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FEDERAL GOVERNMENT UNIVERSITY

COURSE HANDOUTS

Genomics

BIO502

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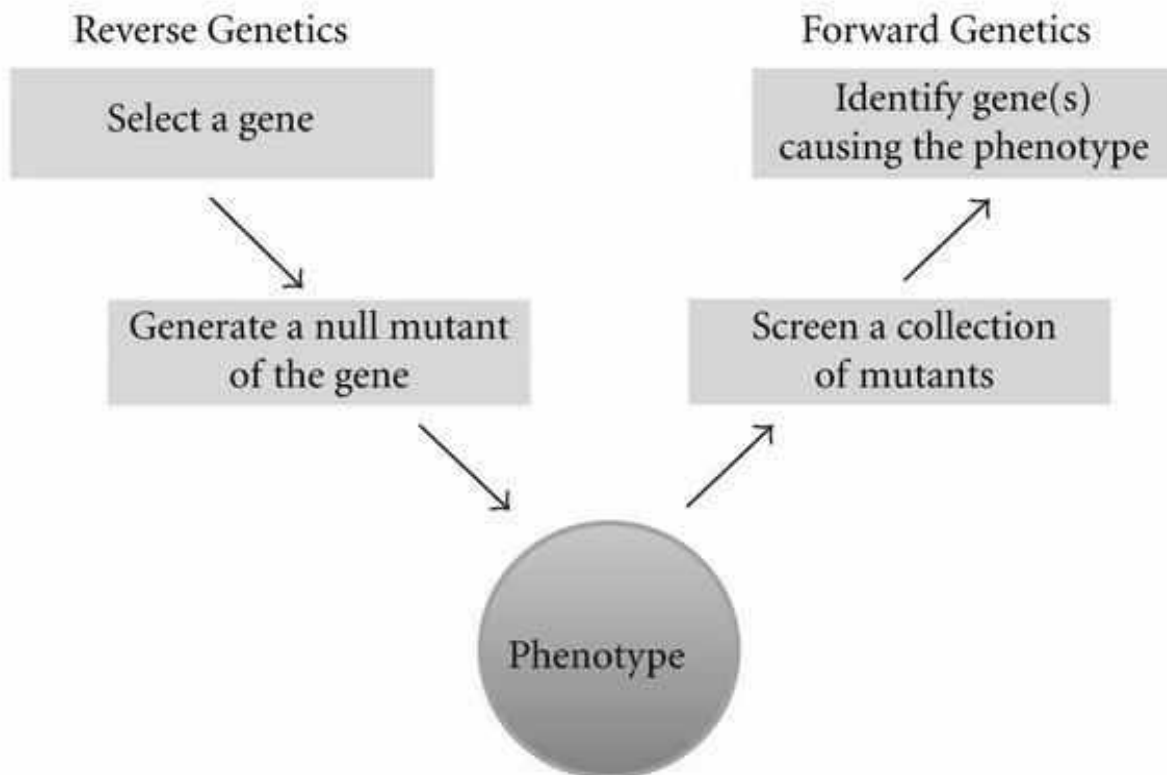
Lesson 1

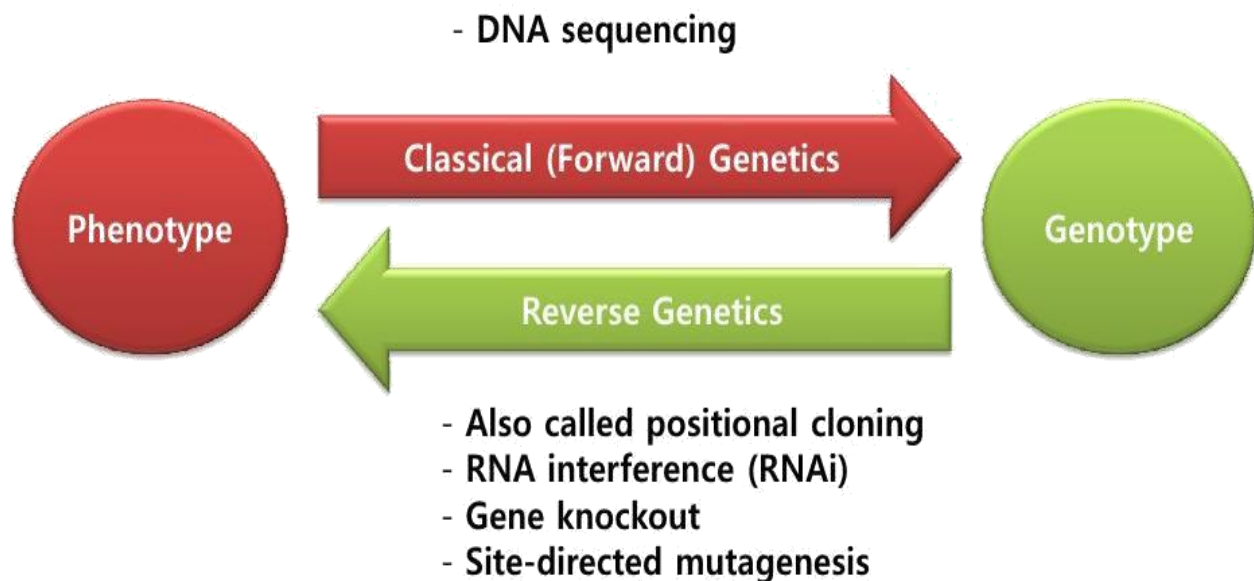
What is Genetics?

Genetics is the study of genes, heredity and variation.

It is considered as a field of Biology.

The principles of heredity were explained by Gregor Mendel in 1866.





Gregor Mendel used garden pea as experimental plant for formulating the laws of heredity, following were the properties of garden pea

Seed in a variety of shapes and colors.

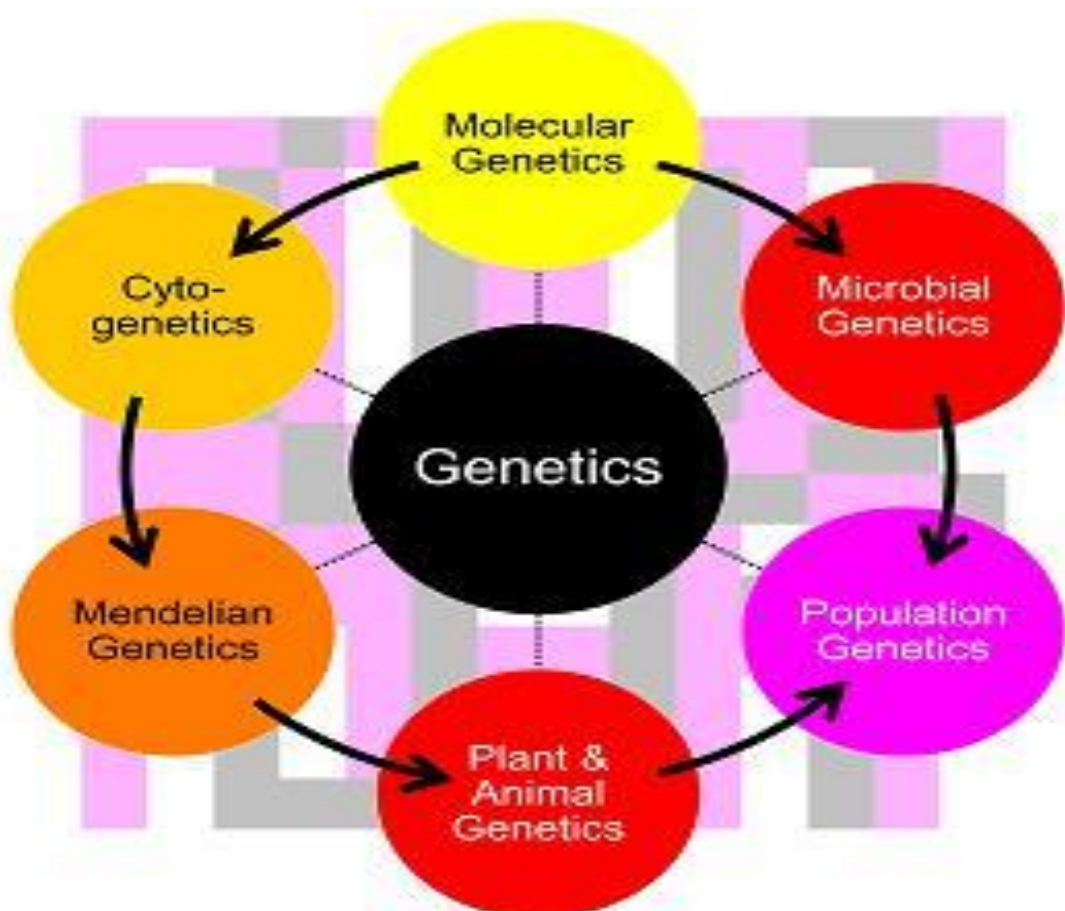
- Self, cross pollinate.
- Takes up little space.
- Short generation time
- Produces many offspring.

Lesson 2

Sub Types of Genetics

There are four sub disciplines of genetics which are as follows, although some of the Geneticist classify Genetics in many sub disciplines

- Transmission (Classical) Genetics
- Population Genetics
- Quantitative Genetics
- Molecular Genetics



Historically, transmission genetics developed first, followed by population genetics, quantitative genetics and finally molecular genetics.

- Transmission or classical genetics deals with movement of genes and genetic traits from parents to offspring. Mendel's Laws. It also deals with genetic recombination.
- Population genetics is the study of traits in a group of population. In this type of genetics we study heredity in groups for traits determined by one or a few genes.
- Quantitative genetics is the study of group hereditary for traits determined by many genes simultaneously such as skin color, height, eye color etc
- Molecular genetics this branch of genetics deals with the molecular structure and function of genes.

Lesson 3

Common Genetics Terminologies

What is Character: A heritable feature (skin color, height etc).

What is Trait: variant for a character (i.e. brown, black, white etc).

What is True-breed: all offspring of same variety.



Different generations of a cross
can be P generation (parents)

F1 generation (1st filial generation)

F2 generation (2nd filial generation)



Pure Cross: A cross between a true breed plant/animal with another true breeds
plant/animal is called pure cross

True breeding X True breeding

WW X ww



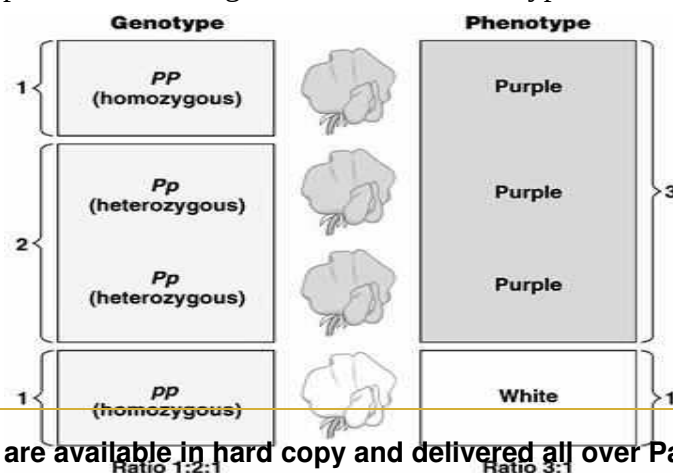
Hybrid Cross:

F1 generation X F1 generation

Ww X Ww



Genotype and Phenotype: Genetic make-up of an organism is called Genotype while
physical appearance of an organism is called Phenotype.





Dominant and Recessive: when one characteristic expresses itself over the other i.e. round over wrinkled was dominant in Gregor Mendel experiments while the trait that does not show through in the first generation is called as recessive trait i.e. wrinkled.

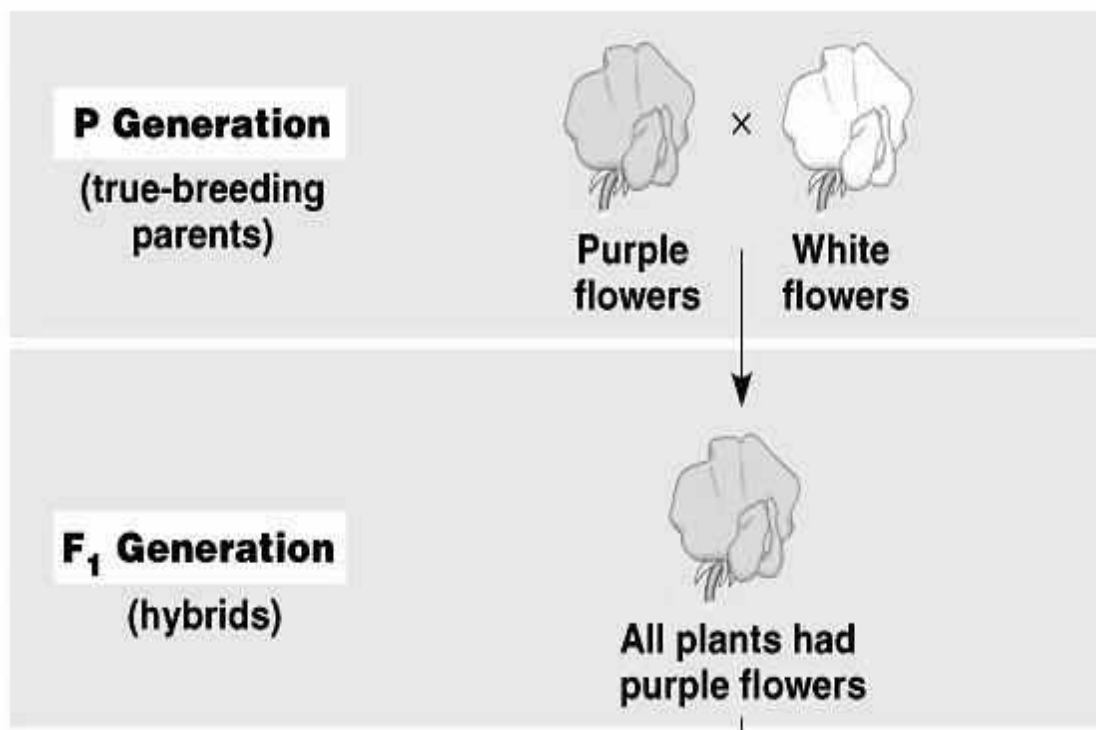
Lesson 4

Mendel's law of dominance

Mendel's law of dominance describes that in a cross of parents, that are pure for contrasting traits, only one form of the trait will appear in the next generation. In the monohybrid cross, one version will be disappeared

Example:

Cross of two true-breeding plants. First plant is with purple color flowers while second is with white color flowers. During F₁ generation, all plants will be with purple color flowers. It can be concluded that purple color dominant to white.



