Unit 3

Genetics & Heredity

Biology 30

Mr. Oosterom

Intro to Genetics

- For centuries, people have known that certain physical characteristics are passed from one generation to the next.
- Using this knowledge, they learned to produce crops and livestock with desired characteristics.
- However, how these characteristics are passed from one generation to the next was unknown to them.

16.1 – Genetics of Inheritance

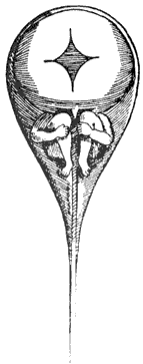
- **Traits** - Distinguishing or unique characteristics which make one organism different from other organisms.
  - Some traits are desirable while others are not.
  - Can you think of any undesirable traits? Desirable?
- It can be observed that traits can be passed down from one generation to the next (ie. Parents to offspring). This transmission of traits is called **heredity** and the traits which are passed on are said to be **inherited**.

What is Genetics?

- **Genetics** is a branch of Biology which is concerned with studying the inheritance of traits and the variations caused by them.
- By studying genetics we gain a better understanding of how we can determine the inheritance of certain traits and patterns of involved in their inheritance.
- The knowledge of genetics which we have today is a far cry from what we knew in the past.

Past Genetics

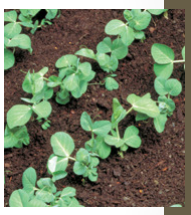
- **Hippocrates** (460 - 377 BC), a Greek philosopher, theorized that every part of the body was involved in the production of the "seeds" which the parent produced. The seeds of the male and female parent fused together to produce a new individual.
- In the 18th century, scientists believed that sperm contained pre-formed embryos. Thus it was the male who had a major contribution to the new individual which was being produced. The contribution of the female was small.
- In 1853, a monk named Gregor Mendel performed a number of experiments which involved pea plants. This study took place over an eight year period and the results of these experiments laid down a basis of inheritance from which other studies were done.



Mendel's Experiments I

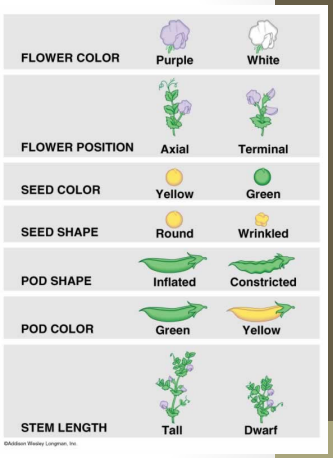
Mendel chose the pea plants because:

1. Pea plants were commercially available throughout Europe at this time.
2. Pea plants are easy to grow and mature quickly.
3. The structure of the pea plants reproductive organs allowed Mendel control which plants reproduced.
4. He cross-pollinated and self-pollinated these plants.
5. Different varieties of the pea plant had different traits which could be observed easily from one generation to the next.



Mendel's Experiments II

- Mendel examined seven different traits in pea plants (shown to the right)
- Each trait had only two possible forms or **variations**.
- In order to perform his experiments, Mendel bred his pea plants until he obtained **purebred** plants. A purebred organism is similar to the parent or parents which produced it. These purebred plants were **true breeding** plants which produced plants with the desired features that Mendel was trying to obtain.
  - For example, a tall parent plant would only produce tall offspring plants.



Mendel's 1st Experiment
The Monohybrid Cross

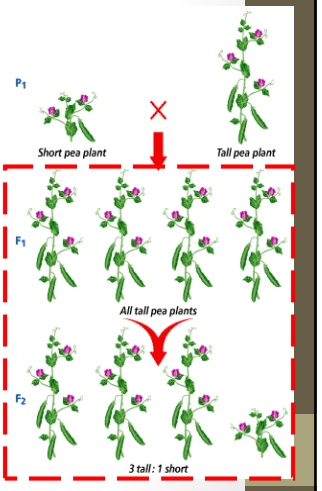
- Once he obtained purebred plants for each of the traits which he was using, he called these the **parent or P generation**.
- He crossed these parent plants to obtain a first generation of offspring which he called the **first filial generation or F1 generation**.
- The plants which were produced in the F1 generation were called **hybrids** because they were the result of a cross between two different purebred plants.
- When two plants from the F_1 generation were crossed, the offspring were called the **second filial generation or F_2 generation**
- Since only **one** trait was being considered in these crosses, they are called **monohybrid crosses**
- See Figure 16.5 on page 529 in your text

Monohybrid cross

- When Mendel performed his cross for the trait of plant height, he crossed a purebred tall plant with a purebred short plant.
  - Mendel expected the offspring to be medium height. What height would you expect the offspring plants to be?
- This was not the case, all the offspring were tall.
- From this observation he concluded that the trait for tall was **dominant** and the trait for short was **recessive**.
- Both forms of the trait were present in the F1 plants, but the short form could not be seen since it was being dominated by the tall form.
- A dominant trait is a characteristic which is always expressed or always appears in an individual.
- A recessive trait is a characteristic which is latent or inactive and usually does not appear in an individual.
- From this Mendel formed what he called the **principle of dominance**.
  - When individuals with contrasting traits are crossed, the offspring will express only the dominant trait.

Law of Segregation

- When Mendel crossed two F_1 offspring to obtain the F_2 offspring he obtained the following results every time
  - Dominant trait expressed in 75% of plants
  - Recessive trait expressed in 25% of plants
  - This 3:1 ratio is called the **Mendelian ratio**



Mendel's Conclusions

- Each parent in the F1 generation starts with two hereditary **factors**. These factors are either both dominant, both recessive, or a combination of dominant or recessive.
- Only one factor from each parent is contributed to the offspring.
- Each offspring inherits only one factor from each parent. If the dominant factor is inherited, it will be expressed. However, the recessive factor will only be expressed if the dominant trait is not present

16. 3 – Introduction

- When Mendel did his experiments with pea plants, he did not know that chromosomes existed in cells.
- In the early 1900s, chromosomes were discovered and observed in cells.

The Chromosome Theory of Inheritance

- In 1902, two scientists Walter Sutton and Theodor Boveri were studying meiosis and found that chromosomes behaved in a similar way to the factors (genes) which Mendel described.
- Sutton and Boveri made three observations
  1. Chromosomes occur in pairs and these pairs segregate during meiosis.
  2. Chromosomes align independently of each other along the equator of the cell during meiosis.
  3. Each gamete (sex cell) receives only one chromosome from each pair.

Chromosome Theory

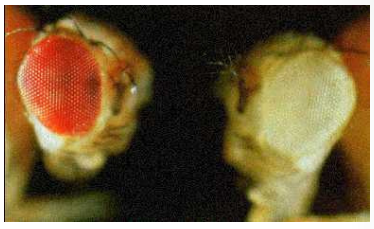
- From the above observations, they formed the **chromosome theory of inheritance**. This theory states
- Mendel's factors (genes) are carried on chromosomes
- The segregation and independent assortment of chromosomes during meiosis accounts for the pattern of inheritance in an organism.

Morgan's Discoveries

- In 1910, an American scientist called Thomas Morgan made a very important discovery from his work with fruit flies

Morgan and his Fruit Flies

- Normal fruit flies have red eyes
- Morgan crossed two red eyed parent flies and obtained a white eyed male. In other crosses, he obtained red eyed females, red eyed males and white eyed males.
- Since the white eye color was only present in the male flies, Morgan concluded that eye color was linked to an organisms sex.



Morgan & Linked Genes

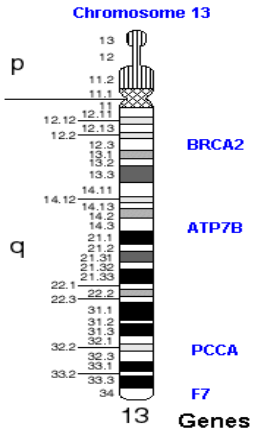
- The gene for eye color in fruit flies was located on the sex chromosome, in this case the X chromosome.
  Such genes are called **sex-linked genes**
- Morgan also stated that genes which are located on the same chromosomes are linked to each other and usually do not segregate (separate) when inherited. These are called **linked genes**

However…

- Morgan found that some genes do segregate
- Morgan created the **gene-chromosome theory** which states that genes exist at specific sites and are arranged in a linear fashion along chromosomes.

