Week 1: Introduction to the unit

- 80% attendance is required to pass the unit.
- Students must achieve 45% on the combined mid semester examination and final examination.
- Students must achieve a final grade of at least 50%

What is genetics?

- Study of genes (unit of heredity) and genetic variation
    - Heredity: transfer of genetic information from one generation to the next
    - Variation: changes in genetic information during heredity (mutation)

What is a genome?

- A genome is a complete set of genetic instruction for any organism.
- All genomes are encoded in nucleic acids – either DNA or RNA

What is genomics?

- Study of the content, organization, and function of genetic information in a whole genome is defined as genomics.

Genetic material: key features

- Must contain complex information.
    - Repository of genetic information (whole genome)
- Must replicate.
    - Mitosis/meiosis
- Must encode the phenotype (expression)
    - Flow of genetic information (central dogma)
- Variability
    - Germline mutation, evolution

DNA (RNA) as genetic material: evidence

- Location (nucleus)
- Stability (metabolism)
- Mutation (sensitive)
- Amount (proportional to chromosome sets)

Genetics: examines the composition, function, effects and inheritance of a single gene or a small number of genes, where as

Genomics: addresses all genes within a genome and their inter-relationships as well as their interactions with the environment to identify their combined influence on the development, metabolism, and function of the organism.

Epigenetics: any inheritable influence on gene activity that does not involve a change in DNA sequence.

Divisions of Genetics

1. Transmission (classical) Genetics: Divisions (based on Mendel's 1st and 2nd laws)

    a. How an individual organism inherits its genetic makeup and how it passes its genes to the next generation (Mendel's law of segregation and independent assortment)
2. Molecular genetics (based on the Central Dogma of Molecular Biology)
    a. How genetic information is replicated, encoded, and expressed (chemical nature of genes, gene structure, organization, and function)
3. Population (and Evolutionary) genetics (based on the theory of Natural Selection proposed by Darwin and Wallace)
    a. Genetic composition of populations
    b. What genetic composition changes over time?
    c. Hardy-Weinberg equilibrium
        i. Constant allele and genotype frequencies from generation to generation without influences from other evolutionary forces

- Structural genomics determines the DNA sequences of entire genomes.
    - i.e., organization and sequence of genetic information contained within a genome.
- Functional genomics determines the functions of genes by using genomic-based approaches.
    - transcriptomics
    - proteomics
- Comparative genomics studies how genomes evolve.
- Phenotype or trait: the appearance or manifestation of a characteristic
    - Traits are not inherited directly. Genes are inherited and along with environmental factors determine the expression of traits.

What is a Chromosome?

- A chromosome is a single DNA molecule with associated DNA bound proteins.

A function chromosome has three essential elements.

- A centromere
- A pair of telomeres at each end
- Origins of replication (not visible microscopically): where DNA synthesis begins.

Centromere

- Constricted region of chromosome (segment of DNA) where kinetochore assembles.
- Kinetochore is a protein complex to which spindle microtubules attach during cell division.

Kinetochore

- The central role of kinetochore is chromosome segregation.
- The kinetochore is a conserved protein complexes that bind to spindle microtubules and regulate chromosome segregation.

Chromosome Mutations

- Variation in the structure and number of chromosomes.
- Two types:
    - Chromosome rearrangements: duplications, deletions, inversion, translocation
        - Unbalanced
            - Duplications (insertion)
                - Doubling of part of a chromosome

        - Effects:
            - Often result in abnormal phenotype
            - Unbalanced gene dosage
            - Extra copies of gene do not pair in meiosis
            - Chromosome is more likely to break at duplicated region during meiosis.
            - Slows down cell division.
    - Deletions
        - Loss of a chromosome segment
        - Effects:
            - Imbalances in gene product
            - Expression of a normally recessive gene
            - Haploinsufficiency
- Balanced
    - Inversion
        - A chromosome segment invert – turned 180 degrees.
        - Inversion causes breaks in some genes and may move others to new locations.
        - Inversions in meiosis:
            - Individuals homozygous for an inversion: no problems during meiosis
            - Individuals heterozygous for inversion: problems occur.
    - Translocation
        - Robertsonian translocation
            - Joining between two long arms and two short arms of two acrocentric chromosomes producing a large metacentric and a very small chromosome
        - Movement of genetic material between nonhomologous chromosomes or within the same chromosome
            - Nonreciprocal
            - Reciprocal
- Changes in the number of chromosomes: aneuploidy, polyploidy

ANEUPLOIDY: change in the number of individual chromosomes

- Nullisomy: loss of both members of a homologous pair of chromosomes, 2n-2
- Monosomy: loss of a single chromosome, 2n-1
- Trisomy: gain of a single chromosome, 2n+1
- Tetrasomy: gain of two homologous chromosomes, 2n+2
- Can involve autosomes as well as sex chromosomes.
- Effect
    - Disrupts gene dosage.
    - Often has severe phenotypic effects.

POLYPLOIDY: change in the number of chromosome sets

Week 2: DNA Structure and Mutations

- DNA -> chromatin -> nucleosome -> chromatosome -> compaction -> chromosome

- Nucleic acids
    - DNA
    - RNA
- Composed of repeating units.

DNA consists of two complementary and antiparallel nucleotide strands that form a double helix.

Special structure can form in DNA and RNA.

- Hairpin structure in single strands of nucleotides, when sequences of nucleotides on the same strand are inverted complements, a hairpin structure forms.
- DNA methylation: methyl groups added to nucleotide bases.

Human cells contain over two meters of DNA.

- Packing process must change during the cell cycle in response to cellular processes.

Euchromatin and heterochromatic

- Euchromatin: undergoes normal processes of condensation and recondensation during cell cycle.
- Heterochromatic: remains condensed throughout the cell cycle, even during interphase

Histones

- Five major types
    - H1
    - H2A
    - H2B
    - H3
    - H4
- They are small, positively charged proteins.

Non-histone Proteins

- Help fold up and pack DNA into chromosome.
- Make up the kinetochore and constitute molecular motors help to move chromosomes during cell division.

Nucleosome: the fundamental repeating unit of chromatin

- Nucleosome is a core particle of chromatin consisting of DNA wrapped about two times around on octamer of eight histone proteins.

Tertiary chromosome structure

- Helix model: nucleosomes arranged in a twisted or supercoiled zigzag ribbon.

Chromatin vs Chromosomes

Chromatin	Chromosomes
- In the nucleus, the DNA double helix is packaged by histones to form chromatin. - Represent DNA folded on nucleoproteins by magnitude of 50.	- The chromatin undergoes further condensation to form the chromosome. - Chromosomes are higher order DNA organization, where DNA is condensed at least 10,000 times onto itself.