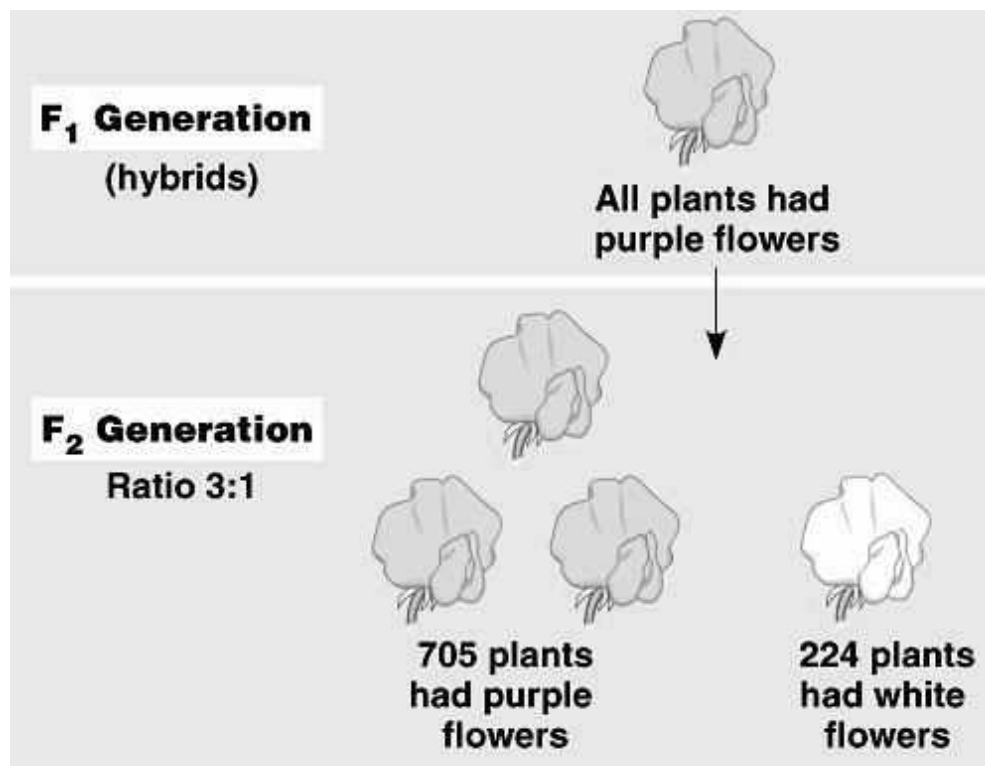
It can be concluded that hybrids will show dominant phenotype

Example:

PP = purple pp = white Pp = purple

Law of dominance and current model of inheritance

Plants of F₁ generation were interbred which produced F₂ plants. Lost-trait was re-appeared that was the formulation of the current model of inheritance.

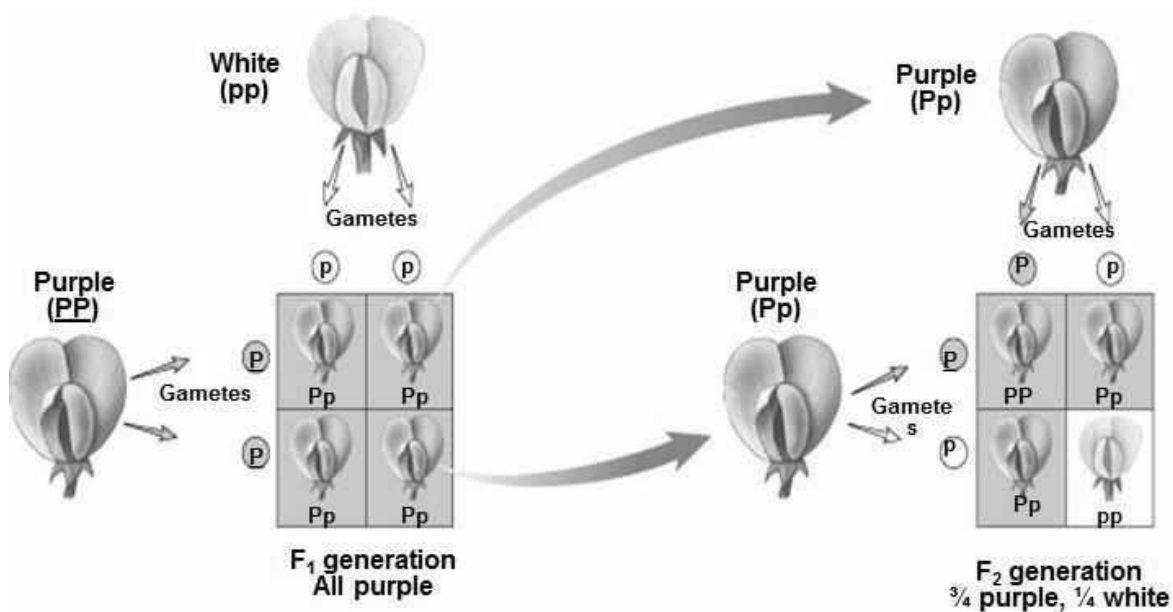


Every gene has two alleles that can code for a trait. One allele is dominant while other allele is recessive. The gene for a particular inherited character resides at a specific locus (position) on homologous chromosome. For each character, an organism inherits two alleles, one from each of the parent.

Lesson 5

Monohybrid cross and Dihybrid cross

Cross-fertilization of true-breeding plants which are different in just one character is called as monohybrid cross. With monohybrid cross, Mendel determined the segregation of alleles at single gene locus.



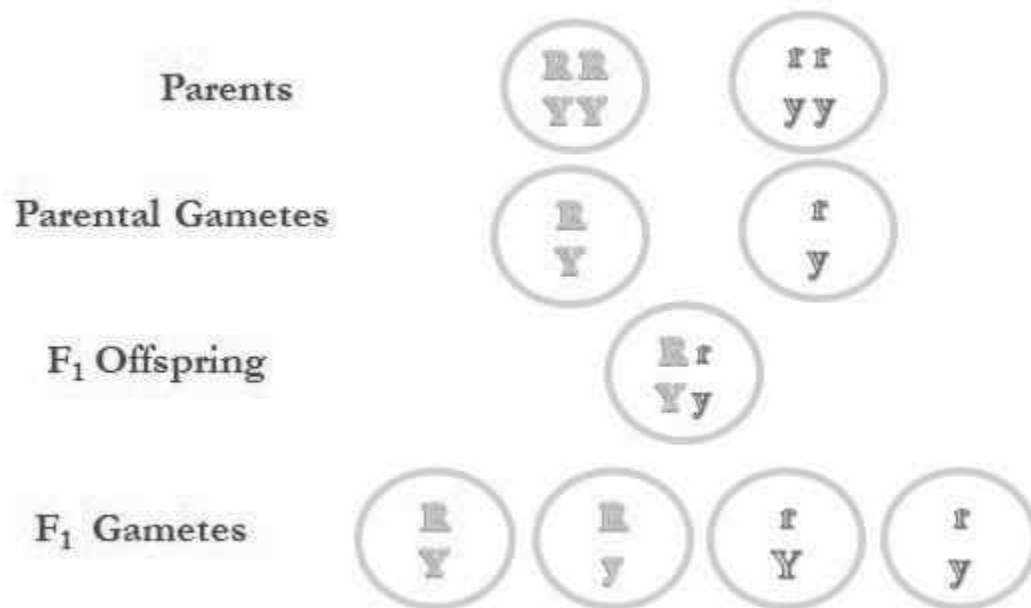
Dihybrid cross determines that alleles at two different gene loci segregate dependently or independently. Segregation is dependent or independent ?

Example:

Seed shape is controlled by one gene while seed color is controlled by a different gene. Mendel crossed two pure-breeding plants: one with round/yellow seeds, other with green/wrinkled seeds.

Dependent segregation: Alleles at the two gene loci segregate together, and are transmitted as a unit.

Independent assortment: Alleles at the two gene loci segregate independently, and are not transmitted as a unit. Plants producing gametes with different allele combinations.



Independent assortment

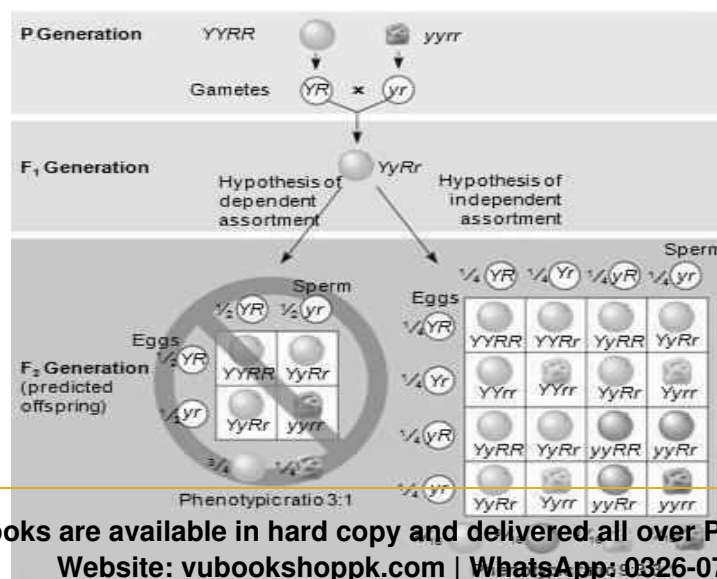
How are two characters transmitted from parents to offspring, if they are away from each other or on different chromosomes? They will transmit

As a package?

○ Independently?

Answer:

independently



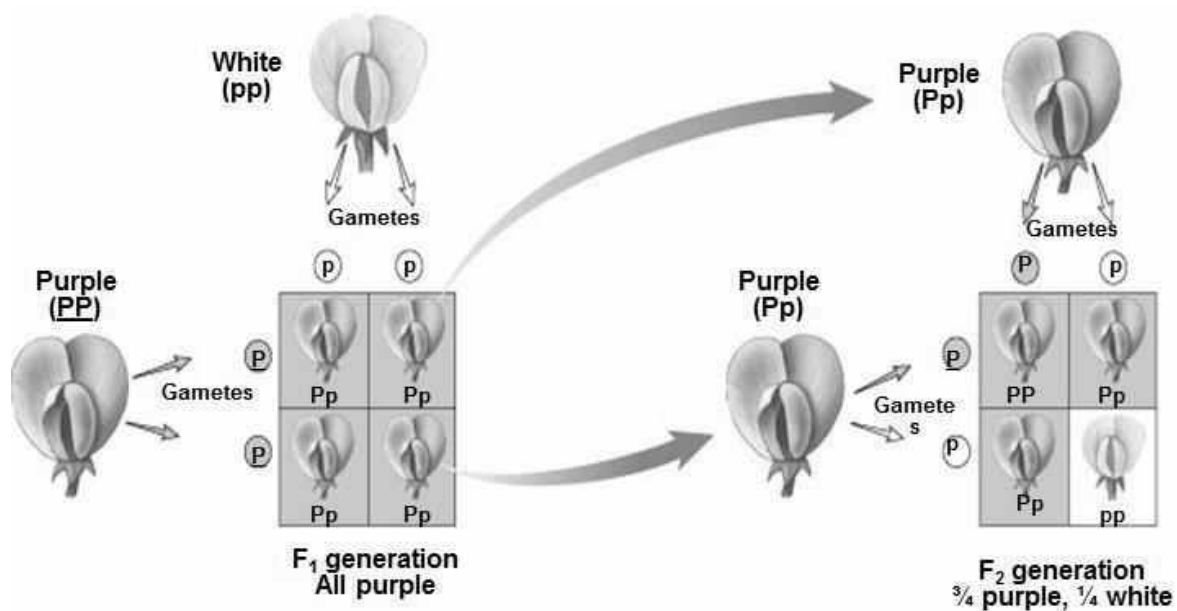
Lesson 6

Law of Segregation

During the formation of gametes, the two alleles responsible for a trait separate from each other. Alleles are then "recombined" during the process of fertilization.