Chromosome 13 Gene Map

- Note that all genes are located in a linear fashion from one end of the chromosome to the other



Sex-Linked Inheritance

- Certain traits depend on the sex of the parent which carries the trait. The genes for these traits are located on the sex chromosomes, X or Y.

Sex-linkage

- transmission of genes which are located on the sex chromosomes is called **sex-linked inheritance**
- Genes which are located on the X chromosome are called X-linked while those on the Y chromosome are called Y-linked. Most sex linked genes are located on the X chromosome

Chromosomes & Gene Expression

Chromosome Inactivation

- Males and females produce the same amounts of proteins. This is coded by genes which are located on the X chromosome.
- Females have two X chromosomes in their cells while males have only one X chromosome.
- one of the two female X chromosomes is inactivated and this inactivated chromosome is called a **Barr body**

Polygenic Inheritance

- Most traits are controlled by one gene, however, some traits are controlled by more than one gene, this is called **polygenic inheritance**.

- Polygenic genes cause a range of variation in individuals called **continuous variation**.

Polygenic Traits in Humans

- Height
- Skin Colour
- Hair
- Eye Colour

Modifier Genes

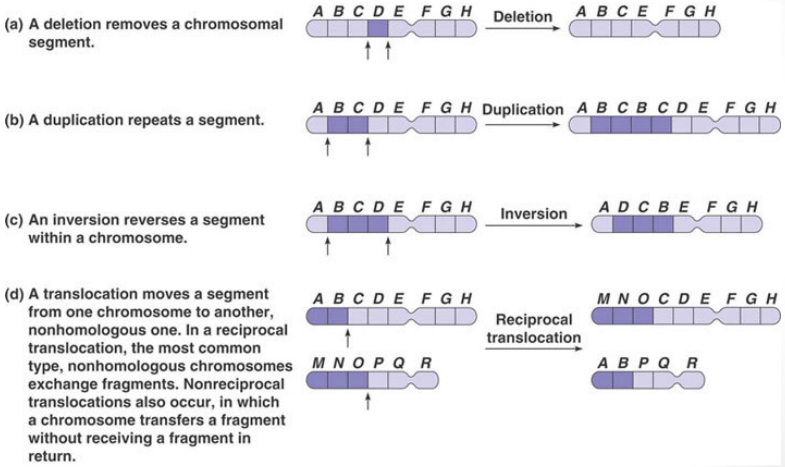
- **modifier genes** – Genes that work with other genes to control the expression of a particular trait.
- In humans, modifier genes help control the trait of eye color.
  - In this case, modifier genes influence the level of melanin present in the human eye to provide a range of eye colors from blue to brown.

Changes in Chromosomes

- **Changes In Chromosome Structure**
  - Changes in the physical structure of chromosomes can occur:

    1. Spontaneously
    2. As a result of irradiation
    3. After exposure to certain chemicals

Structural Changes in Chromosomes



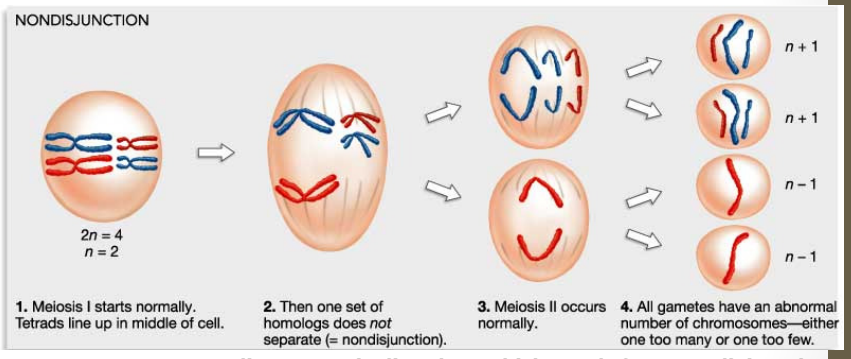
Structural Change & Disorders

- **Deletion**
  - Loss of a piece of chromosome #5
  - Cri-du-chat
  - Affects the larynx making cat sounds
- **Inversion**
  - Some forms of autism
- **Duplication**
  - Duplication in the X chromosome
  - Fragile X syndrome
- **Translocation**
  - Down Syndrome
    - # 14 and 21
  - Lukemia
    - #22 and 9

Nondisjunction

- Sometimes, chromosomes fail to separate from each other during meiosis. This produces gametes (eggs / sperm) which have either too many or too few chromosomes
- If a gamete which does not have the correct number of chromosomes is involved in fertilization, a zygote will be produced which has either too many or too few chromosomes
- This creates an embryo whose cells contain either more or less than 46 chromosomes. These embryos are usually aborted by the mother, but some survive and have genetic disorders

Nondisjunction



Pages 552 – 553 outlines genetic disorders which result from nondisjunction Monosomy, Down syndrome, Turner Syndrome

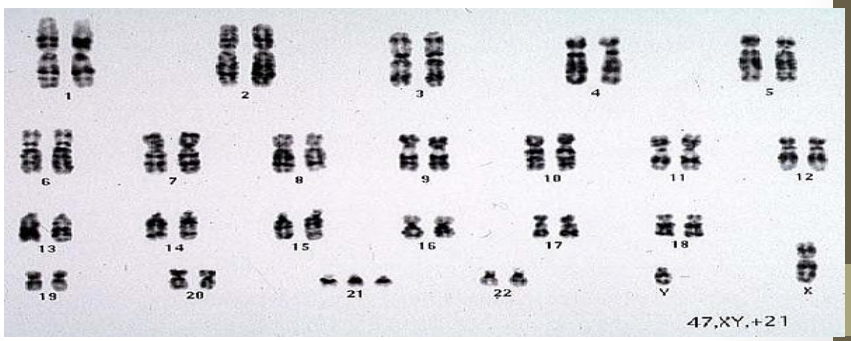
You need to know how each of these disorders arise in an individual for the test as well as the public exam.

Types of Nondisjunction

- **Trisomy** - When an individual inherits an extra chromosome.
- **Monosomy** - When an individual inherits one less chromosome.
- **Three disorders**
  - Down Syndrome
  - Turner Syndrome
  - Klinefelter Syndrome

Down Syndrome (Trisomy 21)

- This occurs when an individual receives three copies of chromosome 21 instead of the normal two.

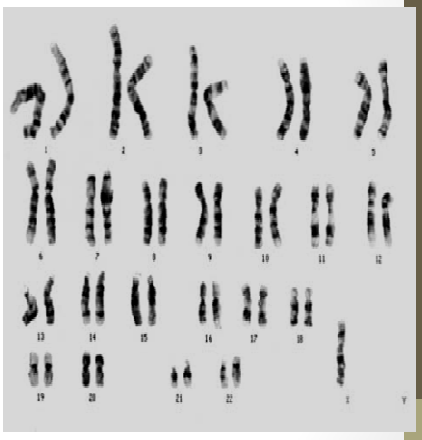


Symptoms of Down Syndrome

- Mild to moderate mental impairment
- A large, thick tongue
- Speech defects
- A poorly developed skeleton
- Short body structure
- Thick neck
- Abnormalities in one or more vital organs

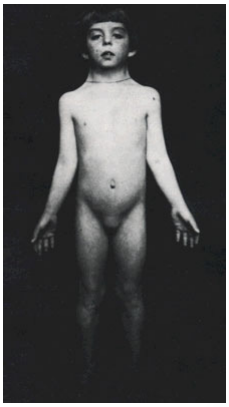
Turner Syndrome

- An individual inherits only a single X chromosome, as well the Y chromosome is missing.
- This results in a female with the genotype XO
  - O represents a missing chromosome



