Biology 5.4
Mutations: Chromosome and Gene Changes

Review of Inheritance

1. Genetics is the study of inheritance
2. Chromosomes are DNA molecules that include segments of codes called genes.
3. DNA is a very dynamic, adaptable molecule and capable of changing.
4. 100-200 changes in the DNA molecule are inherited by each new generation.
5. Gamete formation occurs by meiosis to make inheritance of genetic code possible.
6. Central dogma: DNA transcribes to RNA, which is translated to protein.
7. Change can occur in the DNA, RNA, and/or the protein.

Mutations in the DNA

1. Change in DNA is called mutation
   a. Gene Mutations affect the nucleotide sequence of the genetic code.
   b. Chromosome Mutations affect the number of chromosomes or gene arrangement
2. Change in the genotype may or may not be expressed in the phenotype.
3. Wild type is the common, unchanged DNA in a species population.

Polymorphisms

1. Normal and common phenotype differences within the same species.
2. Differences are common traits in a species (more than 1% of the population). (Green eyes, brown eyes, blue eyes)
3. Differences are **not** new mutations.
4. Monomorphism describes one form of a trait in a species. Dimorphism is two forms.
5. General classification: Genotype and phenotype polymorphisms.
6. Does not include new mutations or rare differences in a species population.
7. SNPs (single nucleotide polymorphisms) are most common, and occur about one in 300 nucleotides.

Gene mutations affect specific genes

1. Point mutation is change in only one nucleotide or base.
2. Change in the wild type code involves substitution or frame shift mutation.
   a. For example: Wild type code: cat tag tac gag
3. **Frame shift** mutation
   a. **Insertion** of nucleotide(s) into the DNA molecule

DNA	RNA	Amino acid
cat ata tac gag	gua uau aug cuc	Val-Tyr-Met-Leu
caa tat ata cga g	guu aua **uau** gcu c	**Val**-Ile-Tyr-Ala

   b. **Deletion** of nucleotide(s) into the DNA molecule (cat **tgt** acg ag)

DNA	RNA	Amino acid
ca**t** ata tac gag	gua uau aug cuc	Val-Tyr-Met-Leu
caa tat acg ag*a*	guu aua ugc ucu	Val-Ile-Cys-Ser

4. **Substitution** of one nucleotide, base, or nucleotide triplet
   a. **Silent** mutation- No change amino acid or in protein function

DNA	RNA	Amino acid
cat ata tac gag	gua uau aug cuc	Val-Ile-Met-Leu
ca**a** ata tac gag	gu**u** uau aug cuc	Val-Ile-Met-Leu

   b. **Missense** mutation- Results in a different amino acid in the protein.
      1) Conservative mutation does not affect the protein function.
      2) Non-conservative mutation changes the protein function.

DNA	RNA	Amino acid
cat ata tac gag	gua uau aug cuc	Val-Ile-Met-Leu
c**g**t ata tac gag	g**c**a uau aug cuc	**Ala**-Ile-Met-Leu

   c. **Nonsense** mutation- Signals a premature stop in the code translation process.

DNA	RNA	Amino acid
cat ata tac gag	gua uau aug cuc	Val-Tyr-Met-Leu
cat at**t** tac gag	gua ua**a** aug cuc	Val-**Stop**

Chromosome Mutations affect chromosomes

1. Change in gene sequence on chromosome
2. Change in number of chromosomes: Aneuploidy mutation
3. Change in number of genomes: Euploidy mutation

Change in Gene sequence and arrangement on chromosome

1. Deletion of chromosome segment.
2. Inversion: Chromosome breaks, reverses position, and reinserts.
3. Duplication: Broken chromosome piece attached to homologous chromosome.
4. Translocation: a piece of chromosome breaks and reattaches to a non-homologous chromosome.

Aneuploidy

1. Change in number of chromosomes for a gain or loss of chromosomes.
2. Nondisjunction: failure of a homologous chromosome pair to separate in first division of meiosis resulting in two gametes one having an extra chromosome and one lacking a chromosome.
   a. Monosomy: Fertilized egg lacking one chromosome (2n - 1)
      1) Turner's syndrome: XO (female). Lacks a matching X or Y. Deformed.
   b. Trisomy: Fertilized egg with extra chromosome (2n + 1)
      1) Down's syndrome: Trisomy of the 21st chromosome
      2) Trisomy X: (XXX, super female). Intellectual disability, also known as mental retardation (CDC, 2017, https://www.cdc.gov/nchs/products/databriefs/db291.htm)
      3) Klinefelter's syndrome: XXY (male). Intellectual disability, also known as mental retardation

Euploidy

1. Change involves the addition or loss of an entire genome.
2. Haploid (1n) or polyploid (3n, 4n, or more) results.
   a. Haploid: 1n, one complete genome (human 23)
   b. Diploid: 2n, two complete genomes (human 46)
   c. Triploid: 3n, three complete genomes
3. Parthenogenesis: the development of an unfertilized egg (complete haploid genome, 1n). *partheno*=virgin; *genesis*=birth. Occurs in amphibians, shrimp, and turkeys.

4. Triploids (three genomes, ***3n***) in plants are sterile because Meiosis requires even number of chromosomes to pair chromosomes. Does not occur in animals.
5. Tetraploids (four genomes, 4n): Common in plants, rare in animals. Human liver cells, Irish potato (rarely fertile gametes).
6. Unmatched genomes. Two complete genomes, but different numbers of chromosomes. Mules: Female horse (n = 32) and Male donkey (n = 31). Therefore, sterile.
7. Euploidy mutations, with a few exceptions, are induced and perpetuated by man.