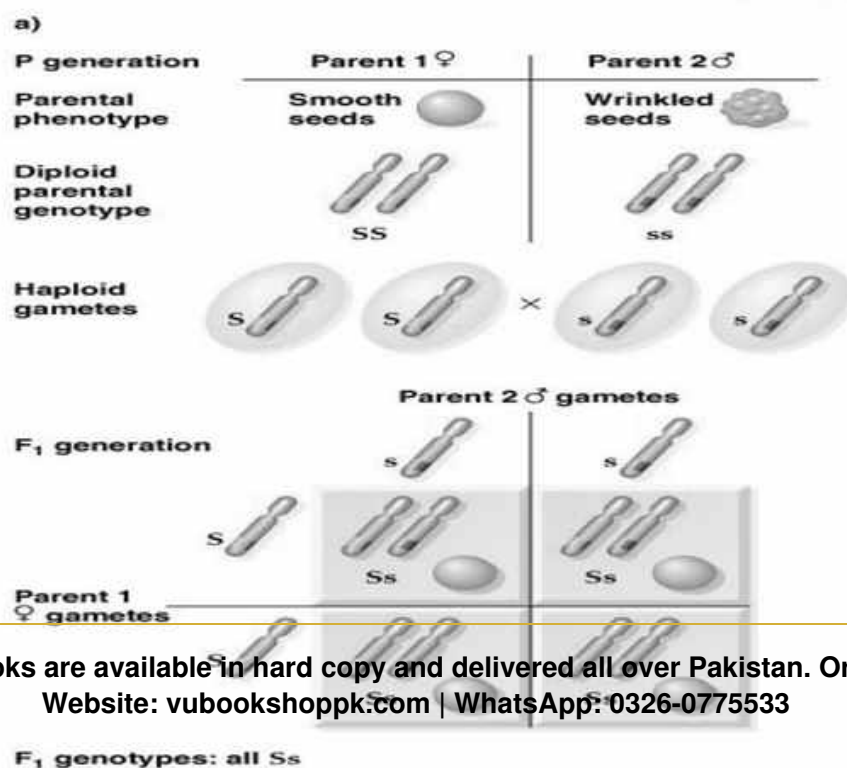
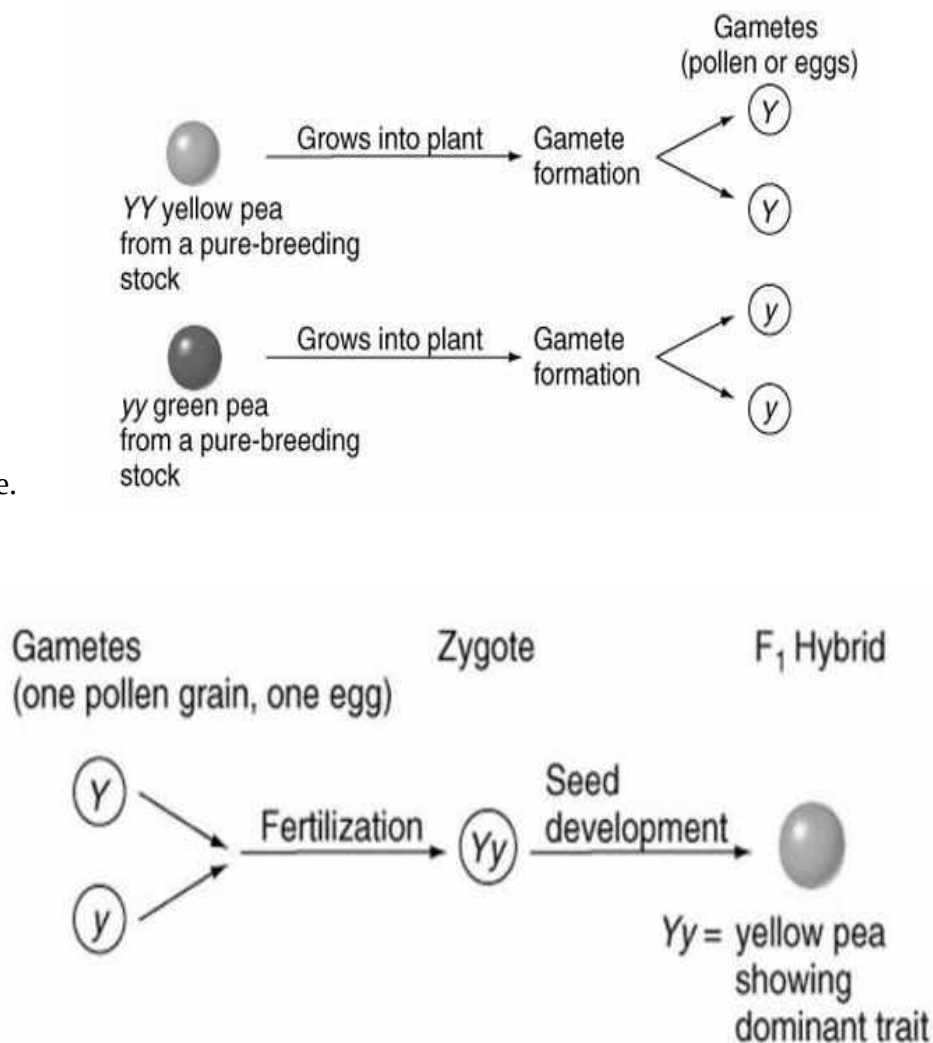
Example 1

During a cross, gametes of each parent first segregate. Then, gametes combine to give new genotype. Resulting phenotype will be according to genotype.



Example 2: Gametes formation, where alleles separate.

During fertilization, gametes re-unite.



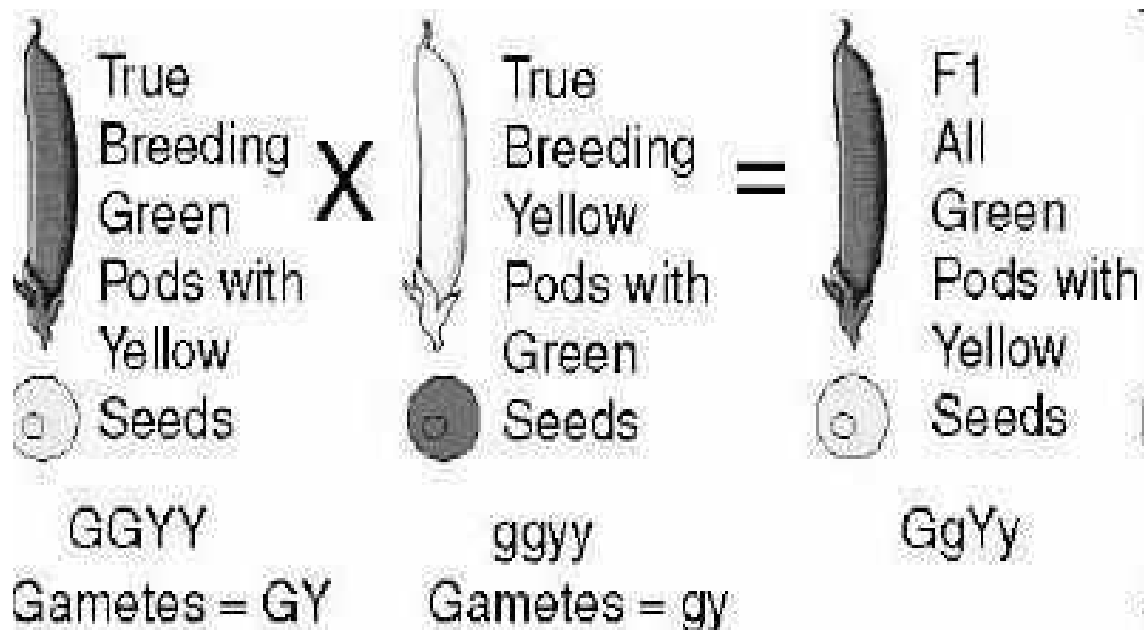
Modern Concept of Segregation states that every gene has two alleles that can code for a trait. Alleles separate during gametogenesis and reunite during fertilization.

Lesson 7

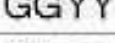
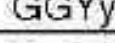
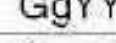
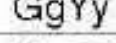
Mendel's Law of Independent Assortment

Alleles for different traits are distributed to sex cells independently of one another. Traits are transmitted to offspring independently of one another.

Example: Dihybrid cross, true-breeding plants for two traits. For example, a plant that had green pod color and yellow seed color was cross-pollinated with a plant that had yellow pod color and green seeds. The traits for green pod color (GG) and yellow seed color (YY) are dominant. Yellow pod color (gg) and green seed color (yy) are recessive. F1 plants heterozygous GgYy

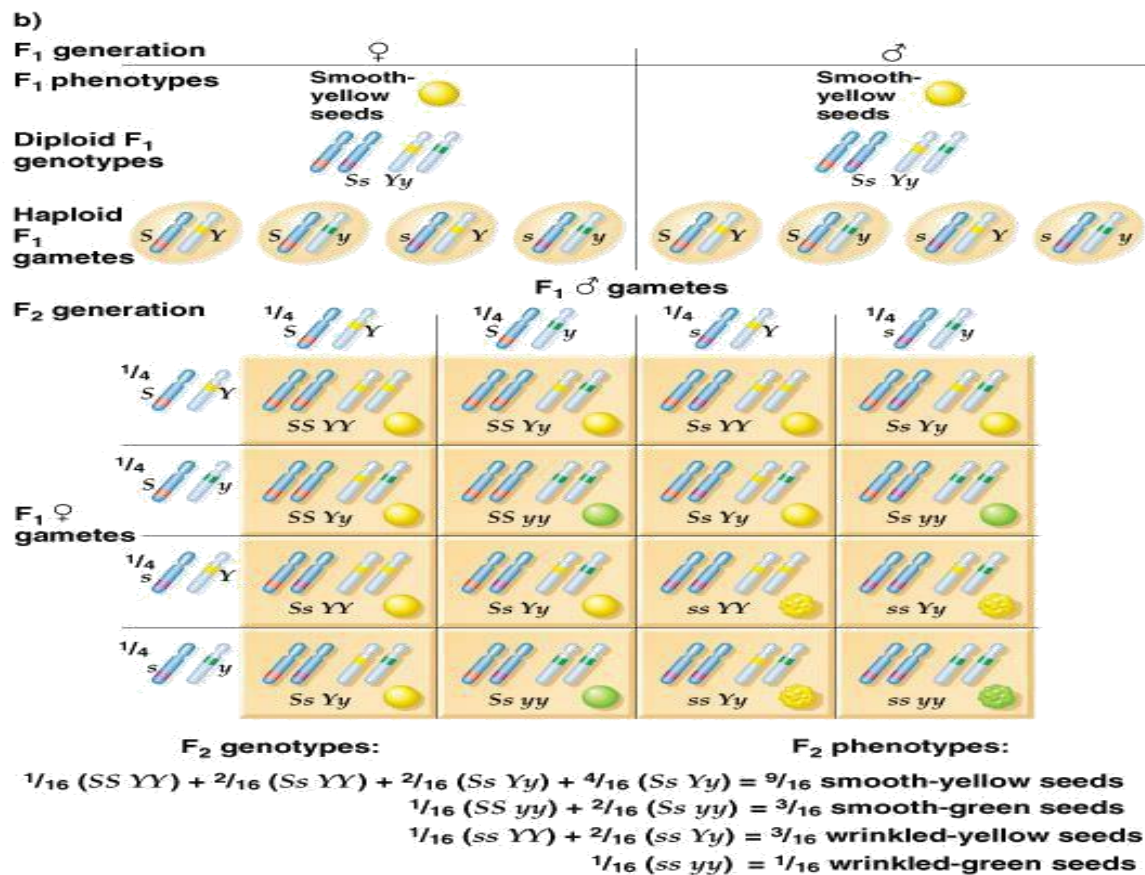


After observing the results of dihybrid cross, Mendel allowed all of the F1 plants to self-pollinate. He referred to these offspring as F2 generation. Mendel noticed a 9:3:3:1 ratio.

				F1	GgYy
		GY	Gy	gY	gy
 F1 GgYy	GY	 GGYY	 GGYy	 GgYY	 GgYy
	Gy	 GGYy	 GGyy	 GgYy	 Ggyy
	gY	 GgYy	 GgYy	 ggYY	 ggYy
	gy	 GgYy	 Ggyy	 ggYy	 ggyy

The results support the hypothesis of independent assortment. The alleles for seed color and seed shape sort into gametes independently of each other.

Modern Concept of Law of Independent Assortment

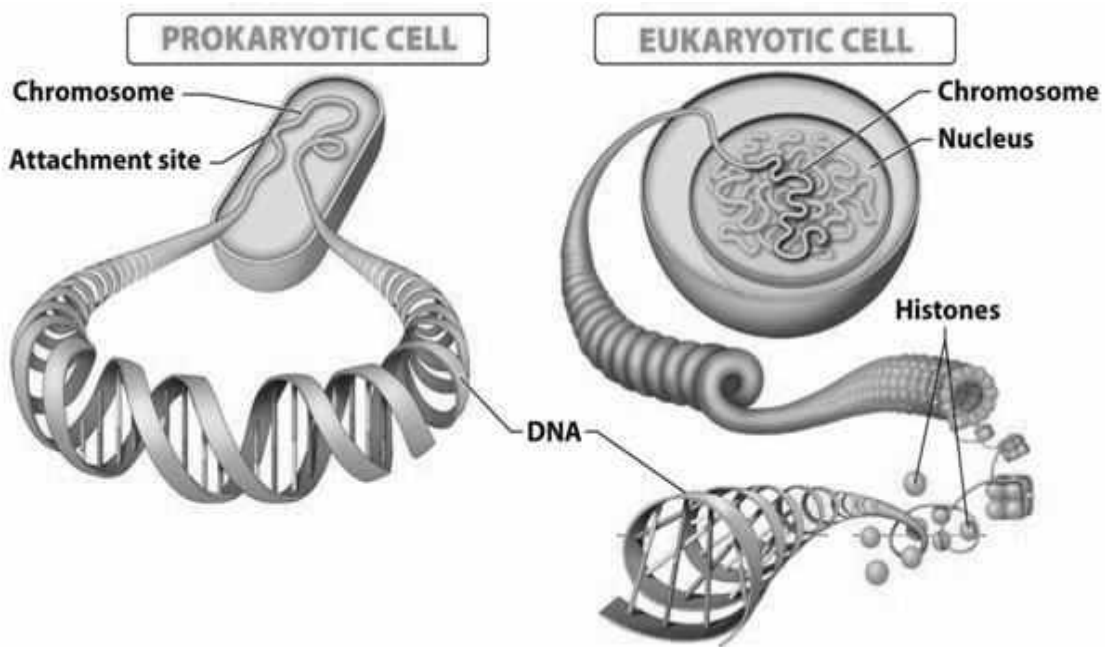


Lesson 8

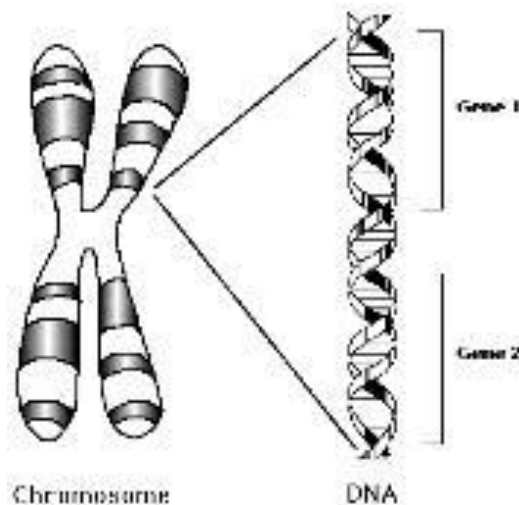
Modern Genetic Concepts

- ✓ Chromosomes and Gene (s)
- ✓ Mendelian Genetics and Non-Mendelian Genetics
- ✓ Genotypes and Phenotypes
- ✓ Mutations and Polymorphism

What is chromosome: Genetic material in cells is organized into chromosomes. Prokaryotes generally have one circular chromosome. Eukaryotes - linear chromosomes in their nuclei.