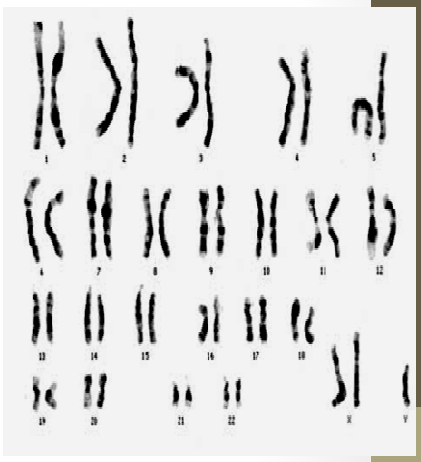
Turner Syndrome Symptoms

- Infertility
- External female genitalia, but no ovaries.
- Webbed neck
- Heart defects
- Kidney abnormalities
- Skeletal abnormalities
- Learning difficulties
- Thyroid dysfunction



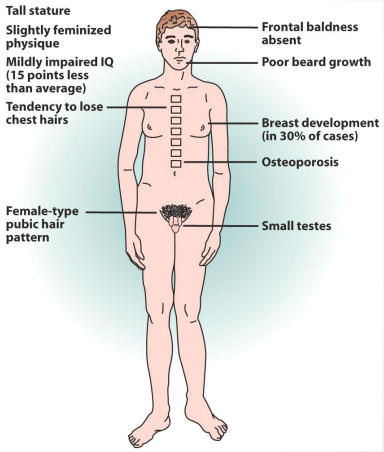
Klinefelter Syndrome

- A male who has an extra X chromosome.
- These individuals have the genotype XXY instead of XY



Klinefelter Symptoms

- Immature male sexual organs
- Lack of facial hair
- Some breast development



Jacobs Syndrome

- Males with an extra Y chromosome, having the genotype XYY
- Symptoms
  - Speech and reading problems
  - Delayed emotional maturity
  - Persistent acne
- Generally XYY males have normal potency and sexual libido, though in rare cases they may also have Klinefelter

Human Genetics / Inheritance Patterns

- The study of human genetics is a complicated field. This is due to a number of reasonsHumans have long life spans.
  1. We produce very few offspring.
  2. Most people do not keep very accurate records of their family history.

Patterns of Inheritance

- There are certain patterns of inheritance which scientists have determined for particular human genetic disorders. These include:
  - Autosomal Recessive Inheritance
  - Codominant Inheritance
  - Autosomal Dominant Inheritance
  - Incomplete Dominance
  - X-linked Recessive Inheritance

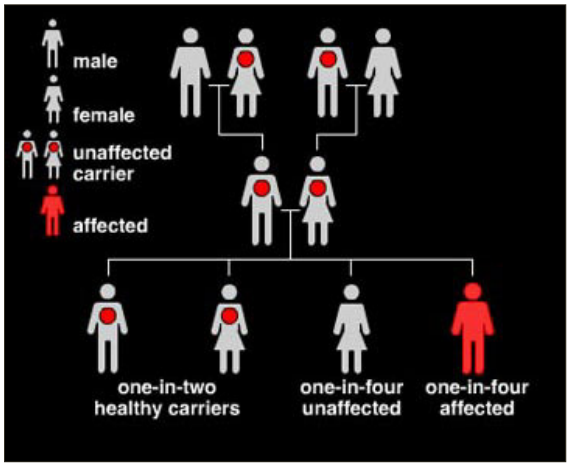
Autosomal Recessive Inheritance

- Disorder is carried on the autosomes (body chromosomes), not sex chromosomes
- Examples include:
  - Tay-Sachs disease
  - Phenylketonuria (PKU)
  - Albinism

Tay-Sachs Disease

- Individuals lack an enzyme in the lysosomes which are located in their brain cells.
  - The lysosomes are unable to break down specific lipids. Thus the lipids build up inside the lysosomes and eventually destroy the brain cells.
- Children appear normal at birth, but experience brain and spinal cord deterioration around 8 months old.
- By 1 year of age, children become blind, mentally handicapped, and have little muscular activity.
  - Most children with their disorder die before age 5.
- There is no treatment for this disorder.

Tay-Sachs



Phenylketonuria (PKU)

- A enzyme which converts a substance called phenylalanine to tyrosine is either absent or defective.
- Phenylalanine is an amino acid which is needed for regular growth and development and protein metabolism.
- Tyrosine is another amino acid which is used by the body to make the pigment melanin and certain hormones

PKU

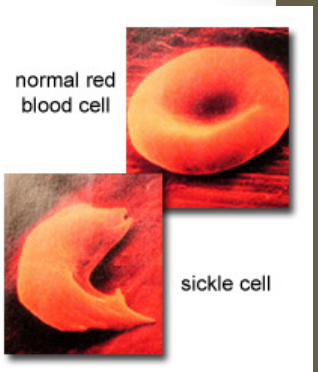
- When phenylalanine is not broken down normally, harmful products accumulate and cause damage to the individual's nervous system.
  - This results in PKU
- Babies who develop PKU appear normal at birth.
  - Can become mentally handicapped within a few months
- Today, testing and proper diet can prevent PKU from occurring in children

Albinism

- Genetic disorder in which the eyes, skin and hair have no pigment.
- People with this disorder either lack the enzyme necessary to produce the melanin pigment in their cells or lack the ability to get the enzyme to enter the pigmented cells.
- Albinos face a high risk of sunburns and eye damage from exposure to the Sun.

Co-dominant Inheritance

- Sickle-cell Anemia
  - Best example of a co-dominant disorder
- Symptoms
  - Defect in the hemoglobin and the red blood cells
  - Defect leads to clots and reduced blood flow to vital organs
  - Low energy, suffer from various illnesses and are in constant pain
  - May die prematurely



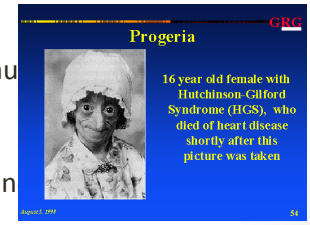
Autosomal Dominant Inheritance

- Genetic disorders which are caused by autosomal dominant alleles, recessive condition is normal
- Very rare in humans, but they do exist.
- Caused by chance mutations or after individuals have passed their child bearing age.
- Two examples:
  - Progeria
  - Huntington's disease

Progeria (Pp)

- Rare disorder causing affected person to age rapidly
- Usually dies by age 10 - 15
- Affects 1 in 8 million newborns
- Results from a spontaneous point mu in a gene
- Mutated gene is dominant over the n condition (pp)

15 yr old male



16 yr old female

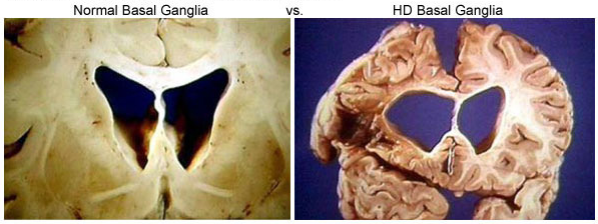
Huntington Disease

- Lethal disorder in which the brain progressively deteriorates over a period of about 15 years
- Symptoms arise after the age of 35
  - After the person has had a chance to pass the allele to their children
- Symptoms include:
  - Irritability and memory loss
  - Involuntary leg / arm movements
  - Symptoms worsen s brain deteriorates
    - Loss of speech and further loss of memory
  - Person dies by 40 – 60 yrs old before they know if their children have the mutant allele

Huntington Diseased Brain

Figure D-4: Effect of HD on the Basal Ganglia

Normal Basal Ganglia vs. HD Basal Ganglia



The basal ganglia of the human brain, showing the impact of HD on brain structure in this region. Note especially that the brain of a person with HD has bigger openings due to the death of nerve cells in that region.

