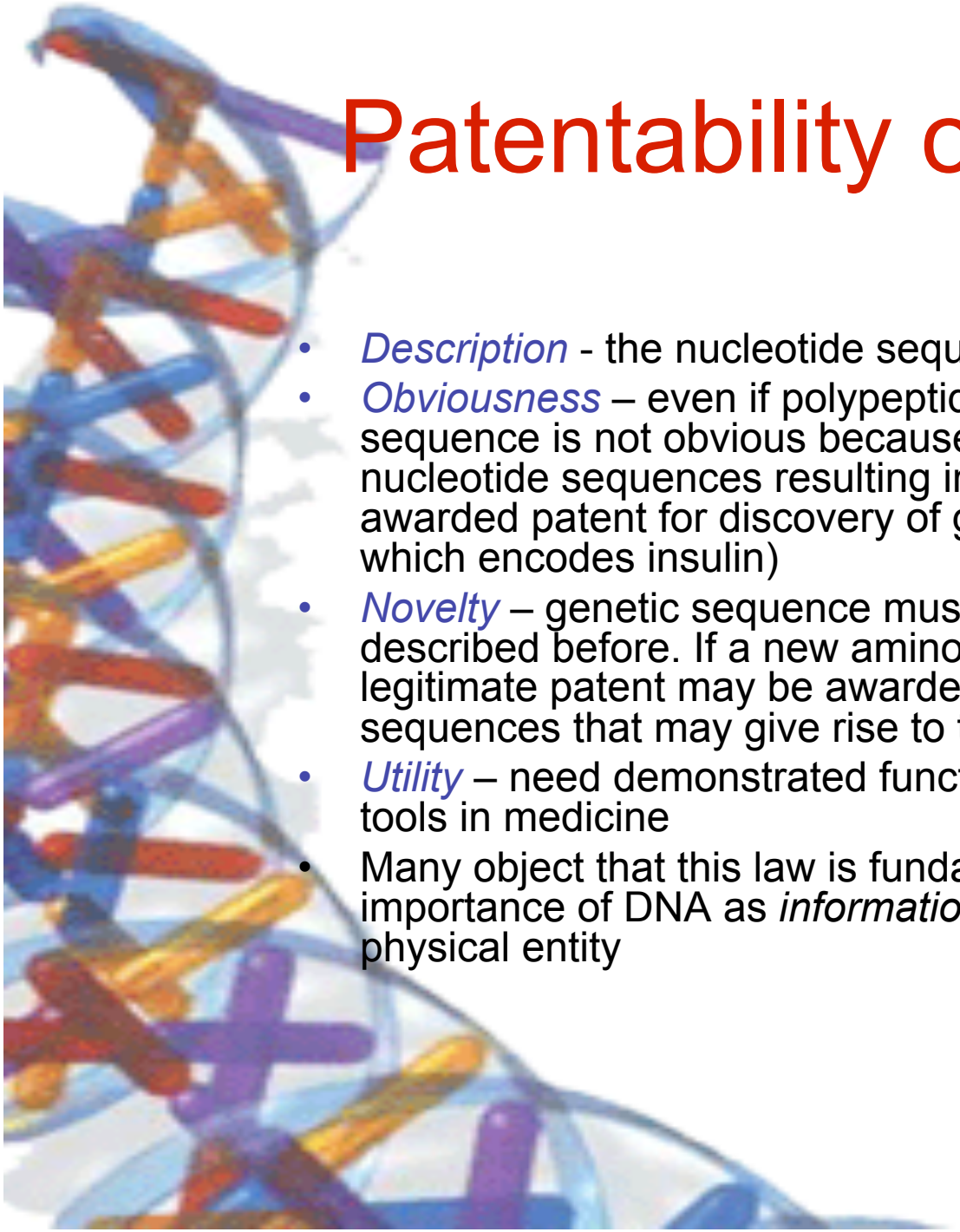


How can we patent DNA?

- Question that most people have asked: How can DNA be considered an invention when it resides naturally within our bodies?
- Answer given by Rebecca Eisenberg, leading expert on biotechnology patent law:

"Those of us who simply use the DNA in our own cells, as our ancestors have been doing for years, should not and need not worry about patent infringement liability. On the other hand, those of us who get shots of recombinant erythropoietin can in fairness expect to pay a premium to the inventors who made these interventions possible."