What is gene : A heredity unit on chromosomes.



Mendelian genetics: Mendelian genetics - genes that obey Mendel's laws. Most genes follow a Mendelian pattern of inheritance, However, there are many that don't.

Non-Mendelian genetics: Patterns of inheritance that deviate from a Mendelian pattern. Linkage - Non-Mendelian. Maternal effect, epigenetic inheritance, Mitochondrial inheritance etc.

Genotype and phenotype: Genetic make-up of an organism while physical appearance of a organism.

Genotype	Phenotype	Phenotype= Blue Eyes	Phenotype=Brown Eyes
EE Homozygous dominant	Detached Earlobes 		
Ee Heterozygous	Detached Earlobes 		
ee Homozygous recessive	Attached Earlobes 		

Genotype=bb	Genotype = Bb or BB
-------------	---------------------

What is mutation: Indicate "a change" while in other disciplines it is used to indicate "a disease-causing change". Mutations may be harmful, beneficial, may have no effect.

Lesson 9

What is Heredity?

Transmission of traits from parents to offspring.

Is transmission blending or particulate.

Is inheritance blending or particulate

Till 19th century ...biologists believed, it was blending.

Problematic, new genetic variations would quickly be diluted, not passed onward.

Blending hypothesis

According to blending hypothesis, genetic material of the parents mixes during fertilization.

Blue and yellow paints blend to make green paint.

Particulate hypothesis

According to particulate hypothesis, parents pass on distinct heritable units.

Those distinct heritable units are now called as genes.

Particulate inheritance

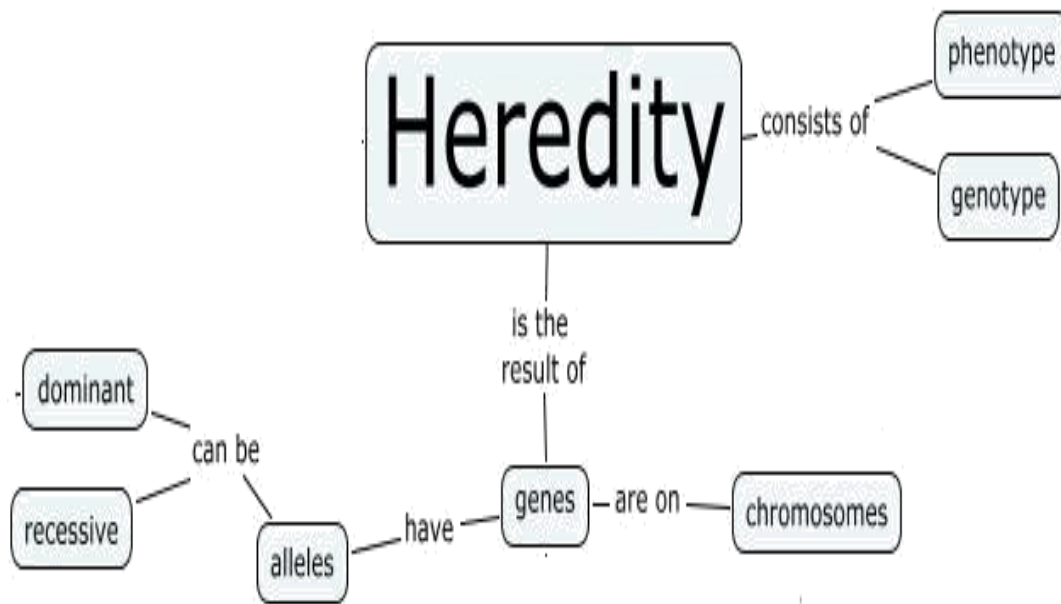
Mendel showed characters, or what we now call alleles, were inherited unchanged.

Pattern of inheritance of these characters gave us the first definition of a gene.

Mendel and particulate inheritance

Mendelian inheritance patterns involve genes that obey Mendel's laws.

Most genes follow a Mendelian pattern of inheritance, However, there are many that don't.

**Heredity**

Heredity is transmission of traits from parents to offspring.

Transmission is particulate.

Lesson 10

Mendelian and Non-Mendelian inheritance

Mendelian inheritance

Gregor Mendel's model of inheritance describes

Each trait is controlled by a single gene.

Each gene has two alleles.

A clear dominant-recessive relationship between alleles.

Mendelian inheritance involve the genes that obey Mendel's laws: Law of dominance Law of segregation Law of independent assortment.

Mendelian inheritance

Phenotypes will obey patterns;

Autosomal dominant

Autosomal recessive

X-linked etc.

Non-Mendelian inheritance

Pattern of inheritance that deviate from Mendelian pattern of inheritance is called as Non-Mendelian inheritance.

Those genes that do not follow principles of heredity formulated by Gregor Mendel.

Examples of Non-Mendelian inheritance

Mitochondrial inheritance

Genomic (parental) imprinting

Incomplete dominance

Co-dominance

Multiple alleles

Epigenetics

Lesson 11

Conclusions of Mendelian inheritance

Mendelian inheritance

Mendel's conclusions were based on three laws:

Law of Dominance

Law of Segregation

Law of Independent Assortment

Conclusion- law of dominance

Cross of true-breeding strains resemble only one of the parents.

Smooth seeds (S) are completely dominant to wrinkled seeds (s)

Conclusion - Law of segregation

Two members of a gene pair segregate (separate) from each other during the formation of gametes.

Conclusion-Law of independent assortment

Alleles for different traits assort independently of one another.

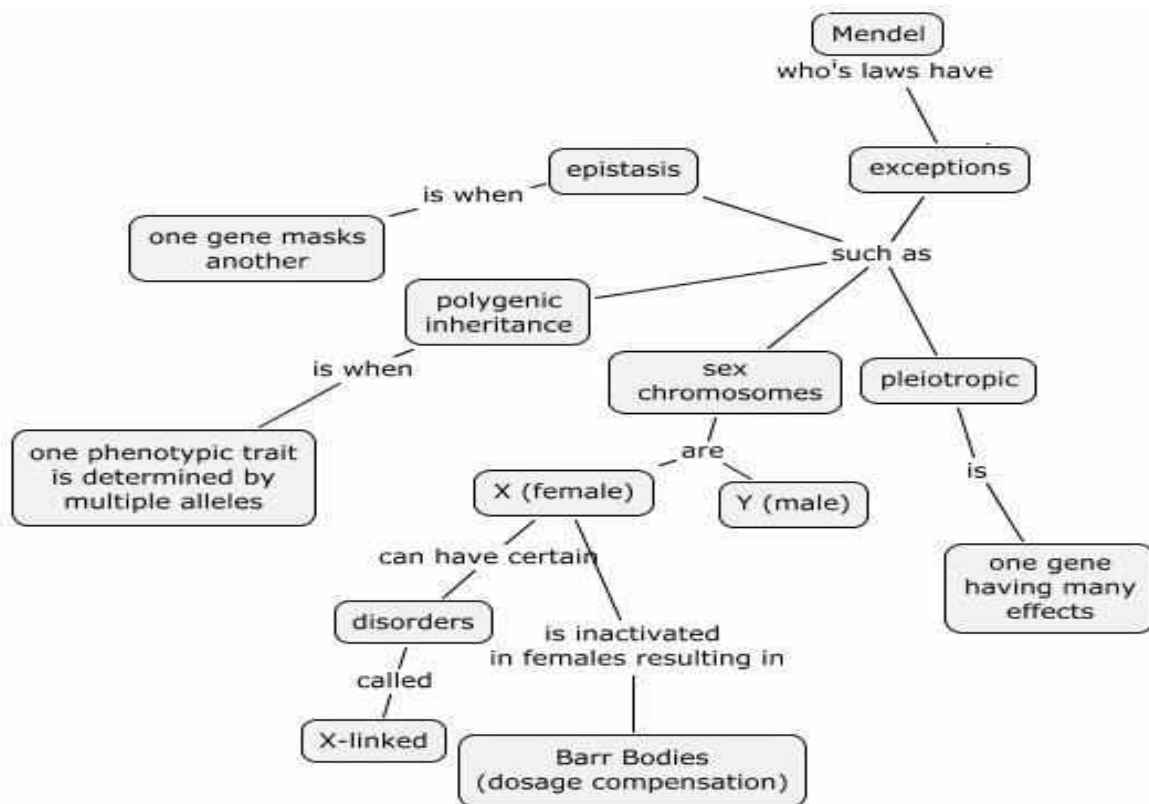
Genes on different chromosomes independently behave.

Lesson 12

Exceptions to Mendelian inheritance

Exceptions to Mendelian inheritance

Incomplete dominance
 Codominance
 Multiple alleles
 Polygenic traits
 Epistasis
 Pleiotropy
 Environmental effects on gene expression
 Linkage
 Sex linkage



Lesson 13

Incomplete dominance

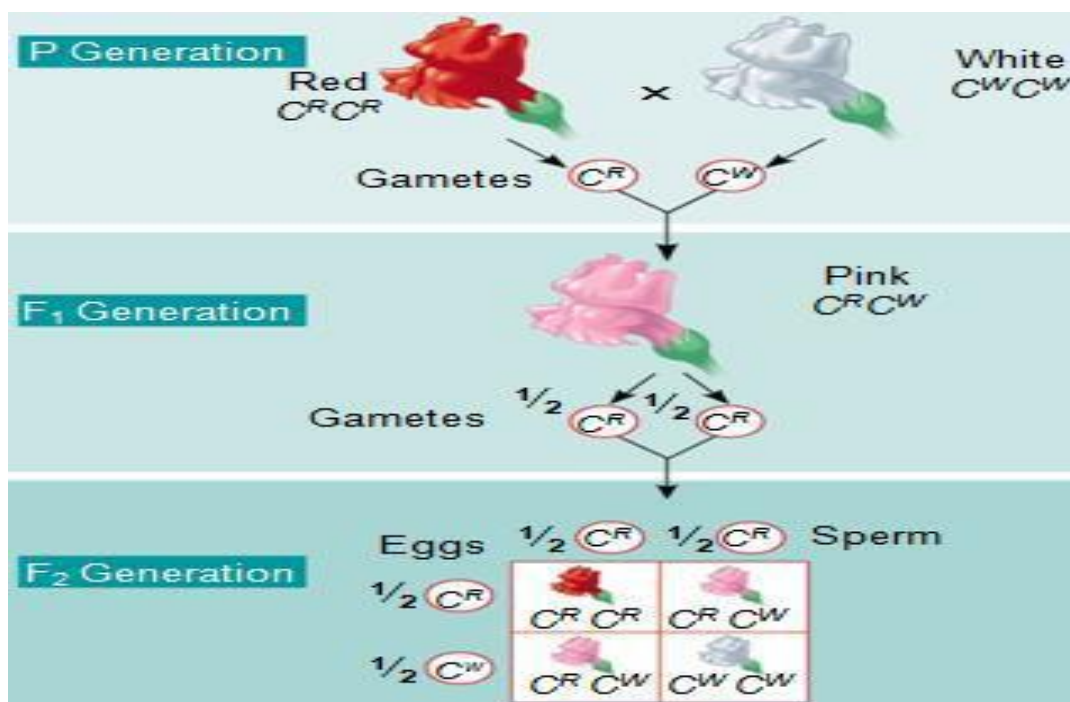
Some alleles for a gene are not completely dominant.

An intermediate phenotype – between two extremes.

None of the allele is dominant.

Incomplete dominance

As none of the alleles is dominant. As a result of a cross, a “new” phenotype appears that is a blend of both alleles.



Example: Japanese 4 o' clock flowers

Genotypes of Japanese 4 o' clock plant

Red flower plant genotype = **RR**

White flower plant genotype = **WW**

Pink flower plant genotype = **RW**

Incomplete dominance is a situation in which neither allele is dominant.

New phenotype appears.

New phenotype is blend of both alleles.

Lesson 14

Co-dominance

A situation, when both alleles appear in the phenotype.

Neither allele is dominant.

Both alleles are expressed in a heterozygous individuals.

Parallel behavior of both allele.

Example 1 : Blood group

Genotype	Phenotype (Blood Group)	Red Blood Cells
$I^A I^A$ or $I^A i$	A	
$I^B I^B$ or $I^B i$	B	
$I^A I^B$	AB	
ii	O	

Example 2: Roan cattle inheritance

Roan color in cattle appears as a mix of red and white colors.

$crcr$ = **red hairs**

$cwcw$ = **white hairs**

$crcw$ = **roan coat**

**Roan cattle inheritance**

Roan color in cattle appears as a mix of red and white.

Example 3: Appaloosa horse

Gray horse dominant to white horse.

Heterozygous is appaloosa –a white horse with gray spots.



- A situation, when both alleles appear in the phenotype and neither of the alleles is dominant.