Source: Singer, Jonathan. Huntington's Disease. Online. Available at: http://ist-socrates.berkeley.edu/~jmp/HD.html

Incomplete Dominance

- Disorder exhibits a phenotype which is midway between the dominant and recessive traits
- Familial Hypercholesterolemia (FH)
  - Normal cells have surface receptors which absorb low-density lipoproteins (LDLs) from the blood.
  - Individuals who have the FH disorder have cells which only have half the normal number of LDL receptors on their surface
  - Person then suffers from high cholesterol because LDLs are not efficiently absorbed from the blood

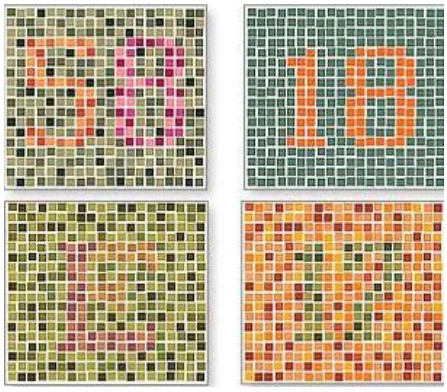
X-Linked Recessive Inheritance

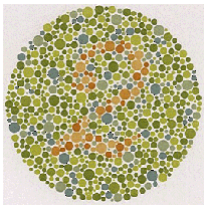
- Disorders linked to genes on the X chromosome
- Are due to the recessive form of the gene, and only occurs if there is no dominant form of the gene present
- Example: Colour blindness

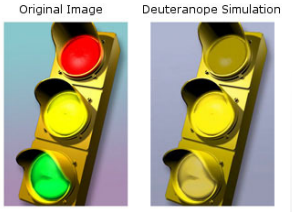
Colour Blindness

- Genotypes: X^cX^c X^cY
- Heterozygous females will have normal vision but they will be carriers → X^cX^c
- Person is unable to distinguish between colours red and green
- Affects about 8% of males and 0.04% of females
- Do sample problems

Can you see the numbers?

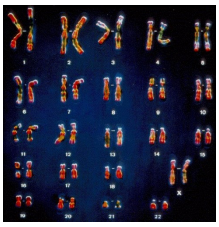


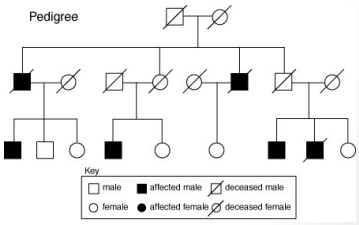




Human Genetic Analysis

- Geneticists are able to analyze the patterns of human inheritance using two methods
  - Examination of karyotypes
  - Construction of pedigrees





Human Karyotype

- Within our body cells, humans normally possess 46 chromosomes.
  - 44 of these are autosomes (body chromosomes)
  - 2 are sex chromosomes.
- A karyotype is a photograph of the chromosomes which are located in the nucleus of a somatic cell
- Once a photograph has been taken of the chromosomes in a cell's nucleus, they are cut out and arranged in pairs according to their size, shape, and appearance.
- By observing the karyotype, disorders may become apparent.

YOU WILL BE DOING A KARYOTYPE LAB FOR HOMEWORK ☺

Constructing Pedigrees

- A pedigree is a chart which shows the genetic relationships between individuals in a family.
- Using a pedigree chart and Mendelian genetics, scientists can determine whether an allele (gene) which is responsible for a given condition is dominant, recessive, autosomal, sex-linked, etc.
- A pedigree can also be used to predict whether an individual will inherit a particular genetic disorder.
- An example of such a disorder is hemophilia. This is a disorder in which a person's blood lacks certain clotting factors, thus the blood will not clot. Because of this, a small cut or bruise may kill an individual.

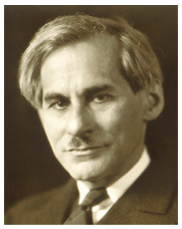
Molecular Genetics

Section 17.1
Isolating the Material of Heredity

- Fridrich Miescher, was the first person to isolate **nucleic acid**
  - He called it **nuclein**
- Nearly 100 yrs later, scientists connected nucleic acids and Mendel's "factors of inheritance"

Components of Nucleic Acids

- Upon closer inspection, Miescher's nuclein was found to be made up of strand-like complexes of nucleic acids and proteins.
- In the early 1900's, **Phoebus levene** made several discoveries about nucleic acids
  - There is, not one, but two types, each differing by a sugar



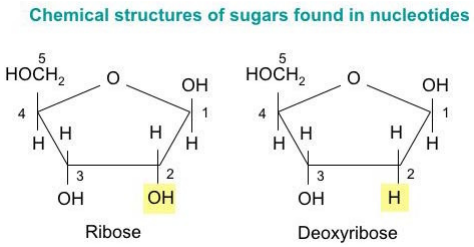
Phoebus Aaron Theodor Levene

Two Types of Nucleic Acid

1. **Ribonucleic Acid**
   - Contained a 5-carbon sugar called **ribose**
   - Also called RNA
2. **Deoxyribonucleic Acid**
   - Contained a different 5-carbon sugar called **deoxyribose**
   - Also called DNA

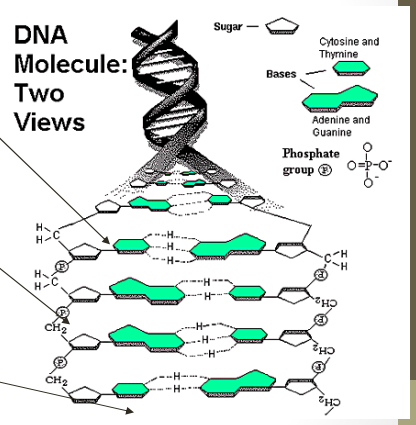
- Levene determined that these nucleic acids were composed of long chains of individual units called **Nucleotides**

Ribose vs. Deoxyribose



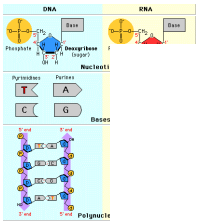
Three Parts of a Nucleotide

1. A 5-carbon sugar
2. A phosphate group
3. A nitrogen base



The Nitrogen Bases

- **DNA Bases**
  - Thymine (T)
  - Cytosine (C)
  - Guanine (G)
  - Adenine (A)



- **RNA Bases**
  - Uracil (U)
    - Replaces thymine
  - Cytosine
  - Guanine
  - Adenine

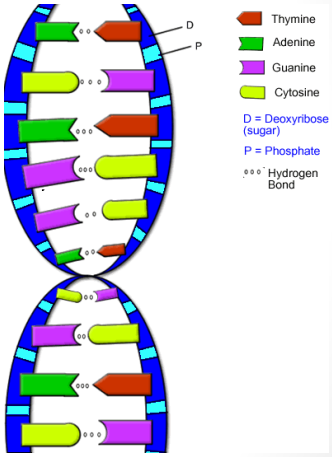
Sugar – phosphate bonds allow long nucleic acid chains to be formed

Erwin Chargaff

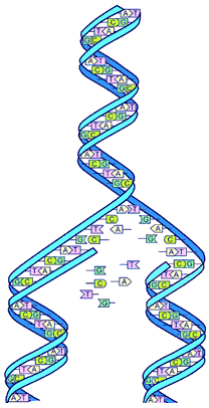
- Late 1940's – Studied DNA and made the following discoveries
  - The 4 nucleotides in DNA are NOT present in equal amounts, as once thought
  - Nucleotide composition varies from species to species
    - Composition within a species, however, is constant

More of Chargaff's Work

- In **any** sample of DNA the following is true:
  - Amount of Cytosine = Amount of Guanine
  - Amount of Thymine = Amount of Adenine
- This constant is called "Chargaff's Rule"



The Double Helix



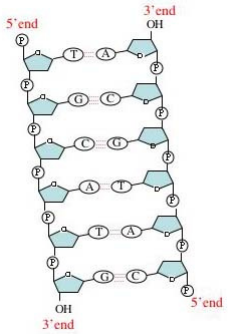
- DNA is made up of two long strands of nucleotides in the shape of a double helix
- In its unwound state, the DNA molecule resembles a ladder (aka Ladder structure)
- Four bases fall in two categories:
  - **Purines** – guanine and adenine
  - **pyrimidines** – cytosine & thymine
- Watson and Crick concluded that a purine always joins with a pyrimidine

Complementary Base Pairing

- Pairing of nitrogenous bases in the centre of the DNA molecule is called **complimentary base pairing**. Pairing can occur in the following ways:
  - Adenine – Thymine → by 2 Hydrogen bonds
  - Thymine – Adenine → by 2 Hydrogen bonds
  - Cytosine – Guanine → by 3 Hydrogen bonds
  - Guanine - Cytosine → by 3 Hydrogen bonds