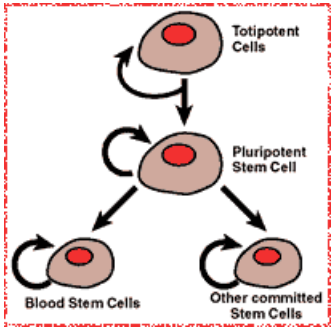


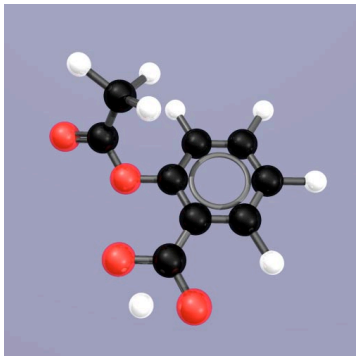
Patentability of Genes

- *Description* - the nucleotide sequence
- *Obviousness* – even if polypeptide sequence is known, the DNA sequence is not obvious because there are many possible nucleotide sequences resulting in same protein (1993 – court awarded patent for discovery of genetic sequence in *humans* which encodes insulin)
- *Novelty* – genetic sequence must be one that has not been described before. If a new amino acid sequence is discovered, a legitimate patent may be awarded for the class of genetic sequences that may give rise to that polypeptide
- *Utility* – need demonstrated function in research methods and/or tools in medicine
- Many object that this law is fundamentally ignorant of the importance of DNA as *information* rather than a chemical and physical entity

Objections to Gene Patents

- Many objections are made because people disagree with the actual biomedical science, not its patentability
- Stem cells provide a key example – two patents were awarded to the University of Wisconsin for purifying and isolating primate embryonic stem cells
- Others believe that genetics breakthroughs are “discoveries” rather than “inventions” because they are naturally occurring phenomena
- However, this view is less understandable since there was much less opposition to the patenting of chemical compounds that were naturally occurring (i.e. aspirin)





Religious Opposition

- Many religious groups became vehemently opposed to patenting genes
- 180 religious leaders representing various groups signed a joint appeal in 1995 and issued statements including:

"By turning life into patented inventions, the government drains life of its intrinsic nature and sacred value."

– Jeremy Rifkin, Foundation on Economic Trends

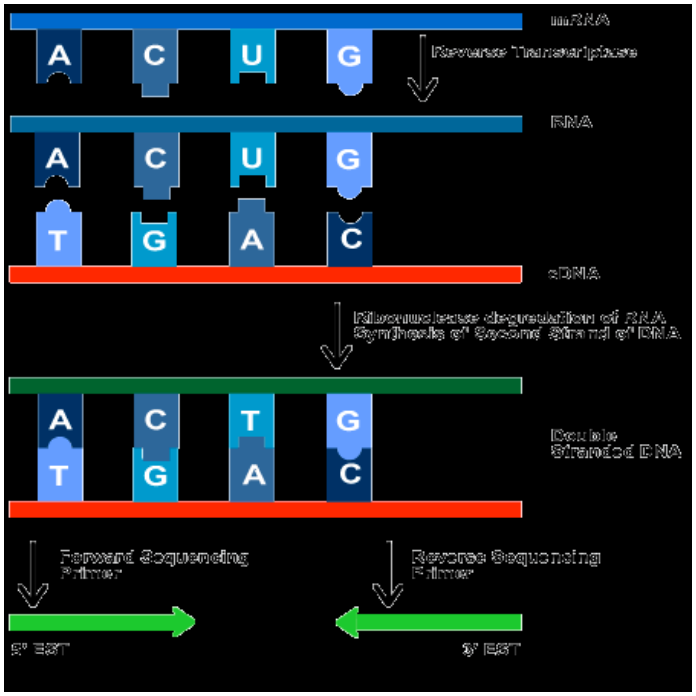
"Altering life forms…is a revolt against the sovereignty of God."

