Chapter 1: Introduction to Genetics

Introduction

- December 1998: deCODE Genetics was granted the right to access the medical records of 270,000 Icelandic residents to create a database. They cross-referenced this information with the Health Sector Database as well as the genealogical database from the National Archives. Ended in 2012.
- Other large-scale databases have developed in Great Britain, Estonia, Latvia and the Kingdom of Tonga.
- Used to analyze human genes for susceptibility to diseases.
- Iceland was selected due to the high level of genetic relatedness within its population, which began 1000 years ago from Scandinavian and Celtic sources. In addition, the health care system is state-supported which allows for good medical records.
- Causes debates over privacy, consent and commercialization.

1.1 Genetics has a Rich and Interesting History

Introduction

- Domestication of animals and cultivation of plants lends itself to the recognition of traits many years ago.
- *On the Seed* by Hippocrates suggested that "humors" in the male parts of the body accounted for offspring's traits.
- Aristotle proposed that the male semen contained "vital heat" which produced offspring similar to the parent.

1600-1850: The Dawn of Modern Biology

- 1600s: William Harvey proposed epigenesist in which an organism follows developmental events following fertilization of an egg.
- Contradicts **preformation:** the fertilized egg contains a miniature adult called a **homunculus.**
- 1830: Matthias Schleiden and Theodor Schwann proposed **cell theory:** organisms are composed of basic units called cells that are derived from similar preexisting structures.
- **Spontaneous generation:** creation of living organisms from non-living components; disproved by Louis Pasteur.

Charles Darwin and Evolution

- *The Origin of Species* published in 1859 by Darwin describing evolutionary ideas.
- He believed existing species evolved over time from preexisting ones.
- **Natural selection:** the most favorable traits will be carried on; explanation for mechanism of evolutionary change; based on the observation of Alfred Russel Wallace that an environment has more organisms than it can support, leading to competition; individuals that can adapt and posses heritable traits survive.
- Darwin lacked genetic knowledge of variation and inheritance.

- Gregor Mendel published his paper on the inheritance of traits using pea plants in 1866. Showed how traits are inherited. His research was not well known until 1900s.
- **Chromosomal theory of inheritance:** closed the gap in Darwin's theory; heredity and development depend on genetic information in genes, contained in chromosomes and passed on through gametes.

1.2 Genetics progressed from Mendel to DNA in less than a century

Mendel's Work on Transmission of Traits

- Pea plants; decade long experiment; Augustinian monk.
- Showed that traits are passed from parents to offspring in predictable ways
- **Genetics:** branch of biology concerned with heredity and variation

Chromosome Theory of Inheritance: Mendel and Meiosis

- 20 years after Mendel's work, we discovered chromosomes.
- **Diploid number (*2n*):** number of chromosomes; 46 in humans
- **Homologous chromosomes:** chromosomes in diploid cells exist in pairs
- **Haploid number (*n*):** cells produced from meiosis only receive one chromosome from each pair.
- **Mitosis:** chromosomes copied; each daughter cell receives identical set of chromosomes to parent.
- **Meiosis:** gamete formation; cells receive one chromosome from each chromosome pair.
- Walter Sutton and Theodor Boveri: behavior of chromosomes in meiosis is similar to behavior of genes in gamete formation noted by Mendel.
- **Chromosome theory of inheritance:** inherited traits controlled by genes on chromosomes that are transmitted through gametes; genetic continuity throughout generations.

Genetic Variation

- *Drosophila melanogaster*: fruit fly used for studying inheritance of traits.
- **Mutation:** heritable change in DNA sequence; source of genetic variation
- **Allele:** alternative forms of a gene
- **Phenotype:** observable features, such as eye color
- **Genotype:** set of alleles for a given trait
- Geneticist can map the location of a gene on the chromosome using mutations

The Search for the Chemical Nature of Genes: DNA or protein?

- White-eye mutation in fruit flies showed that he trait was on a single chromosome.
- Proteins and DNA are major chemical components of chromosomes
- 1944: researchers at Rockefeller Institute showed that DNA carried genetic information in bacteria; did not convince many scientists.
- Further work on viruses proved that DNA, not protein, carried genetic information and scientists turned their attention toward deducing the structure.

1.3 Discovery of the Double Helix

Structure of DNA and RNA

- 1953: James Watson and Francis Crick described structure of DNA; along with Maurice Wilkins they received the Nobel Prize in 1962.
- Each linear strand of DNA is made up of **nucleotides:** A (adenine), G (guanine), T (thymine) or C (cytosine).
- The two strands of DNA are complements of each other AT and CG are pairs.
- RNA contains ribose instead of deoxyribose (in DNA).

Gene Expression

- Phenotype is expressed as a result of the order of the nucleotides in DNA through a series of steps.
- **Transcription:** in eukaryotes, one strand of DNA is used to construct a complementary strand of RNA. That RNA molecule moves to the cytoplasm where the mRNA binds to the **ribosome.**
- **Translation:** the synthesis of proteins under the instruction of mRNA.
- **Genetic code:** the information encoded in the mRNA; series of nucleotide triplets called **codons.**
- There are 20 different amino acids found in proteins.
- **TRNA:** transfer RNA; assembles proteins; recognize the code in the RNA and carry the correct amino acids to construct the protein in translation.

Proteins and Biological Functions

- Proteins are end product of gene expression
- Diversity of life arises from proteins that are long and each position can be one of 20 amino acids.
- **Enzymes:** biological catalysts; largest category of proteins; allows cellular metabolism to happen at body temperature and lower activation energies
- **Hemoglobin:** oxygen binding molecule in red blood cells
- **Insulin:** pancreatic hormone
- **Collagen:** connective tissue molecule
- **Actin and Myosin:** contractile muscle proteins

Linking Genotype to Phenotype: Sickle Cell Anemia

- Caused by mutant form of hemoglobin
- A mutation in the beta-globin causes a change in one DNA nucleotide, change in codon 6 in mRNA, GAG to GUC.
- A person with two mutant copies of the genes has sickle cell anemia.

1.4 Development of Recombinant DNA Technology

- **Restriction enzymes:** used by bacteria to cut DNA of invading viruses; can be used to produce a reproducible set of fragments
- **Vectors:** carrier DNA molecules; insertion of DNA fragments into vectors that form **recombinant DNA.**