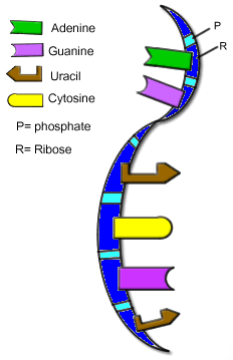
  - The two strands run **anti-parallel** (opposite directions) and are not identical to each other

Anti-parallelism



RNA

- Three differnces from DNA
  1. Sugar is a ribose, while DNA has a deoxyribose
  2. RNA has uracil instead of thymine as in DNA
  3. RNA is only a single strand



Organization of Genetic Material

- Scientists examine cells to determine how DNA is organized within a cell
- There are two main types of cells:
  - Prokaryotes (bacteria)
  - Eukaryotes (everything else)
- Structure of the DNA varies in each type of cell

Eukaryotic Genes

- All cells have double-stranded DNA
- DNA is arranged into **chromosomes** within the nucleus
- Each chromosome contains a double stranded DNA molecule and a protein called a **histone**
- A typical chromosome contains:
  - 60% Protein
  - 35% DNA
  - 5% RNA
- Chromosomes are joined together to form a long, fibrous material called **Chromatin**

Genes and the Genome

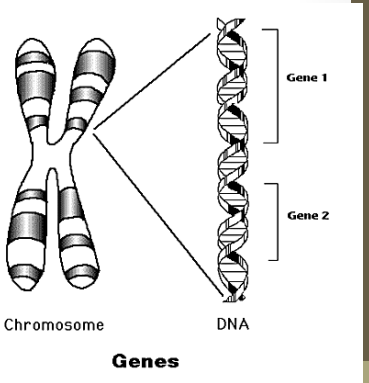
- Studies have shown that there are patterns in how heredity information is organized at the molecular level that are shared by different organisms. They are:
  - How individual genes are organized
  - How the individual's genome is organized

Genes

- A gene is a subunit of DNA
- Chromosomes in a cell carry genes
- Different species have their own unique arrangement of genes
  - Though many genes are common between species

What IS a Gene?

- Portion of inherited information that defines o particular trait of an organism's physical characteristics
- Are responsible for coding proteins and some non-protein products



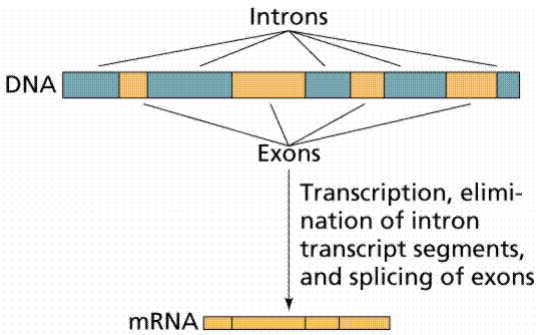
Arrangement of the Genome

- Each chromosome has its own unique arrangement of genes
  - Gene density varies among chromosomes
    - Ex. Ch. # 4 has about 200 genes, while Ch. # 14 has about 1450 genes
- Different organisms have different numbers of genes
  - An ameoba has about 7000 genes while humans have about 35,000 genes

Eukaryote Genes

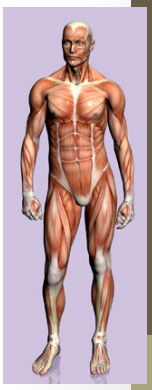
- Each genes if made up of two different regions
  - Exons → Coding or **ex**pressed regions of a gene
  - Introns → Non-coding nucleotide sequences
    - Can make up over 50% of the length of a gene
- More complex organisms tend to have more introns, while simple organisms like bacteria or yeasts have none or few introns

Introns and Exons



Section 17.3
DNA Replication

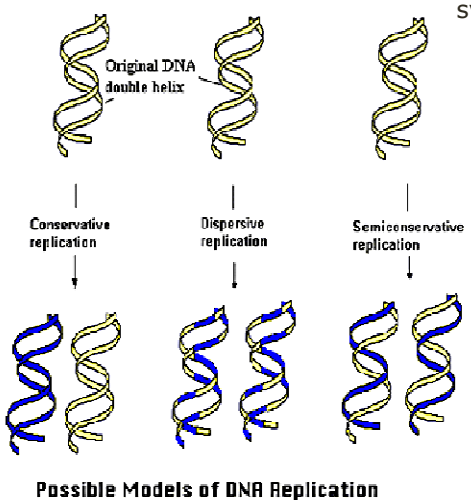
- Humans have about 1 trillion cells
- Each of these cells is genetically identical to the zygote from which they formed
- For this to happen:
  1. The genome must be copied quickly
  2. The genome must be copied accurately



The Replication Process

- DNA replication is a process from which two molecules of DNA are made from one
- Called a semi-conservative model
  - Meaning each of the two new DNA molecules contains one original (parent) strand and one new strand

Possible Modes of Replication



Possible Models of DNA Replication

•The two original strands of DNA are shown in yellow (light); newly synthesized DNA is blue (dark)

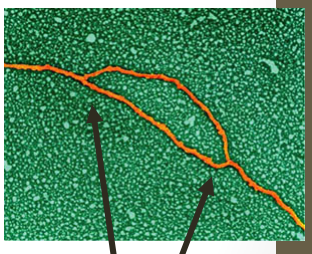
- **Conservative replication** would leave intact the original DNA molecule and generate a completely new molecule.
- **Dispersive replication** would produce two DNA molecules with sections of both old and new DNA interspersed along each strand.
- **Semiconservative replication** would produce molecules with both old and new DNA, but each molecule would be composed of one old strand and one new one

Three Stages of the Replication Process

1. Initiation
2. Elongation
3. Termination

1. Initiation

- The DNA double helix begins to unwind itself
- DNA is a tightly bound stable structure for most of a cell's life
- DNA unwinds at special points along the strand called **replication forks**
- Enzymes called **helicases** are responsible for unraveling short segments of DNA



Replication forks

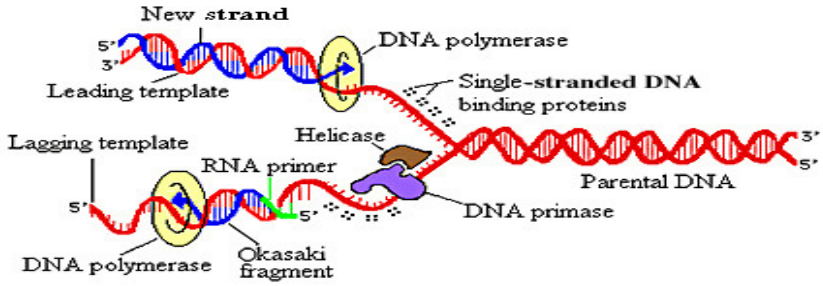
2. Elongation

- Assembly of two new DNA strands begins
- An enzyme called **DNA polymerase** helps to attach new nucleotides to the DNA strand
- Newly replicated DNA can be found in short segments called **Okazaki fragments** ranging from 1 to 2 thousand nucleotides in lenth

Still Elongating

- Replication occurs in the 5' to 3' direction of one DNA strand while it occurs in the 3' to 5' direction on the other strand. The enzyme **DNA primase** begins this process
- **Leading strand** - The strand replicating in the 5' to 3' direction
- **Lagging strand** – The strand replicating in the 3' to 5' direction
- Okazaki fragments are joined together by an enzyme called **DNA ligase**

Replication Processes



Collaboration of Proteins at the Replication Fork

Replication Animation

3. Termination

- The stage when the new DNA molecules reform into helices or double helices
  - Daughter DNA strands rewind forming their stable helical structure
- Each new daughter DNA molecule is slightly shorter than its parent
  - Chromosomes lose about 100 base pairs with each replication

Telomeres & Chromosome Shrinkage

- In eukaryotic cells special regions called **telomeres** which have the base sequence TTATGGG are attached to the ends of each chromosome
- These sequences have no role in the development and thus the chromosome can lose them with each replication and not lose any important genetic information

Like the hard ends on your shoelaces, telomeres are the protective bits of DNA at the ends of your chromosomes.