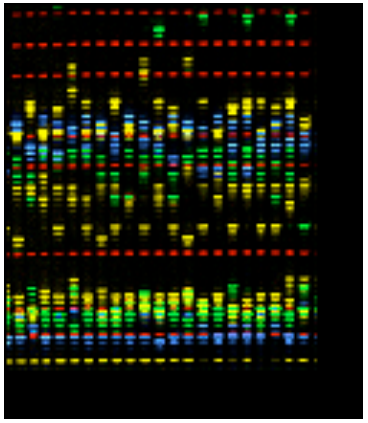
– Baptist cleric

- Similar sentiments to those being voiced right now in the debate over stem cells

Expressed Sequence Tags (ESTs)

Expressed Sequence Tags are sequenced portions of cDNA fragments, which are produced from mRNA

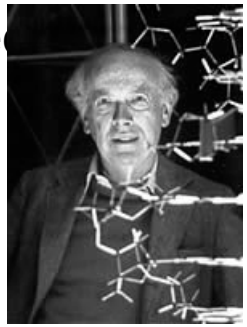


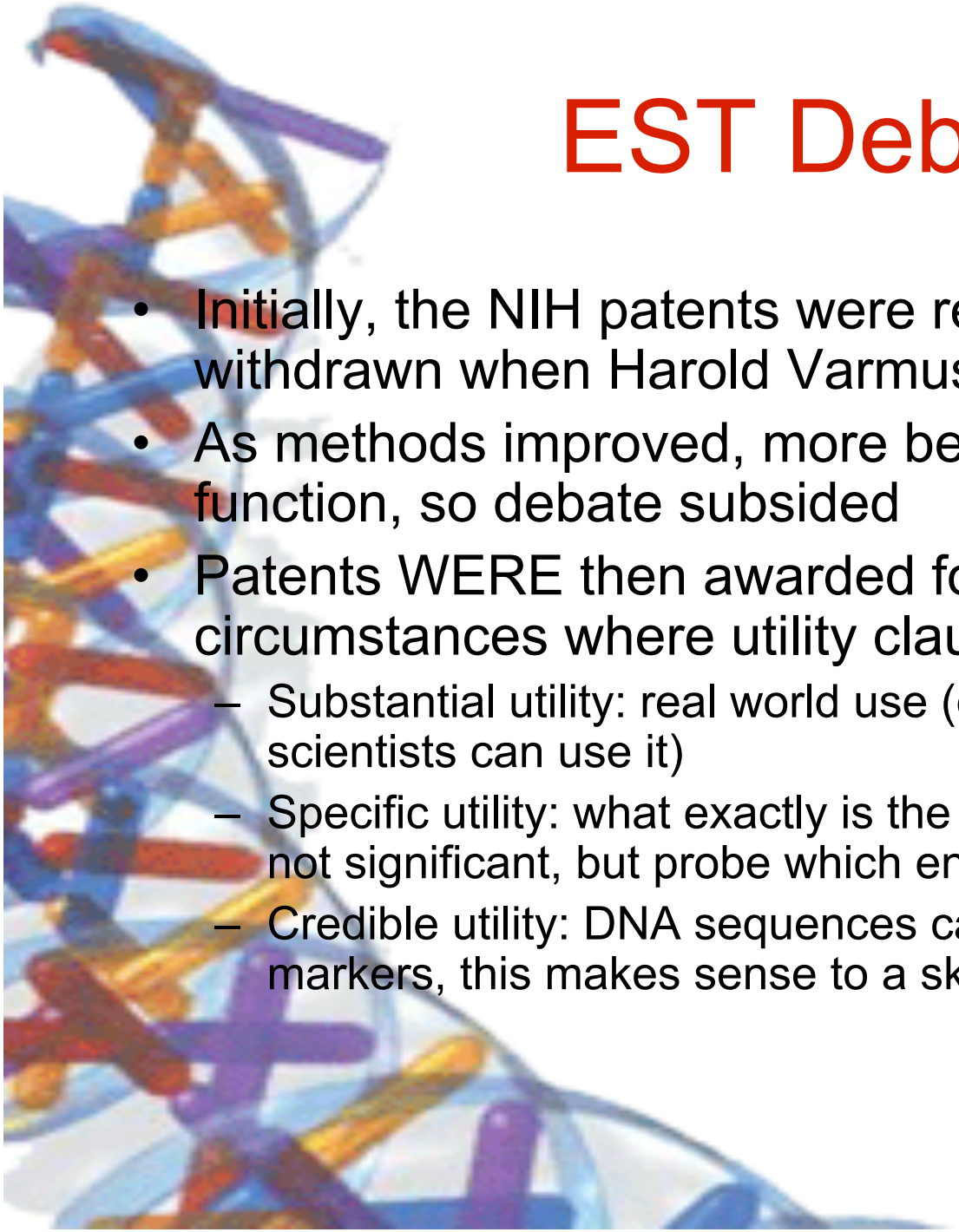


They are useful in probing for the presence of certain genes in various cells and tissues in various developmental stages, and allow scientists to study only those portions of the genome that are “important”