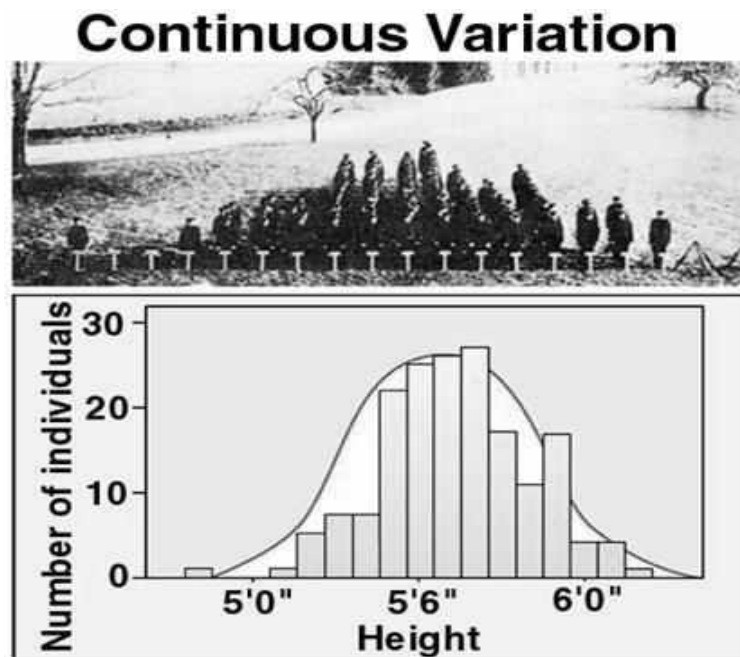
Lesson 15

Polygenic traits

Most traits are not controlled by a single gene locus, but by the combined interaction of many gene loci. These traits are called polygenic traits.

Example: Humans Height

Graph for continuous variation



Example: Humans eyes color is controlled by many genes.



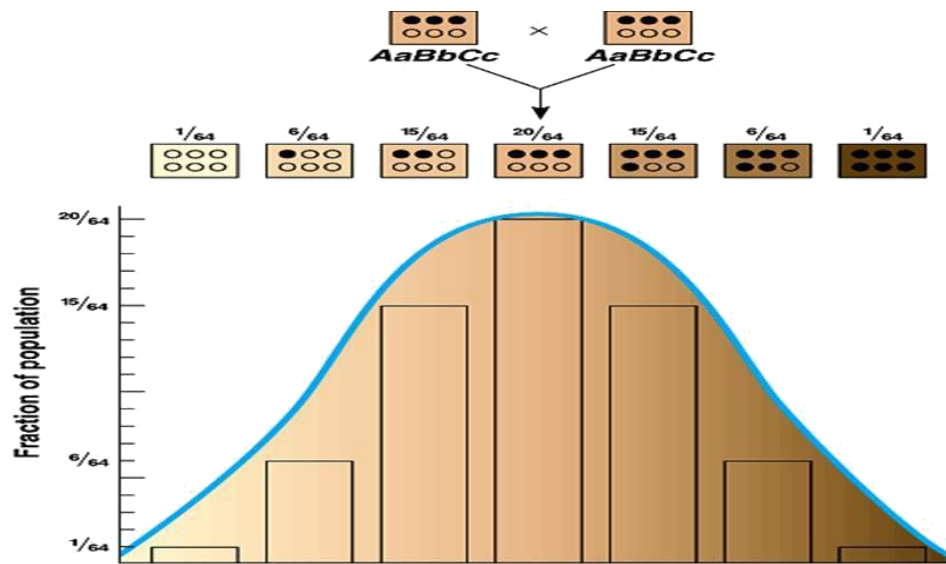
Pigmentations in humans

Qualitative traits usually indicate polygenic inheritance; effect from two/more genes.

Skin color pigmentation in humans is controlled by at least three separately inherited genes.

Pigmentation in humans

Controlled by three genes.



Conclusion

Polygenic traits are those traits which are controlled by additive effect of many genes.

Qualitative traits are usually polygenic in nature.

Lesson 16

Epistasis

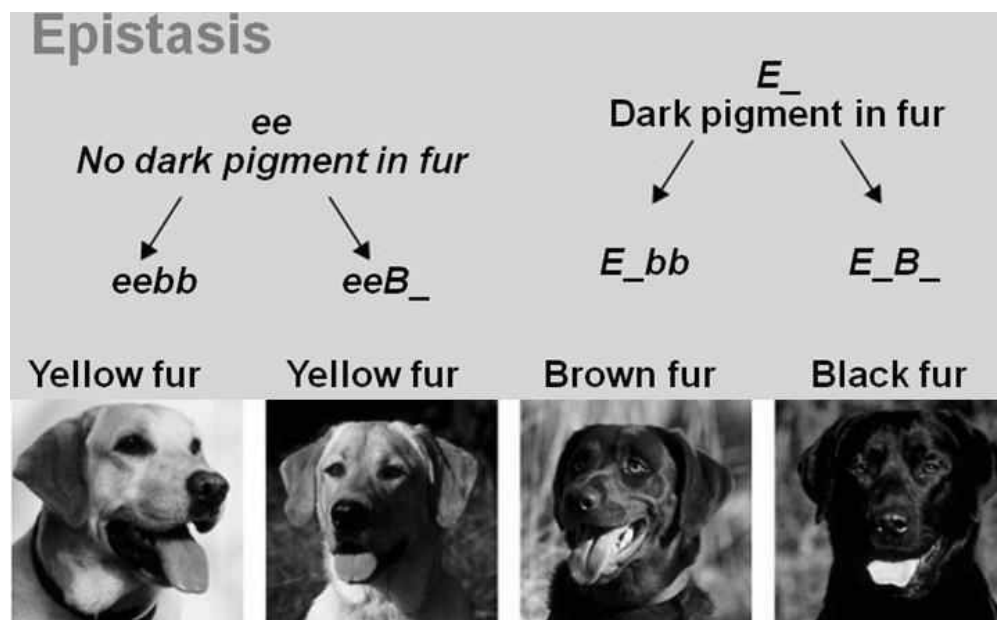
Alleles at one gene locus can hide or prevent expression of alleles at second gene locus.

Labrador retrievers one gene locus affects coat color by controlling pigment eumelanin deposited in the fur.

Example

A dominant allele B for black, recessive allele b brown coat, a second gene (e) locus controls eumelanin deposited in fur.

Dogs homozygous recessive at this locus (ee) will have yellow fur no matter which alleles are at first locus.



Example: Epistasis in horses fur

Horse coloration involves 2 or more gene pairings.

EE or Ee is for black.

ee is for red (sorrel).

Other genes can add effects to base colors.

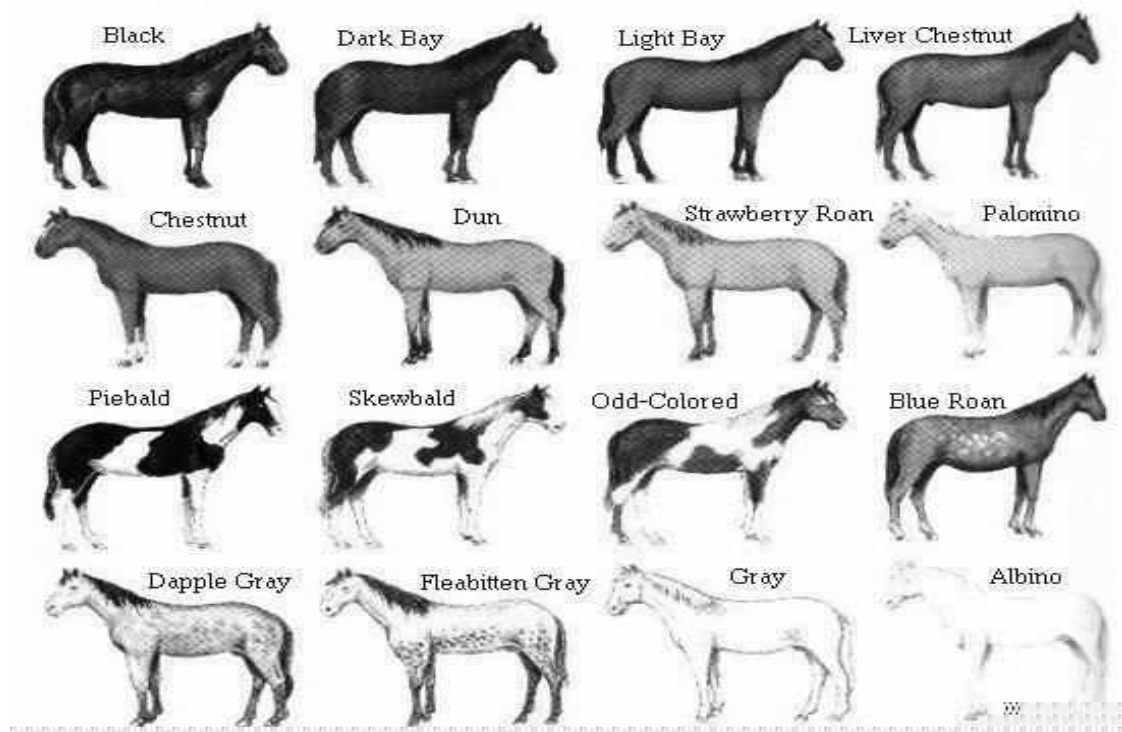
Bay is AA, EE – black with agouti gene;

Buckskin is AA, EE, CcrC – bay with cremello gene,

Dun is AA, EE, Dd – bay with dun gene;

Palomino is ee, CcrC – sorrel with cremello gene.

Equine's Color's and Marking's



Alleles at one gene locus can hide or prevent expression of alleles at second gene locus is called as epistasis.

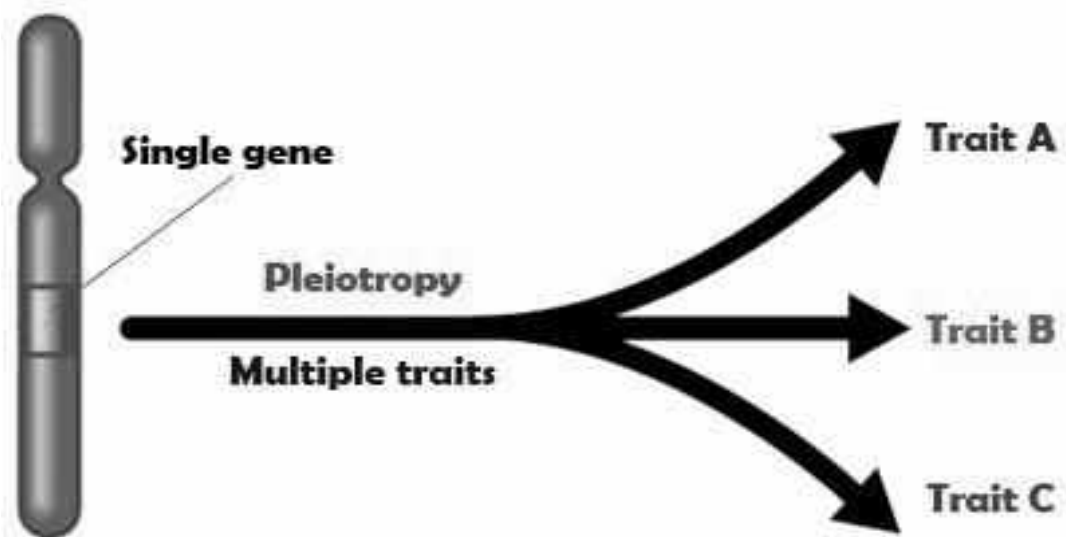
Lesson 17

Pleiotropy

The ability of a gene to affect an organism in many ways is called pleiotropy.

Pleiotropy refers to an allele which has more than one effect on the phenotype.

This phenomenon occurs when a single gene locus produces more than one traits.

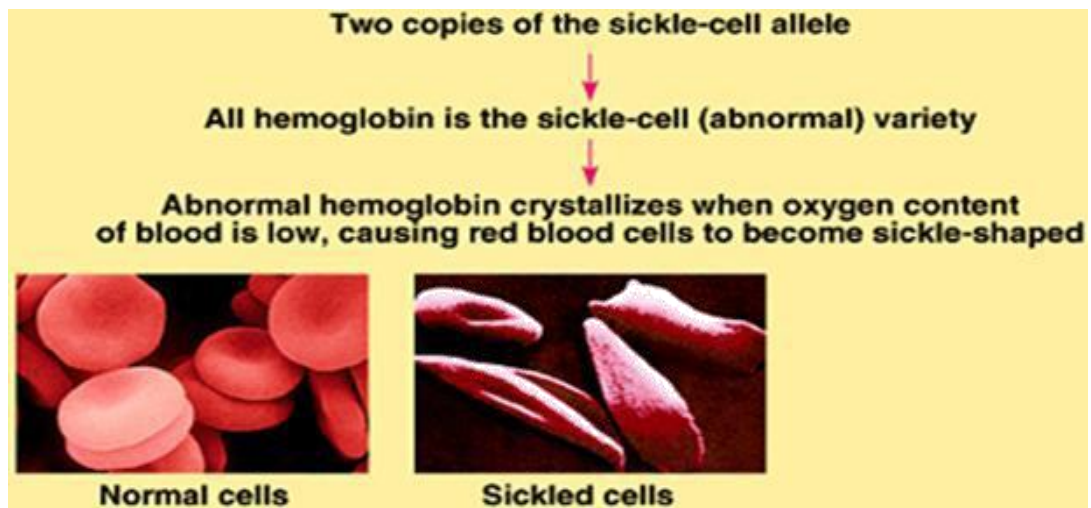


Pleiotropic effects in humans

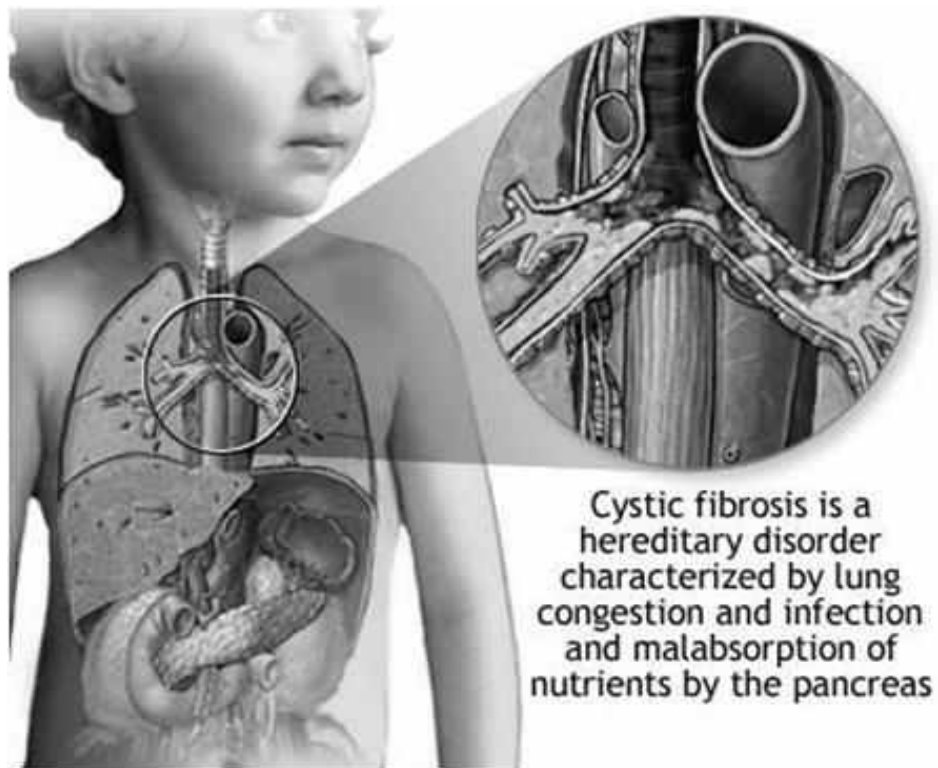
Example:

Sickle cell anemia

Cystic fibrosis



Cystic fibrosis



Huntington disease

One gene – more than one phenotypes

Phenotype 1: progressive dementia at age of 40-50 years

Phenotype 2: death in about 5 years after onset of disease.

Lesson 18

Environmental effects

Environmental effects on Gene expression

The phenotype of an organism depends not only on which genes it has (genotype), but also on the environment under which it develops.

Interaction - genotype and environment

Although scientists agree that phenotype depends on a complex interaction between genotype and environment.

Debate and controversy about the relative importance of both.

Environmental effects

Allele expression may be affected by environmental conditions.

Examples:

Coat color in arctic foxes

Himalayan rabbits

Siamese cats

Explanation

✓

ch allele affected by temp >33 C tyrosinase enzyme inactivates and reduces melanin pigment.



Himalayan rabbits



Siamese cats



Environmental effect on phenotype

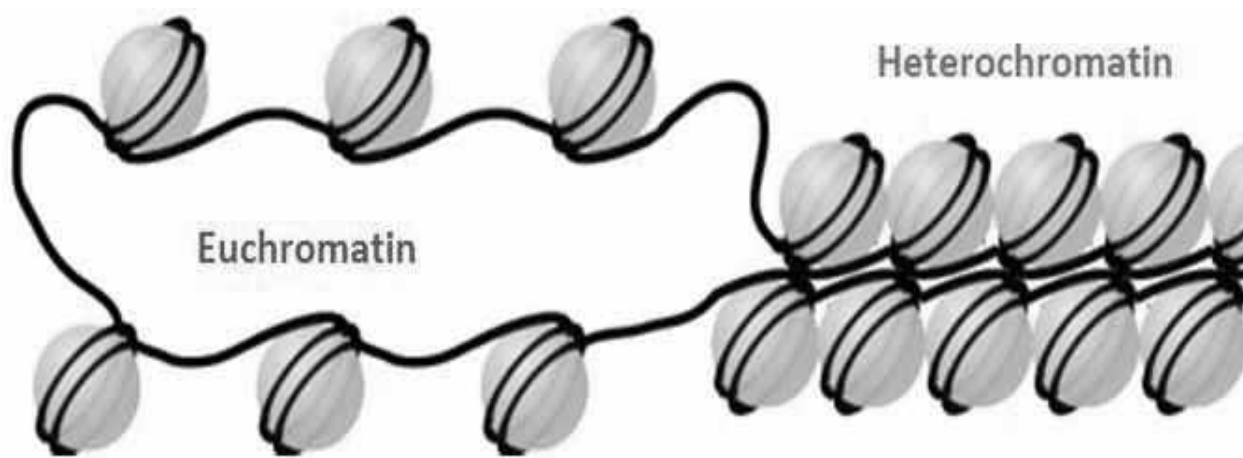
pH of the soil will change the color of hydrangea flowers.



There is a strong impact of environment on the expression of certain traits.

Lesson 19

Euchromatin and Heterochromatin: Chromosomes may be identified by regions that stain in a particular manner when treated with various chemicals. Several different chemical techniques are used to identify certain chromosomal regions by staining. Darker bands are generally found near the centromere or on the ends (telomeres) of the chromosome. The position of the dark-staining is heterochromatic region or heterochromatin. Light staining regions are Euchromatin region or Euchromatin.

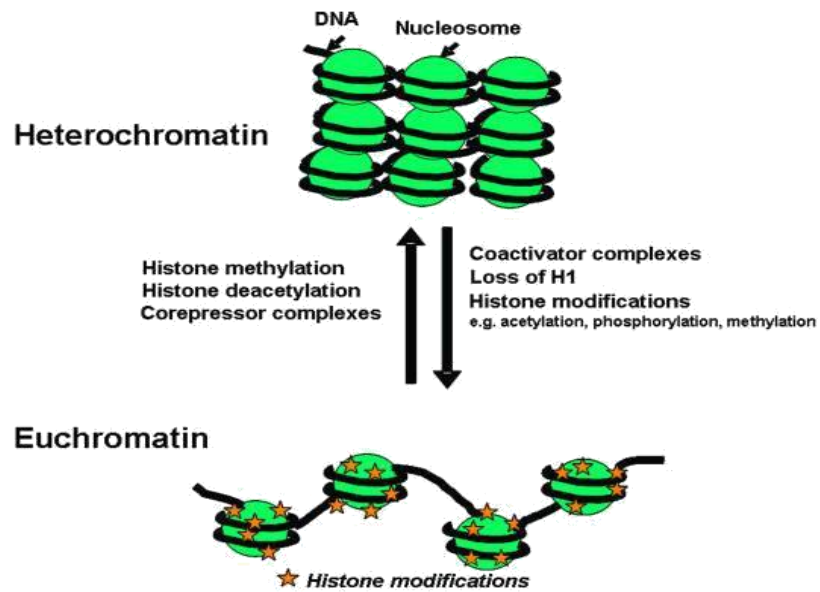


Heterochromatin Heterochromatin is classified into two groups:

1. Constitutive
2. Facultative

Constitutive heterochromatin remains permanently in the heterochromatic stage. It does not revert to the Euchromatin stage.

Facultative heterochromatin consists of Euchromatin that takes on the staining and compactness characteristics of heterochromatin during some phase of development.



Lesson 20

Staining and banding chromosomes

Staining procedures

Staining procedures have been developed in the past two decades and these techniques help to study the karyotype in plants and animals.

Feulgen staining

Cells are subjected to a mild hydrolysis in 1N HCl at 60 °C for 10 minutes.

This treatment produces a free aldehyde group in deoxyribose molecules.

Q Banding

Q bands are the fluorescent bands observed after quinacrine mustard staining with UV light.

The distal ends not stained by this technique.

R Banding

The R bands (reverse) are those located in the zones that do not fluoresce with the quinacrine mustard, that is they are between the Q bands and can be visualized as green.

C Banding

The C bands correspond to constitutive heterochromatin.

The heterochromatin regions in a chromosome distinctly differ in their stainability from euchromatic region

Human chromosome banding patterns

Human body cells contain 46 chromosomes in 23 pairs – one of each pair inherited from each parent.

Q-banding	Quinacrine	Chromosome arms; mostly repetitive AT-rich DNA	Under UV light, distinct fluorescent banded pattern for each chromosome.
G-banding	Giemsa	Chromosome arms; mostly repetitive AT-rich DNA	Distinct banded pattern for each chromosome; same as Q-banding pattern except single additional band near centromere of chromosomes 1 and 16
R-banding	Variety of techniques	Chromosome arms; mostly unique GC-rich DNA	Reverse banding pattern of that observed with Q- or G-banding
C-banding	Variety of techniques	Centromere region of each chromosome and distal portion of Y chromosome; highly repetitive, mostly AT-rich DNA	Largest bands usually on chromosomes 1, 9, 16, and Y; chromosomes 7, 10, and 15 have medium-sized bands; size of C-bands highly variable from person to person

Lesson 21

Nucleosomes

The nucleosome is composed of a core of eight histone proteins and DNA (147 bp) wrapped around them.

The DNA between nucleosomelinker DNA.

Linker DNA 20-60 bp.

NUCLEOSOMES ASSEMBLY

Nucleosomes are assembled immediately after DNA replication.

Two molecules each of four types of histones are packed by DNA to form a Nucleosomes.

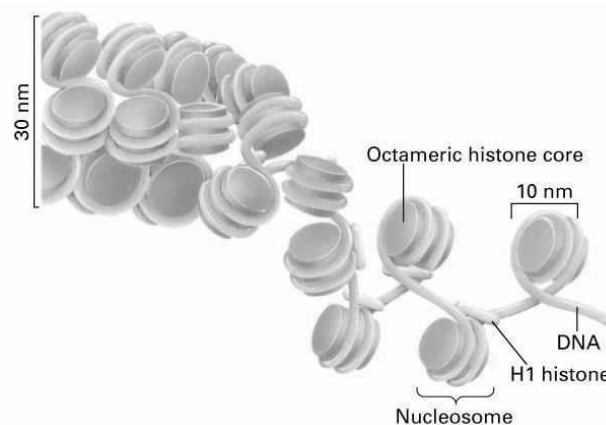
Histones

Histones are small, positively charged (basic) proteins

Nucleosomes- Five histones:

Five abundant histones are H1, H2A, H2B, H3 and H4.

The core histones share a common structural fold, called histone-fold domain.



Lesson 22

Chromatin and chromosomes

Chromatin

The complexes between eukaryotic DNA and proteins are called chromatin.

The major proteins of chromatin are the histones – small proteins containing a high proportion of basic amino acids arginine and lysine.

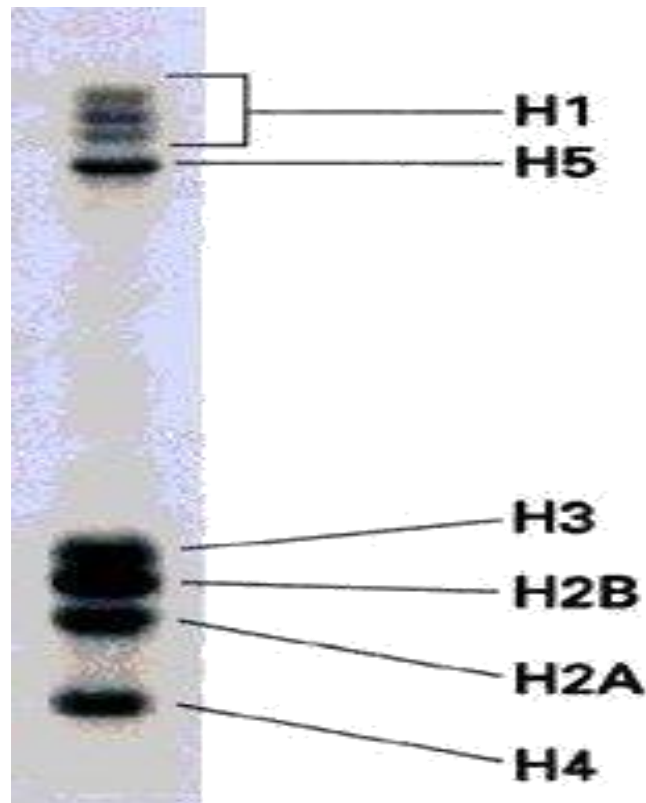
There are 5 major types of histones: H1, H2A, H2B, H3, and H4 – which are very similar among different sp of eukaryotes.

The histones are extremely abundant proteins in eukaryotic cells.

Molecular weight and number of amino acids

Histone	Mol. Wt	No. of Amino acid	Percentage Lys + Arg
H1	22,500	244	30.8
H2A	13,960	129	20.2
H2B	13,774	125	22.4
H3	15,273	135	22.9
H4	11,236	102	24.5

Histones - size and molecular weight

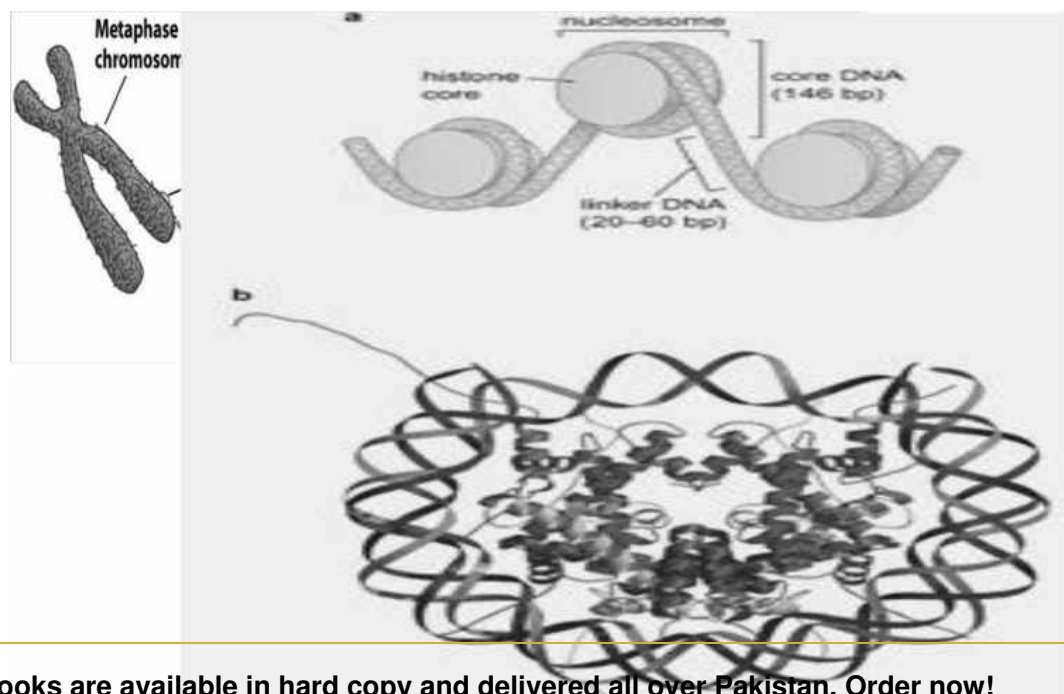


Non-histones

Chromatin contains an approximately equal mass of a variety of nonhistone proteins.

