Genetic Variation

- Chromosomal
  - Duplications/Deletions
- Sequence variation
  - Single mutation in gene
- SNP

Single Nucleotide Polymorphism
Linkage analysis

Graphics from NCI Understanding Gene Testing
Why SNPs in Mapping?

• Numerous
• Stable
• Easy to score
• In genes (sometimes)
GATACAATGCATCATA
GATGCAATG\textcolor{red}{T}\textcolor{red}{A}\textcolor{red}{T}\textcolor{red}{C}\textcolor{red}{A}\textcolor{red}{T}\textcolor{red}{A}\textcolor{red}{T}\textcolor{red}{C}\textcolor{red}{A}\textcolor{red}{T}\textcolor{red}{A}\textcolor{red}{T}CATA
GATGCTATGCGCATCATA
Human SNPs

• 2 chromosomes differ ~1/1,000 bases

• More chromosomes → more sites

• Potential for 30 million variable sites

• Expanded type of study design for genetic studies
SNP Genotyping Tools

330,000-650,000 SNPs per array

Courtesy, S. Gabriel NHGRI
Increase in Genetic Information

• High throughput technologies have increased ability to generate genotypes

• Lead to increase in “collections” of data:
  – Independent lab studies
  – Consortium studies: HapMap
  – “Open source”
  – Forensic

• Even small studies can hold large datasets
  – CNSS study generated 1.8M genotypes
Sources of Genetic Information

• Not only nuclear DNA!
  – RNA
  – Protein
  – Mitochondrial

• Many tissues - all cell types
  – Blood
  – Skin
  – Paraffin samples after surgery

• Family History
Genetic Information- who cares?

- Permanent
- Personal
- Powerful
- (Potentially) Predictive
Genetic Information

• Permanent
  – DNA is stable and easily stored
  – Database genetic information
  – Confidential

• Personal
• Powerful
• (Potentially) Predictive
Genetic Information

• Permanent
• **Personal**
  – Individual Information
  – Family Information
• Powerful
• (Potentially) Predictive
Genetic Information

- Permanent
- Personal
- **Powerful**
  - Genetic code of life
  - Linkage to health and disease
  - Links an individual to family
    - Paternity/Maternity
  - Forensic
- (Potentially) Predictive
Genetic Information

- Permanent
- Personal
- Powerful
- (Potentially) Predictive
  - Susceptibility markers disease
  - Diagnostic tests
ELSI: Ethical, Legal, and Social Issues

• Privacy and confidentiality of genetic information.

• **Fairness in the use of genetic information** by insurers, employers, courts, schools, adoption agencies, and the military, among others.

• **Psychological impact, stigmatization, and discrimination** due to an individual’s genetic differences.

• **Reproductive issues** including adequate and informed consent and use of genetic information in reproductive decision making.

• **Clinical issues** including the education of doctors and other health-service providers, people identified with genetic conditions, and the general public about capabilities, limitations, and social risks; and implementation of standards and quality-control measures.

U.S. Department of Energy Genome Programs, Genomics and Its Impact on Science and Society, 2003
ELSI Issues (cont.)

• Uncertainties associated with gene tests for susceptibilities and complex conditions (e.g., heart disease, diabetes, and Alzheimer’s disease).

• Fairness in access to advanced genomic technologies.

• Conceptual and philosophical implications regarding human responsibility, free will vs genetic determinism, and concepts of health and disease.

• Health and environmental issues concerning genetically modified (GM) foods and microbes.

• Commercialization of products including property rights (patents, copyrights, and trade secrets) and accessibility of data and materials.
From Genes to Proteins

Genes contain instructions for making proteins.

Proteins act alone or in complexes to perform many cellular functions.
METABOLIC PATHWAYS

- Carbohydrate
- Energy
- Lipid
- Nucleotide
- Amino Acid
- Other Amino Acids
- Complex Carbohydrates
- Complex Lipids
- Cofactors and Vitamins
- Macromolecules
The Next Challenge...

Individual

Family

Society