- One theory: chromosome shrinkage is related to symptoms of aging

Err is to human… and DNA replication

- Though we would like to believe that DNA replication is an orderly step by step process, this is usually not the case. Just as we make mistakes, so can the replication process
  - Wrong bases may be inserted into the new DNA
  - Nucleotide bases may be damaged (ie. By radiation)
- When this happens, mutations or other serious problems can occur in the DNA molecule

Proofreading and Correction

- To prevent errors from occurring, the enzyme DNA polymerase is able to check to see whether bases are actually bonding together by hydrogen bonding
  - No H-bonding means there is a base mismatch
  - The incorrect base is replace with the correct one
- DNA replication involves dozens different enzymes and other proteins working together as a **replication machine** to get the job done correctly and virtually error-free

DNA Repair Animation

Section 17.4 Protein Synthesis & Gene Expression

- DNA stores information in the form of a code that we call the **genetic code**
- Genetic code is based on the order of the base pairs that make up the DNA molecule
- The sequence of nucleotide determines the sequence of amino acids within a protein

Genetic Code

- Transfer of genetic information from DNA to protein is called **genetic expression** which occurs in two stages:
  1. **Transcription**
     - Information is copied from DNA onto an RNA molecule (inside the nucleus of the cell)
  2. **Translation**
     - RNA moves from the nucleus to the cytoplasm where it helps to make a polypeptide (protein)

Codons Based on RNA Nucleotides

Second base in codon

First base in codon	U	C	A	G	Third base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

The Genetic Code

- Using combinations of three nucleotides, the DNA molecule creates code words that represent the 20 amino acids (Pg. 590 table 17.2)
- Each set of three bases is called a **codon**
  - Some amino acids (AA) are coded for by more than one codon, while others, only by one
  - Each set of 3 amino acids is called a **reading frame**
- Codons are represented by the RNA base sequences

How Reading Frames Work

NORMAL CODE	ALTERED CODE
DNA Sequence	**Deletion in DNA**
TAC GCC GAC TTA G	**TAC GCC GCT TAG**
RNA Sequence	**New RNA sequence**
AUG CGG CUG AAU	**AUG CGG CGA AUC**
Amino acid sequence	**New AA sequence**
met – arg – leu - asn	**met – arg – arg - iso**

How does this work?

- DNA sequence: T-A-C-A-G-T-A-T-C

Find the complimentary RNA sequence

- RNA sequence: A-U-G-U-C-A-U-A-G

Match each codon with the amino acid to get the sequence

- AA sequence: Met – Ser – Stop
  (methionine / start – serine – stop)

3 Characteristics of the Code

1. Redundancy
   - More than one codon can code for the same amino acid – lots of repetition
2. Continuous
   - Code reads as a series of 3-letter codons without spaces, punctuation or overlap
3. Universal
   - Code is virtually the same in all organisms making is possible to transfer information

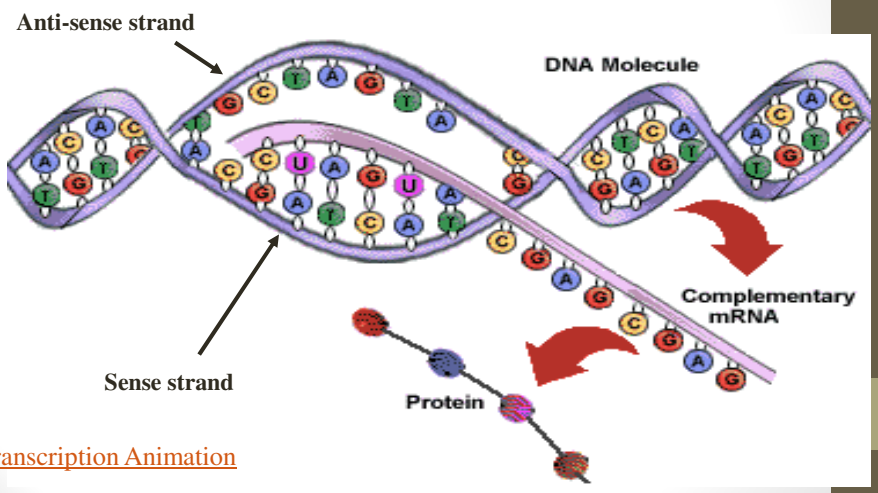
Transcription I

- Process by which a small portion of the DNA is copied onto a special type of RNA called messenger RNA or mRNA
- mRNA carries information from the nucleus of a cell to the cytoplasm to become a protein
- RNA polymerase is the catalyst for the production of the RNA molecule

Transcription II

- DNA has two strands
  - Sense strand and Anti-sense strand
- ONLY the sense strand is transcribed into RNA
- RNA polymerase opens up the DNA double helix allowing the mRNA to be formed from exposed nucleotide bases
- Transcription continues along the DNA until a stop codon is reached. The RNA and polymerase separate and a special nucleotide sequence is added to the 3' and 5' ends

Transcription Illustrated

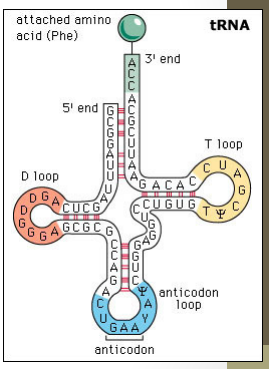


Transcription Animation

Translation I

- The reading of mRNA by a ribosome so that proteins can be formed in the cytoplasm

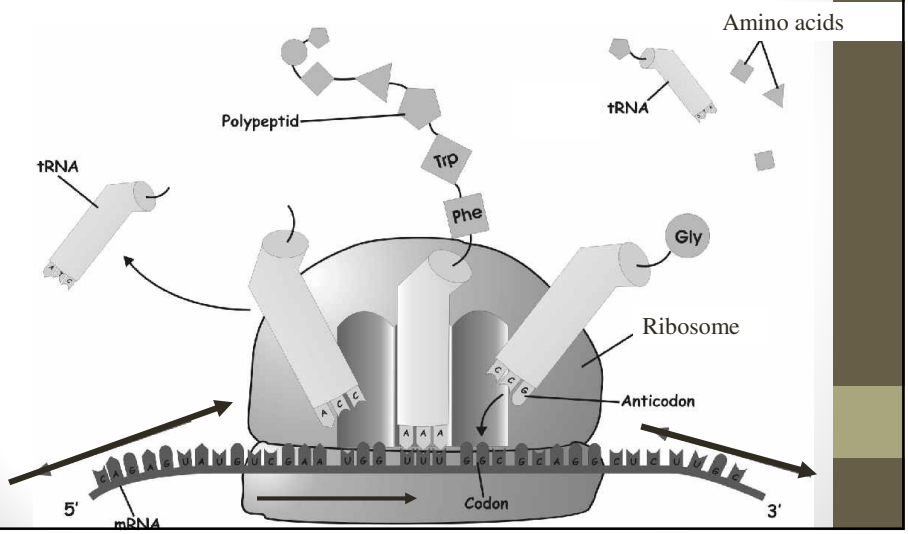
1. mRNA comes in contact with a ribosome
2. **Transfer RNA (tRNA)** joins to the mRNA. One end of the tRNA carries an amino acid which will be used to make a protein. The opposite end has a 3-base nucleotide sequence called an **anti-codon** that joins with a sequence of mRNA codons



Translation II - Animation

- After the first tRNA binds to the mRNA a second will join next to it, adding its amino acid to the chain. When the third tRNA binds the first tRNA molecule is "bumped" out of the ribosome. With each new tRNA a new amino acid is added to the polypeptide chain.
- The cycle of amino acids linking together is repeated until a "stop" codon (UAA, UAG or UGA) is reached. Once this tRNA is read, the amino acid is released from the ribosome and the protein is formed

Translation Illustrated

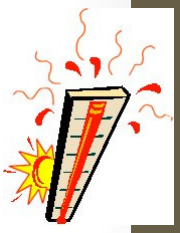


Regulating Gene Expression

- Every living cell has the ability to respond to it environment by changing the kinds and amounts of polypeptide (proteins) it produces
  - By controlling this process, the cell can regulate gene expression
- There are a number of factors that control the rate of transcription and translation

Factors Effecting Gene Expression

- Changes in temperature or light
- Presence or absence of nutrients in the environment
- Presence of hormones in the body
  - Development of an organism is governed by this regulation of gene expression