More than a thousand different types of proteins, which are involved in a DNA replication and gene expression.

The DNA of prokaryotes is similarly associated with proteins, some of which presumably function as histones do, packing DNA within the bacterial cell.



Chromosomes

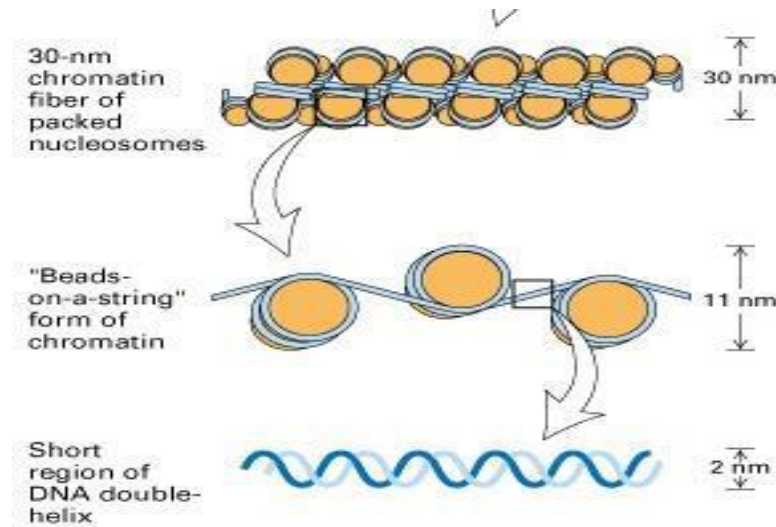
- Tightly packaged DNA
- Found only during cell division
- DNA is not being used for macromolecule synthesis

Chromatin

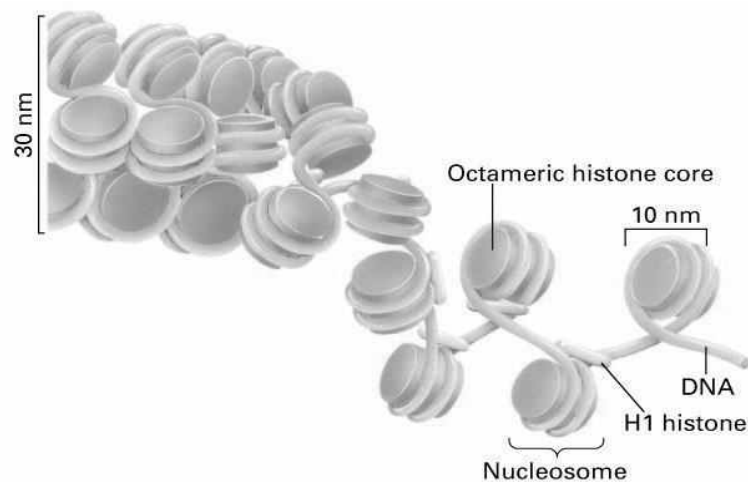
- Unwound DNA
- Found throughout Interphase
- DNA *is* being used for macromolecule synthesis