Debate over Patenting ESTs

- ESTs (Expressed Sequence Tags) are cDNA fragments with known sequence but often unknown function
- Structure vs. function: which is enough?
- Current law requires thorough description of sequence, and demonstrated function of the sequence in research, not necessarily exact biological function of protein
- In late 1990's patent office received over half a million applications for EST patents, largely filed by Craig Venter with the NIH
- Debate occurred over whether a research tool should be patented or made public to expedite advances
- Many respected scientists disagreed with the NIH position, and feared that future research would be hindered if EST gene fragments were patented
- James Watson called it "outrageous" and "sheer lunacy" and resigned as head of the NIH genome project
- European governments condemned it

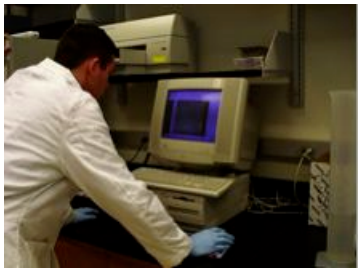




EST Debate

- Initially, the NIH patents were rejected, and then withdrawn when Harold Varmus took over NIH
- As methods improved, more became known about EST function, so debate subsided
- Patents WERE then awarded for EST sequences in circumstances where utility clause was satisfied:
  - Substantial utility: real world use (demonstration of how scientists can use it)
  - Specific utility: what exactly is the biological use (“gene probe” is not significant, but probe which enables locating gene X is)
  - Credible utility: DNA sequences can be used as diagnostic markers, this makes sense to a skilled scientist