Mutations

- The genome of an organism is not stable
  - The overall structure of DNA is constantly changing
- Changes that take place within genes provide, what we call, **genetic variation** Permanent changes in the DNA are called mutations
  - Some mutations are inheritable, while others are not
- **Germ cell mutations** – Mutation in DNA of the gametes (germ cells). Can be passed on
- **Somatic cell mutation** – Mutations in the body cells. Cannot be passed on to offspring (ie. Cancer)

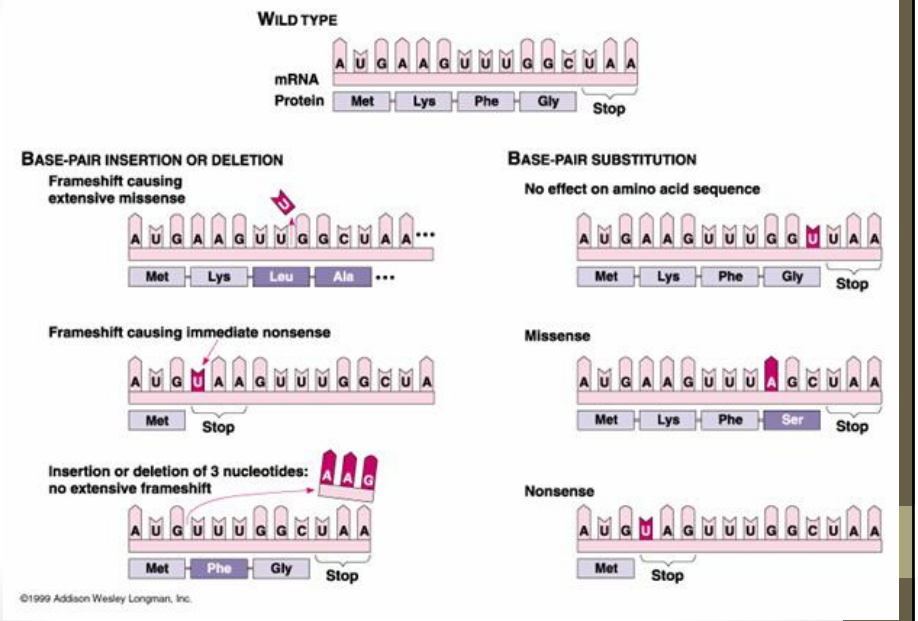
Genetic variations make all humans and races different from one another

Types of Mutations

- **Point mutations** – small changes in the nucleotide sequence of genes. Maybe be one nucleotide replacing another, deletion or insertion
- **Silent mutations** – Has no negative effect on the cells in which they occur. May be in exons or simply in "unused" DNA
- **Mis-sense mutations** – Cause slight alteration of a protein. May be beneficial or harmful depending on the protein(s) affected
- **Nonsense mutations** – Make a gene unable to code for a functional protein. Usually caused by changes to the start/ stop codons

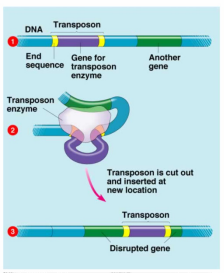
Nucleotide Insertions/ Deletions

- One or two nucleotides in a sequence of codons can produce a **frameshift mutation**
  - This is when a nucleotide insertion or deletion causes and entire frame of a gene to be altered
  - See page 597 – fig. 17.33 for an example



Chromosomal Mutations

- Involve the rearrangement of genetic material which affects genes
- May involve:
  - Exchange of portions of chromosomes between sister chromatids or chromosomes
  - Loss of chromosome pieces
  - Duplication of chromosome segments



- Barbara McClintock found jumping genes called **transposons** that are short strands of DNA capable of moving from one location to another. (pg 597-598)

Causes of Mutations

- **Spontaneous mutations** – caused by molecular interactions that occur naturally inside a cell. The rate of these mutations varies among different organisms
- Environmental factors can increase the rate of mutations. These are called **induced mutations**
- **Mutagen** – Any substance or event that increases the rate of mutation in an organism
  1. **Chemical**
  2. **Physical**

Physical Mutations

- Agents which can forcibly break a nucleotide sequence causing random changes in one or both strands of DNA
  - X-Rays
  - Gamma rays
  - Ultraviolet (UV) radiation

Effects of radiation

Chemical Mutations

- A molecule that can enter a cell's nucleus and cause mutations by reacting with the DNA
- Chemical mutagens insert themselves into the DNA molecule and this cause a mutation
  - Chemicals in the air
  - Chemicals in cigarettes / smoke
  - Heavy metals

One of the most common mutagens around

Mutations: General Information

- Each organisms genes undergoes 1000's of mutations during a lifetime
- Most mutations are repaired by the cell's own enzymes
- Some mutations cannot be repaired, and these build up over the lifetime of the cell leading to cellular damage
- Cancer is an example of a disorder caused by accumulated mutations – cells begin to divide uncontrollably
- Any mutagen which can cause cancer is called a **carcinogen**

18.1 - Diagnosis & Treatment of Genetic Disorders

- Until recently, it was very difficult to determine the health of an unborn baby.
- Today, with new research and technology, information can be gathered during fetal development and can even be predicted before conception

Genetic Counseling

- A genetic counselor is a medical professional who gathers detailed information from individuals who have a history of genetic disorders in their family. This information is gathered through interviews, blood tests, and discussions with geneticists.
- After gathering the necessary information, the counselor will then construct a family pedigree.
- The counselor can also use the information to predict the probability of a child inheriting a particular disorder.
- Once this information is communicated to the parents, they then need to make a decision as to whether or not they should conceive a child.

Diagnosis

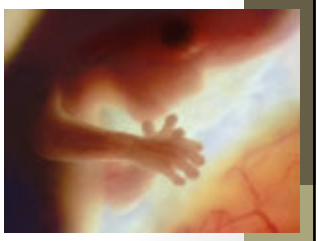
- **Diagnosis can occur at two stages**
  1. Pre-implantation diagnosis
  2. Prenatal diagnosis

Pre-implantation Diagnosis

- Pre-implantation diagnosis is performed before pregnancy has occurred.
- Sperm and eggs of prospective parents are placed inside a glass dish with a growth medium. Several eggs are fertilized and allowed to develop. After two days, eight cells have formed.
- One of these cells is removed and a karyotype is produced, the remaining cells continue to divide.
- Karyotype is analyzed for any genetic disorders. If none are found, the hollow ball of cells is placed in the female's uterus to continue its development.

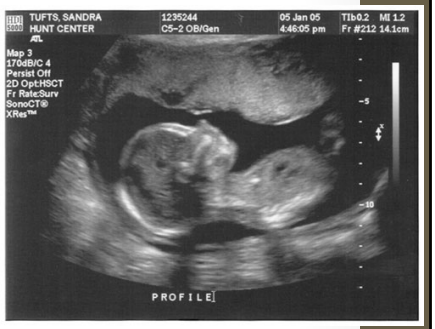
Prenatal Diagnosis

- Performed after a woman has conceived a child.
- There are several methods which can be performed here ;
    1. Ultrasound
    2. Amniocentesis
    3. Chorionic villus sampling
    4. Fetoscopy



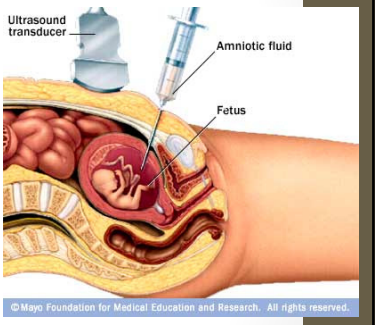
Ultrasound

- Involves sending sound waves through the amniotic fluid which the fetus is suspended in.
- The sound waves bounce of the fetus and are used to create a black and white image of the fetus.
- The image is studied to determine any physical abnormalities such as missing limbs, a malformed heart, etc.



