

The Human Genome Project

The Science, the Applications and the Issues

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Outline of this Presentation

- Video Introduction to the Human Genome Project (HGP)
- Introduction to the molecular biology of the human genome
- History of the HGP
- Video on how the human genome was sequenced
- Developments after the release of the first draft
- Benefits and general applications of the Human Genome Sequence (HGS)
- Video on ethical, legal and social issues (ELSI)
- Conclusion

Exploring our molecular selves

From "The Human Genome Project" CD-ROM produced by the National Human Genome Research Institute, National Institutes of Health (US)

The Human Genome

- Genome: the totality of genetic information in an organism
- 23 chromosomes (diploid content = 46)
- ~100,000 genes
- ~ 3 billion bases
- just the genome sequence alone would require 3 gigabytes of computer storage space

The Human Genome

***From Genes to Proteins:
How our genome makes us what we are
(with help from the environment)***

History of the Human Genome Project (HGP)

- The US Department of Energy (DOE) and the Human Genome
- 1983 - National Laboratories of the DOE begin producing libraries of human chromosomes
- 1988 - DOE and US National Institutes of Health (NIH) sign a memorandum of understanding outlining their cooperative effort in genome research

History of the HGP

- 1988 - HUGO (Human Genome Organization) founded by genome scientists
- 1989 - DOE and NIH establish a working group to study the Ethical, Legal and Social Implications (ELSI) of the HGP
- 1990 - DOE and NIH present a 5-year HGP plan to the US Congress. This marks the beginning of the 15-year project

History of the HGP

- 1998- Celera Genomics and Incyte Pharmaceuticals (both private companies) announce plans to sequence the human genome before the public funded HGP is completed
- 2000- Craig Venter of Celera and Francis Collins of NIH (representing the HGP) jointly announce the completion of a "working draft" of the human genome
- 2001 - Publication of the Human Genome Sequence in the journals *Nature* and *Science*

History of the HGP: From bacteria to humans

- 1995- First bacteria genomes to be sequenced completely (*Haemophilus influenzae* and *Mycoplasma genitalium*)
- 1996- yeast genome completed (*Saccharomyces cerevisiae*)
- 1998- worm genome completed (*Caenorhabditis elegans*)
- 1999- sequence of first human chromosome (chromosome 22) completed
- 2000- "working draft" of the entire human genome completed

Project Goals of the HGP

- Identify all the 100,000 genes in the human genome
- Complete the sequence of 3 billion bases of the human genome
- Store the human genome information in databases
- Develop tools for analysis of the data
- Transfer technologies to the private sector
- Address the ELSI that may arise from the HGP

Whose DNA was actually sequenced?

- The HGP sequenced a composite genome from several different people
- The sequence was generated from 10 to 20 primary samples that were taken from many anonymous donors
- Donors belong to diverse ethnic and racial backgrounds

How was the Human Genome sequenced?

From "The Human Genome Project" CD-ROM produced by the National Human Genome Research Institute, National Institutes of Health (US)

Information derived from the HGP

- ▶ size of human genome: 3.1647 billion base pairs (bp)
- ▶ number of human genes: ~30 000
- ▶ genes vary in length and can cover thousands of bases
avg. size: ~3,000 bp
- ▶ less than 2% of the human genome codes for proteins
- ▶ ("junk DNA") make up at least 50% of the human genome
- ▶ almost all (99.9%) nucleotide bases are exactly the same in all people

Benefits and Applications

- Medical benefits
- Microbial genome research
- DNA forensics
- Evolution and human migration
- Risk assessment

Benefits of HGP Research Medical Benefits

- ▶ improved diagnosis of disease
- ▶ earlier detection of predispositions to disease
- ▶ rational drug design
- ▶ gene therapy and control systems for drugs
- ▶ pharmacogenomics "personal drugs"
- ▶ organ replacement

DNA in a bottle

Benefits of HGP Research Microbial Genome Research

- ▶ environmental monitoring
- ▶ protection from biological and chemical warfare
- ▶ safe, efficient toxic waste cleanup



Pictures from Microsoft™ XP

Benefits of HGP Research DNA Forensics

- ▶ identify potential suspects at crime scenes
- ▶ identify crime and catastrophe victims
- ▶ establish paternity and other family relations
- ▶ match organ donors with recipients in transplant programs

Benefits of HGP Research Risk Assessment

- assess health damage and risks caused by exposure to:
 - mutagens
 - radiation
 - cancer-causing toxins
- reduce the likelihood of heritable mutations

What remains to be done on the “working draft” of the human genome

- Proofread
- Fill gaps
- Sequence the remaining 7%
- Find all the Open Reading Frames (ORFs)
- Find the genes that do not code for proteins
- Find the regulatory sequences
- Elucidate interactions between genes and other molecules
- Identify gene functions

Recent Developments since February 2001

- January 2003 – human chromosome 14 sequence completed
- December 2002 – draft of mouse genome sequence completed
- December 2001 - Human chromosome 20 sequence completed
- Goal: finish human genome sequences 100% by 2003

Ethical, Legal and Social Implications (ELSI) of HGP

ELSI of HGP

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Please remember...

- That we are greater than the sum of our parts (or genes)
- That our genes do not determine by themselves our fates
- That genetic information can be powerful, and can do both harm and good

Sources of all images and information

Except when otherwise indicated

- www.ornl.gov/hgmis and links therein
- Videos were from “The Human Genome Project” CD-ROM produced by the National Human Genome Research Institute, National Institutes of Health (US); www.nhgri.nih.gov

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