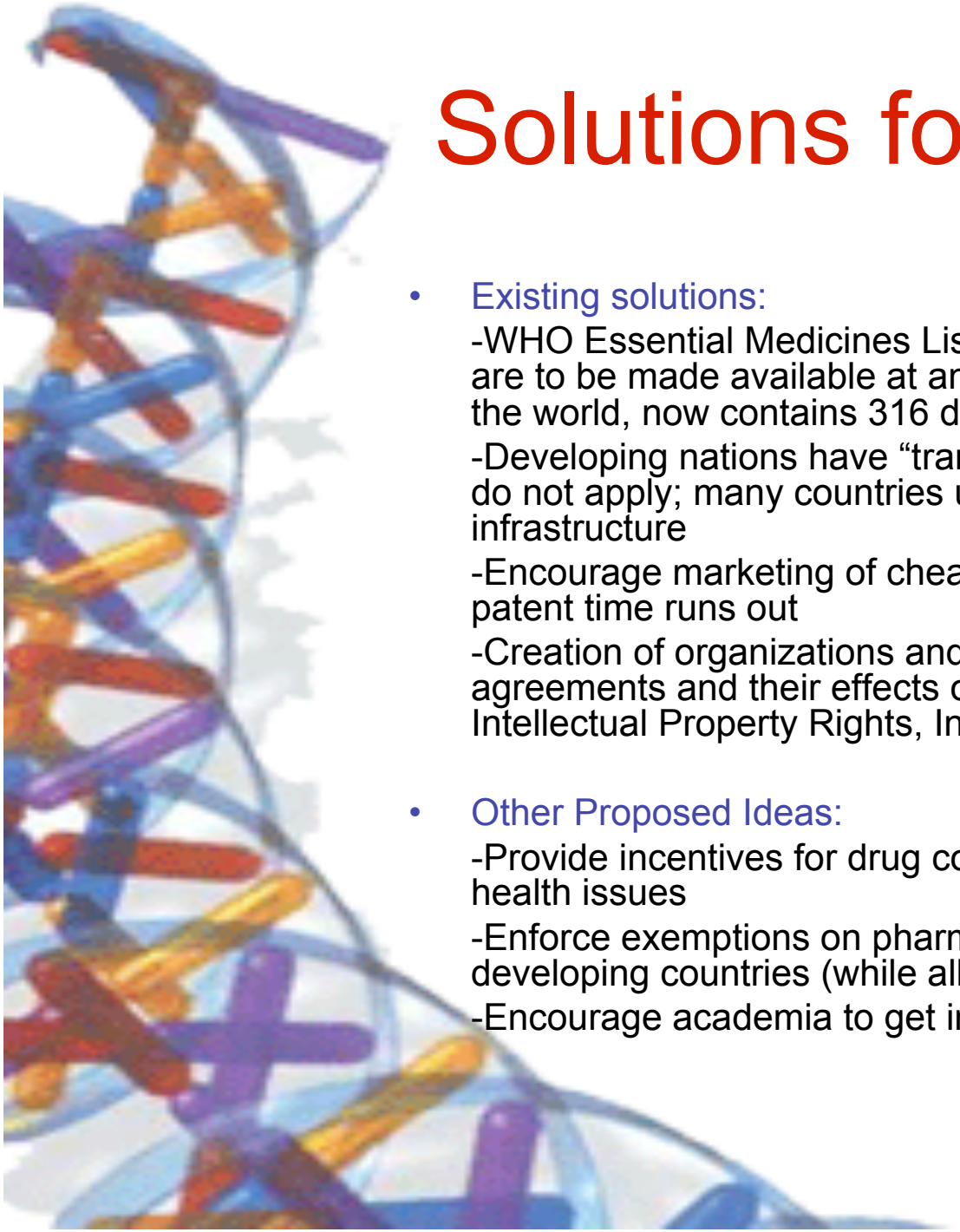
Computational Methods in Bioinformatics



- Methods used for patentable research are controversial
- Public notion that research must entail physical experimentation: in 2000 reporters described researchers who file for patents without “doing a single experiment or getting a pipette wet”
- Patent Act states: “Patentability shall not be negatived by the manner in which the invention was made”
- Thus, courts ruled otherwise, permitting bioinformatics discoveries to be patented
- Use of consensus sequences, BLAST searches with high thresholds (at least 10^-8 for protein sequences) yielded patent awards
- Current status of the law permits patents for sequences with function determined solely by homology (NIH opposed this)

Third World IP Policy

- Dilemma arises because often drugs don't reach developing world due to cost
- However, eliminating patent rights over pharmaceuticals is not a viable solution because drug development is expensive and incentive structure is vital
- History shows that biotechnology "follows profits"; for many years now companies have focused on drugs that targeted not infectious diseases afflicting millions but rather 'diseases of the rich' such as depression and impotence



Solutions for Public Health

- Existing solutions:

  -WHO Essential Medicines List (created in 1977)– drugs which are to be made available at an affordable price to people around the world, now contains 316 drugs, over ten of which are for AIDS

  -Developing nations have “transition period” during which patents do not apply; many countries use this time to develop infrastructure

  -Encourage marketing of cheaper generic products as soon as patent time runs out

  -Creation of organizations and coalitions which monitor trade agreements and their effects on health, ie Commission on Intellectual Property Rights, Innovation, and Public Health

- Other Proposed Ideas:

  -Provide incentives for drug companies to direct R&D at global health issues

  -Enforce exemptions on pharmaceutical products sold in developing countries (while allowing profits in developed world)

  -Encourage academia to get involved in public health effort

Role of Academia

- Bayh-Dole Act allowed patent rights for academia – inventions made with federal funding are patentable

- However, many feel that universities should focus on “neglected” diseases rather than go after patents

  -April 21, 2005: Nature published article criticizing universities, an editorial advocated internal incentives for research on diseases with lower potential patent revenue

- Effect of commercial patents on research in academia:

  -Research exemption, but this has been weak

  -Studies have shown that patents have led to a decline in certain clinical testing at major medical centers and hospitals due in large part to increased costs

Conclusions

- Need intellectual property protection for open disclosure of discoveries and incentive system
- Genetic material can be patented if it meets the requirements for other inventions, but we must be weary of the distinction between information and tangible matter
- Drug discovery is depending increasingly upon genetic advances, and it is important that incentives exist such that neither is kept hidden
- Exceptions must be made in patent law, however, for biomedical innovations due to the stark consequences of unaffordable pricing in the developing world

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