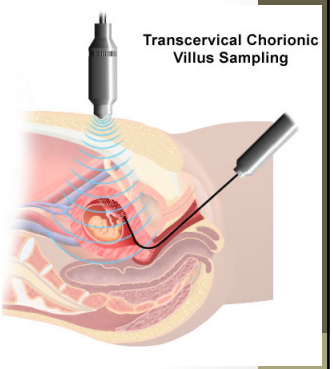
Amniocentesis

- A small amount of the amniotic fluid around a fetus is extracted with a long thin needle.
- This fluid is placed in a special nutrient rich medium and the cells are allowed to multiply for several weeks until there are enough cells to get a karyotype of the fetal cell's chromosomes.
- Observation of the karyotype will allow scientists to see disorders such as Down Syndrome, etc.
- Due to a potential risk to the fetus, this procedure cannot be done before the fourteenth week of pregnancy.



Chorionic Villus Sampling (CVS)

- Performed around the ninth week of pregnancy.
- Cells are removed from the membrane called the chorion which surrounds the amniotic sac.
- The chorion membrane contains fetal cells which have genetic information inside them.
- These cells are grown in a special medium until a karyotype can be made.
- The karyotype is then used to diagnose a genetic disorder.



Fetoscopy

- an endoscope, a long tube with a camera on one end, is inserted through a small incision which is made in the woman's abdomen.
- Procedures such as drainage of excess fluid surrounding the brain and blood transfusions can be performed on the fetus while still in the womb.
- Allows for the safe collection of blood samples from the fetus.
- Genetic material from the blood sample can be used to create a karyotype or to test for a number of different genetic disorders.
- Identification of proper blood type and detection of blood disorders are also possible using the process of fetoscopy.

18.3 The Chimera: From Legend to Lab

- In Greek mythology, the **Chimera** is a fire breathing monster which had the head and shoulders of a lion, the body of a goat, and a serpent for a tail.
- Today, geneticists use the term chimera to describe a genetically engineered organism which contains genes from unrelated species.
- In 1973, the first chimeric organism was created by two scientists, **Stanley Cohen and Herbert Boyer,** who developed a bacteria which could express an amphibian gene. This work is the foundation of the genetic engineering which is done today

Inserting Animal Genes Into Bacterial Cells

- In 1990, scientists produced the first **transgenic** or genetically engineered product which was approved for use in North America.
- In cattle, the growth hormone **somatotropin** makes them grow bigger, develop large udders, and produce extra milk.
- Scientists took the gene which is responsible for coding this hormone and successfully cloned and inserted it into a bacterial vector.
- In order to insert a gene from one organism (eukaryotic) into another (prokaryotic), two requirements must be met:
  1. Researchers must isolate the target gene from the eukaryotic organism's genome.
  2. They must ensure that the eukaryotic gene can be correctly expressed by the prokaryotic organism.

Inserting DNA into Plant or Animal Cells

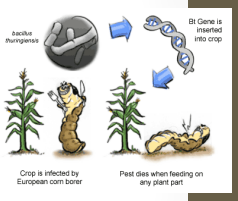
- In some cases plant or animal cells can be used as a cloning vector instead of bacterial cells.
- Plant and animal cells can be grown in special culture dishes, however, since they are difficult to culture it is harder to insert foreign DNA into them.
- Several methods have been developed to solve this problem:
  1. Bacteria plasmids (DNA) can be used to infect a plant cell by inserting the bacteria's DNA into the plant's DNA.
  2. Special devices such as a DNA particle gun can be used to open pores in the cell's nuclear membrane and DNA particles can be fired directly into the nucleus of the plant cell.

Putting Genetic Technologies To Use

- Any new strains of organisms which are developed by the use of genetic technologies must be examined by government agencies to determine the benefits and risks before they are used for commercial use.
- Different countries have different standards with regards to the use of these new strains of organisms.
- Genetic engineering technologies are being put to use in a variety of fields including agriculture, medicine, and environmental protection.
- As more transgenic organisms are produced, needs for standards and criteria will have to be developed

Herbicide - Resistant Corn

- Over 50 types of genetically modified crop plants have been approved for use in Canada.
- An example of such a plant is herbicide resistant corn.
- Scientists have isolated and cloned a bacterial gene which provides resistance to certain herbicides.
- DNA fragments from this gene were sprayed onto gold particles and fired into corn cells. The cells developed into corn which were resistant to the herbicide.
- Since the corn is resistant to herbicides, farmers can apply them to their fields to control weeds, but not damage the corn plants.
- This form of transgenic corn does not present a risk to human health and was approved for use in Canada in 2001.

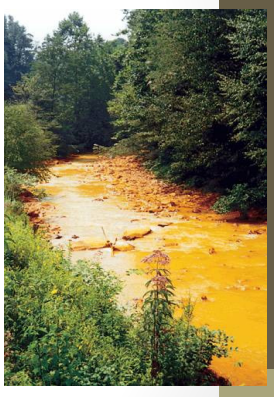


Human Insulin

- In 1982, a form of human insulin which was synthesized by transgenic bacteria was approved for use in the United States. This was the first example of a genetically engineered pharmaceutical product.
- By developing a process for inserting the human gene for insulin into bacteria, scientists were able to produce high volumes of human insulin.
- This lowered the cost of insulin treatment and reduced the number of side effects.
- Since this time, other pharmaceutical products have been produced using bacterial vectors.

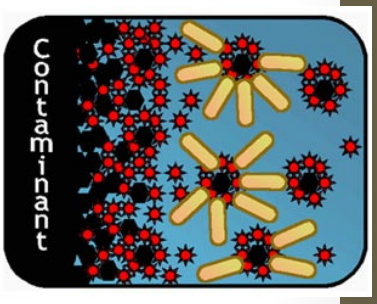
Bioremediation: PCB Eating Bacteria

- PCBs or polychlorinated biphenyls are a by-product of a number of industrial processes.
- These compounds are highly toxic and environmentally persistent. They build up in the soil and accumulate in food chains, thus presenting a risk to animal and human populations.
- Since cleanup of areas which are contaminated with PCBs is difficult and expensive, biotechnology companies are developing recombinant bacteria which can break down PCBs into harmless compounds.
- The use of living cells to perform environmental remediation tasks is called **bioremediation**.



Other Forms of Bioremediation

- Bacteria which can clean up oil spills.
- Bacteria which filter air from factory smokestacks.
- Bacteria which remove heavy metals from water



Better Nutrition

- Millions of people worldwide suffer from malnutrition due to lack of sufficient foods and balanced diets. This can lead to disease.
- Development of genetically modified foods such as rice, wheat, etc. which contain a number of necessary vitamins and other materials is an answer to these problems.
- Foods which are higher in nutrients will prevent malnutrition and limit the amount of disease in people who live in poorly developed countries.

Weighing the Risks

- Genetically modified products such as corn, golden rice, etc. have been marketed as demonstrating the benefits of genetic engineering.
- However, along with the benefits come a number or risks.
- Potential risks from the use of transgenic organisms include:
  1. Environmental threats
  2. Health effects.
  3. Social and economic issues

Environmental Threats

- The creation of herbicide resistant crops encourages farmers to use more herbicides to protect their crops. These herbicides leach into the water supplies and various ecosystems causing problems in non-target or even wild organisms, limiting biodiversity
- Herbicide resistant crops may crossbreed with other plants such creating what are called super-weeds. These weeds would then be very difficult to destroy.
- As insects feed on herbicide resistant crops, they may eventually develop into what are called super-bugs. These insects may then become resistant to certain pesticides

Health Effects

- Not enough is known about the long-term effects of transgenic products.
- Consumption of transgenic products may have effects which do not show up in studies done today, but may occur at a later time

Social & Economic Issues

- Some people argue that transgenic crops will help rid the world of hunger. Others argue that world hunger is a result of uneven food distribution, not food shortages, thus we do not need transgenic crop production.
- Others argue that if development of transgenic organisms continues by large companies, control of the world's food supplies could be controlled by large corporations.
- A final concern is that we, the human species, are treating other living organisms as commodities which we can manipulate, patent, and sell at our will.

$$$$

Transforming Animal DNA

- Researchers hope to create certain organisms through the process of **artificial selection**.
- By the process of artificial selection, humans are able to select particular traits by breeding certain organisms. This is also called **selective breeding**.
- Scientists have chosen to use the method of artificial selection because it is much more difficult to insert foreign DNA into animal cells than it is in plant cells