How mutations occur

1. Spontaneous mutations: occur naturally about one in one billion cells.
2. Induced mutations: Exposed to a mutagen such as radiation, chemical, mechanical

Where mutations occur

1. Somatic mutation
   a. Occurs in body cells
   b. Are not inherited
   c. Occurs during mitosis cycle
2. Germ mutation
   a. Occurs in germ cells
   b. Are inheritable
   c. Occurs during meiosis cycle
3. Inherited mutations
   a. Must be in germ cells or gametes
   b. Must be viable
   c. Must be reproducible (no sterility)
   d. Must involve mutated gametes in conception

Results of mutations

1. No change
2. Phenotype change
3. Cancer
4. Deformity
5. Death
6. Sterility
7. Inheritable trait

Mutation musings

1. Oncogene- A gene that can cause cancer.
2. Male gametes have higher rate of mutations than female gametes.
3. Jumping genes, called transposons (transposable elements TEs), jump from one location in the genome to another.
4. Transposons are regulatory genes.
5. Some estimate that 41% of human DNA is made of transposons.
6. Epigenetics is the study of chemical reactions and factors that influence the activation and deactivation of the genes. (http://learn.genetics.utah.edu/content/epigenetics/intro)

Genetic engineering

1. Intentionally altering the genetic code.
2. Advantages include overcoming genetic diseases and increasing food production and quality.
3. Disadvantages include creating deadly diseases, political manipulation to produce a desired race of people.

4. Recombinant DNA: combining DNA from two sources.
5. Human insulin gene in bacteria.

CRISPR

1. A naturally-occurring defense mechanism found in a wide range of bacteria.
2. In the 1980s, scientists observed a repetitious pattern of DNA sequences in some bacterial genomes.
3. Within these repetitions are found unique sequences.
4. Named this pattern "Clustered Regularly Interspaced Short Palindromic Repeats," or CRISPR.
5. The unique sequences in between the repeats match the DNA of viruses that infect bacteria. So, it is thought that CRISPR is one part of bacterial immune system.
6. The second part of the defense mechanism is a set of enzymes called Cas (**C**RISPR-**AS**sociated proteins), which can precisely snip DNA and slice out invading viruses.
7. The genes that code for Cas are always sitting somewhere near the CRISPR sequences.
8. As the CRISPR region fills with virus DNA, it becomes a molecular most-wanted gallery, representing the enemies the microbe has encountered.
9. The viral DNA code is used to turn *Cas* enzymes into precision-guided weapons.
10. The bacterial DNA is copied into an RNA molecule and *Cas* enzymes cradle it as they drift together in the cell.
11. If encountering matchable genetic material from a virus in the cell, the RNA latches on tightly and the *Cas* enzymes chop the virus DNA in two, preventing the virus from replicating.
12. The best known Cas enzyme is called Cas9.
13. Cas9 comes from *Streptococcus pyogenes,* better known as the bacteria that causes strep throat. Together, they form the CRISPR/Cas9 system.
14. Once the cut is made, the DNA repair enzymes go to work. And if a replacement gene is added to the nucleus, then it can be fitted into the cut. Thus, a targeted mutant can be cut and replaced with a normal gene.

Chimeras

1. A single organism made up of cells containing two sets of DNA each one from a different species.
2. Not the same as recombinant DNA and hybrids.
3. Hybrids result from fertilization of egg.
4. Transgenic organisms result from DNA of one species incorporated into the DNA of another.
    a. Geep are the offspring of a cross between sheep and goats.
    b. Blue roses are modified with pansy genes.
    c. Golden rice: modified rice that produces beta-carotene.
5. In 2002, Karen Keegan discovered that she had blood cells with different DNA in her than other body tissues. She absorbed some of the cells from a dead fraternal twin while still in the womb.
6. Some researchers have inserted human cells into animal embryos attempting to grow human organs for transplants. President Trump admin prevented attempts to lift a ban on such chimeras.

Eugenics

1. The practice of breeding humans for desired traits.
2. Refers to *good* or *desirable* genes.
3. Rome, Germany, and America have participated in human eugenics.
4. Genetic screening involves pedigree charting, karyotying, and phenotype analysis.
5. DNA probes are pieces of DNA with a nucleotide sequence that match known genes.
6. Ultrasonic scanning, fetoscopes, and amniocentesis are used to analyze the unborn.

Artificial reproduction

1. Artificial insemination
2. Surrogate mothers
3. Test-tube fertilization

Ethics of genetic engineering

1. Genetic engineering is a tool that can be used for good or evil.
2. As with any tool, its use for good is determined by the users.
3. We need Christian scientists to control the use of tools.
4. Ilia Ivanov, also known as the "Red Frankenstein", attempted to produce a human-ape hybrid in the 1920's.

Genetic homeostasis

1. Organisms manifest genetic stability by resisting change.
2. As a result of genetic homeostasis, variation is limited to a kind.

Genomic Entropy

1. Dr. John Sanford, Cornell University geneticist and inventor of the genetic gun,
2. 100-200 net mutation accumulations per generation. Very small percent of DNA.
3. 6 billion nucleotides (3 billion pairs) in humans. 600 million mutations for 1% = 3 million generations.
4. "If the mutations aren't 'bad' enough, selection can't 'see' them, cannot eliminate them, and the mutations will accumulate."
5. The net accumulation of mutations and lost information from generation to generation leads to an inevitable extinction.
6. This phenomenon is observed in eukaryotes and to some extent in prokaryotes.
7. "The central part of Sanford's argument is that mutations … are accumulating so quickly in some creatures (particularly people) that natural selection cannot stop the functional degradation of the genome—let alone drive an evolutionary process that can turn apes into people." [creation.com]
8. **A review of** *Genetic Entropy & The Mystery of the Genome* **by John C. Sanford**, Ivan Press, Lima, New York, 2005