Lesson 23

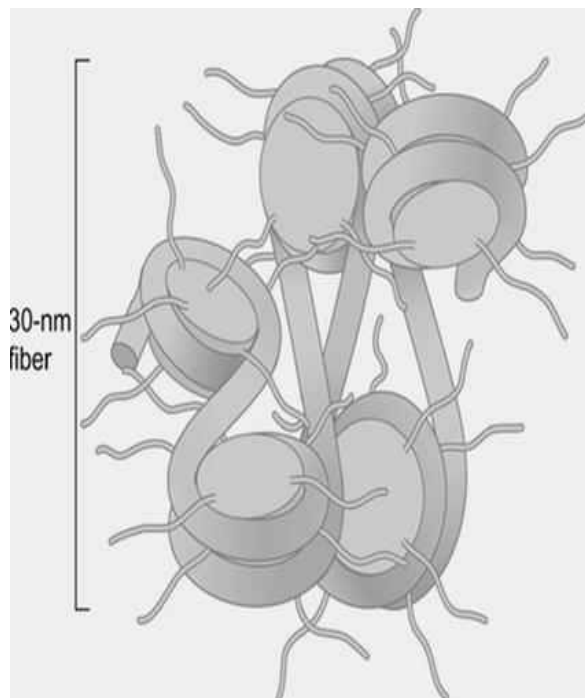
Higher order chromatin folding



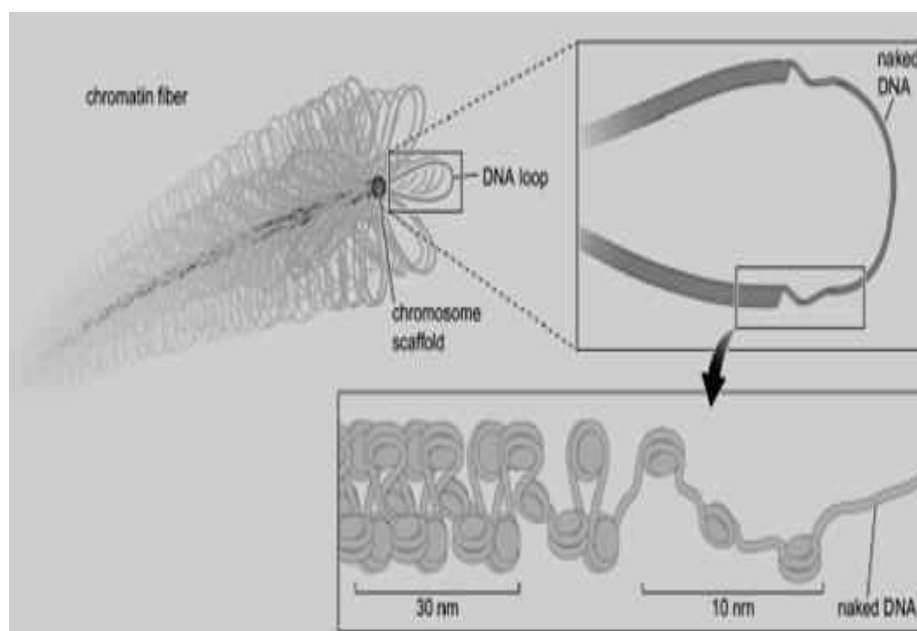
Nucleosomes and higher order



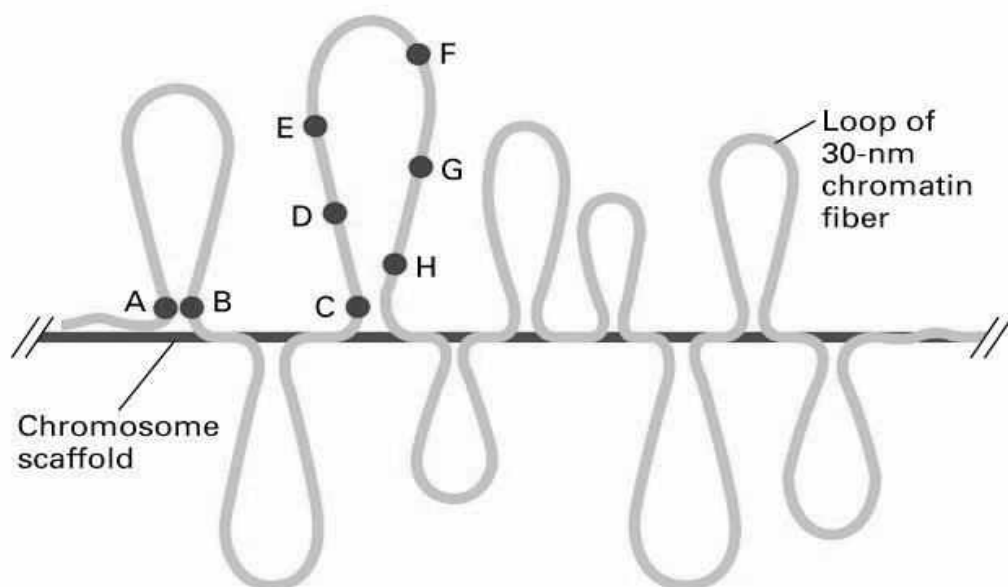
30 nm fibre

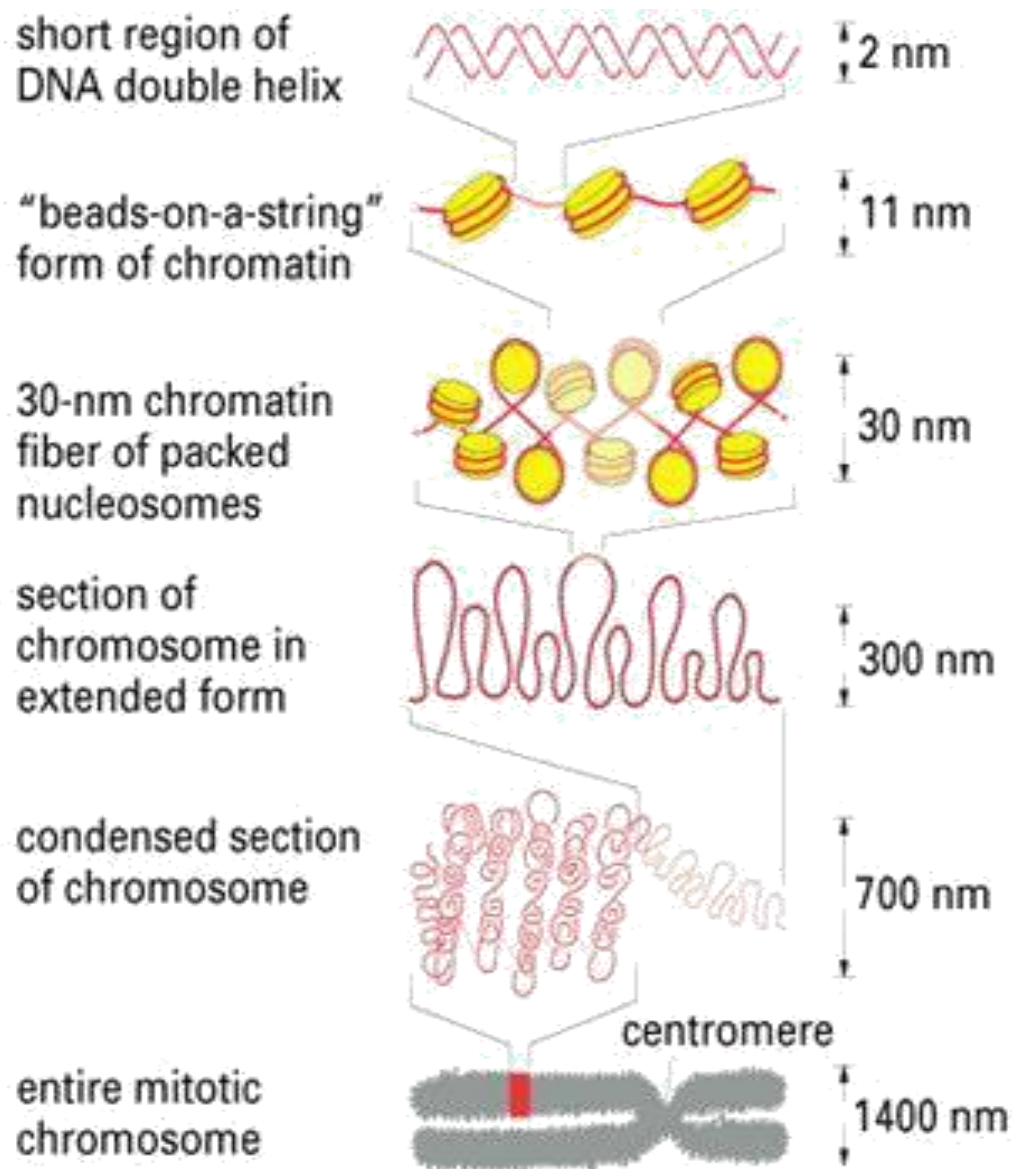


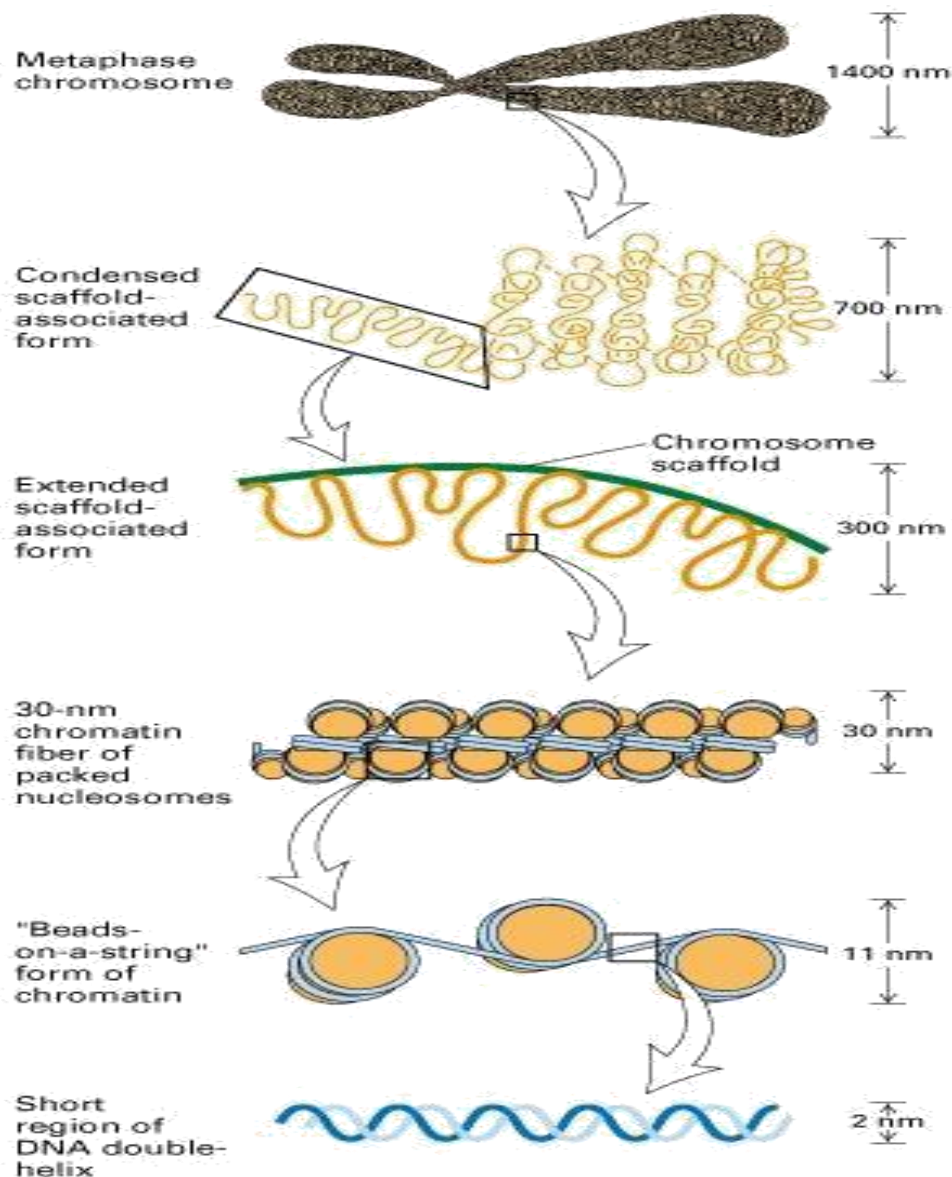
300 nm fibre



300 nm fibre







The mechanism by which the “beads-on-a-string” nucleosome chain folds into various higher-order chromatin structures in eukaryotic cell nuclei is still poorly understood. The various models depicting higher-order chromatin as regular helical fibers and the very opposite “polymer melt” theory imply that interactions between nucleosome “beads” make the main contribution to the chromatin compaction. Other models in which the geometry of linker DNA “strings” entering and exiting the nucleosome define the three-dimensional structure predict that small changes in the linker DNA configuration may strongly affect nucleosome chain folding and chromatin higher-order structure. Among those studies, the cross-disciplinary approach pioneered by Jörg Langowski that combines computational modeling with biophysical and biochemical

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experiments was most instrumental for understanding chromatin higher-order structure in vitro. Strikingly, many recent studies, including genome-wide nucleosome interaction mapping and chromatin imaging, show an excellent agreement with the results of three-dimensional computational modeling based on the primary role of linker DNA geometry in chromatin compaction. This perspective relates nucleosome array models with experimental studies of nucleosome array folding in vitro and in situ. I argue that linker DNA configuration plays a key role in determining nucleosome chain flexibility, topology, and propensity for self-association, thus providing new implications for regulation of chromatin accessibility to DNA binding factors and RNA transcription machinery as well as long-range communications between distant genomic sites.

Lesson 24

Kinetochores

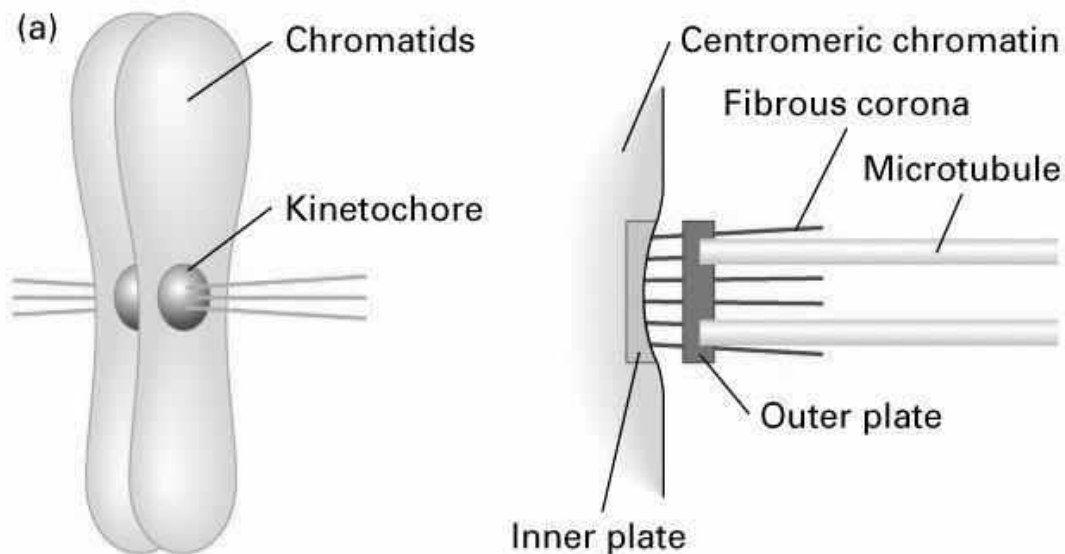
Within the centromere region, locations where spindle fibers attach which consist of DNA as well as protein.

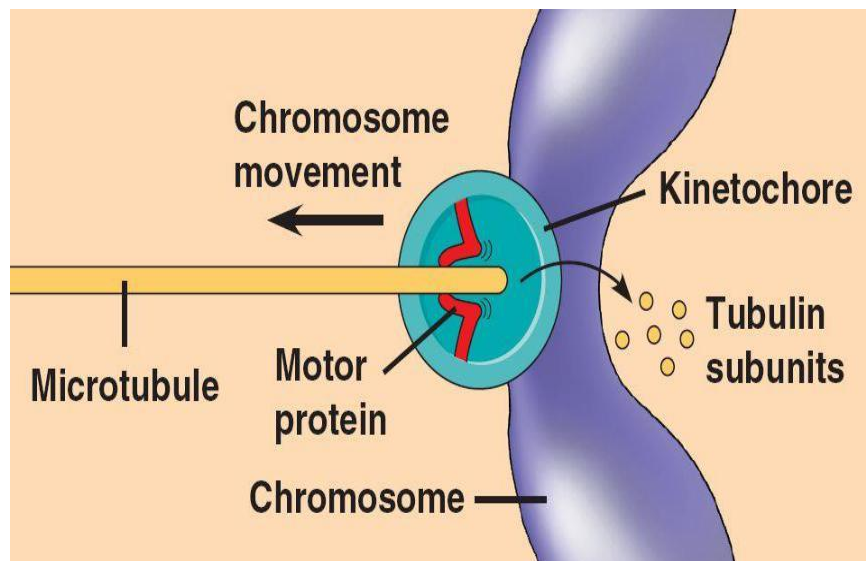
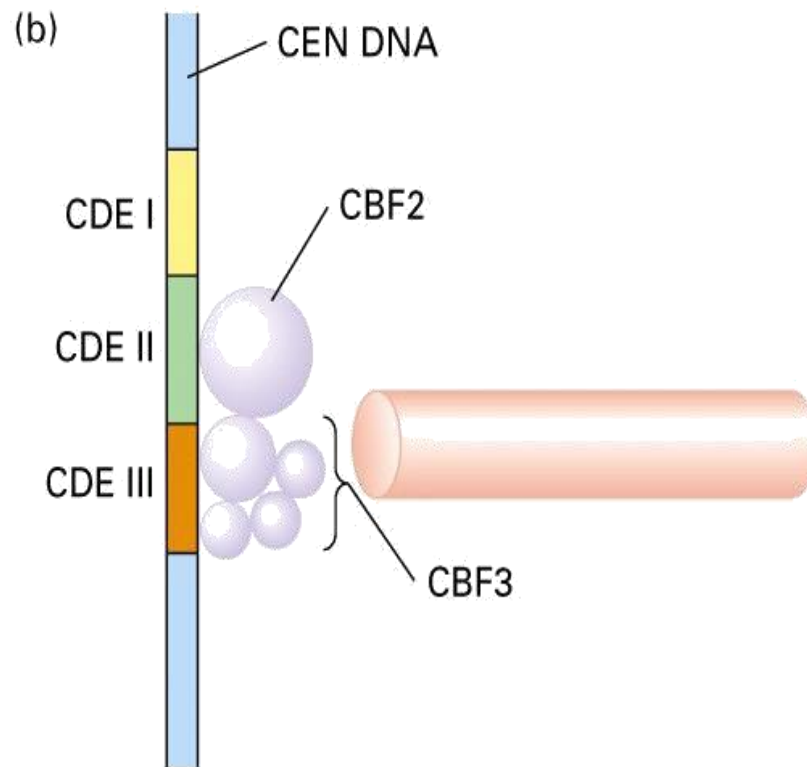
The actual location where the attachment occurs is called the kinetochore and is composed of both DNA and protein.

The DNA sequence within these regions is called CEN DNA ..120 base pairs long and consists of sub-domains, CDE-I, CDE-II and CDE-III.

Mutations in the first two sub-domains have no effect upon segregation.

But a point mutation in the CDE-III sub-domain completely eliminates the ability of the centromere to function during chromosome segregation.





Lesson 25

Karyotyping

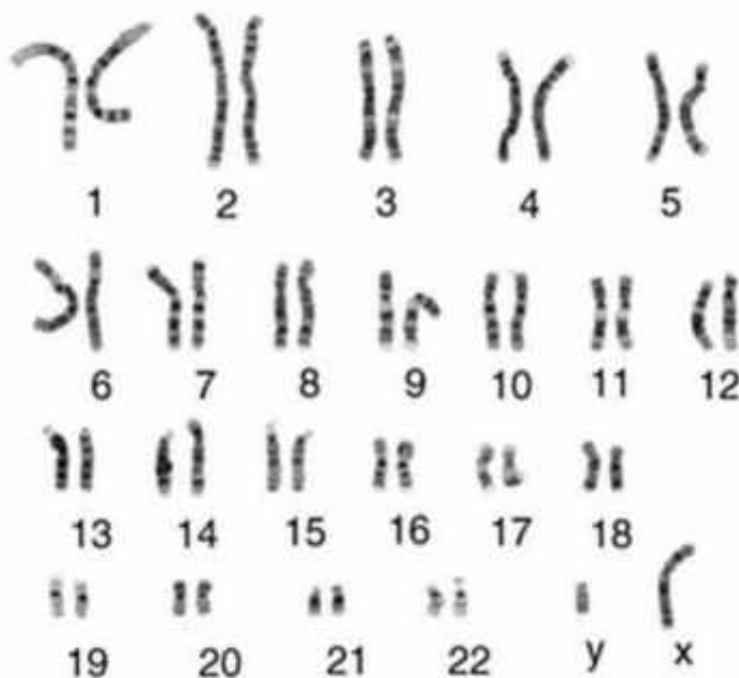
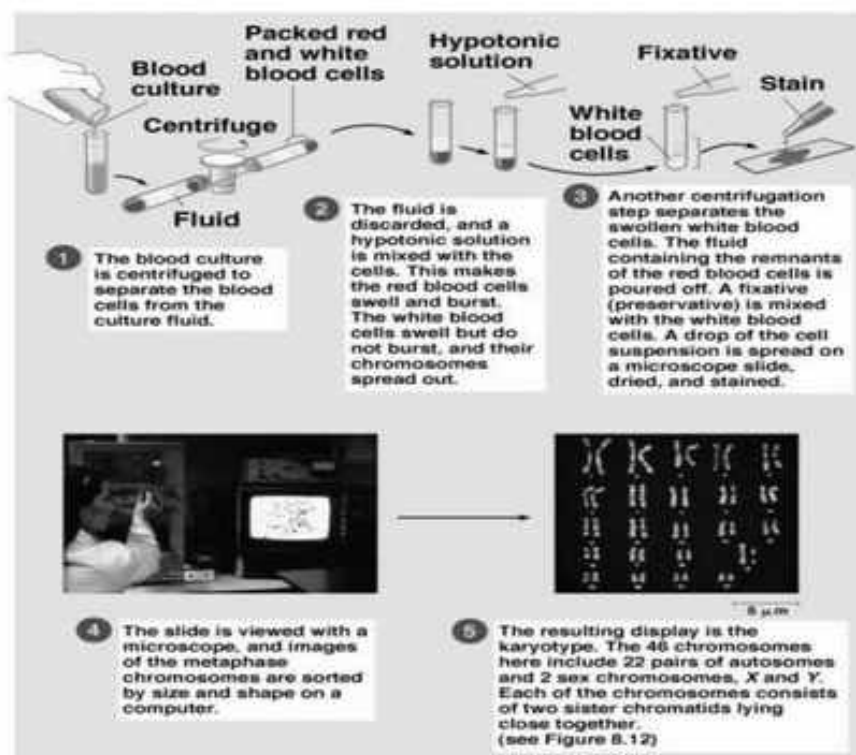
IDENTIFYING CHROMSOMES

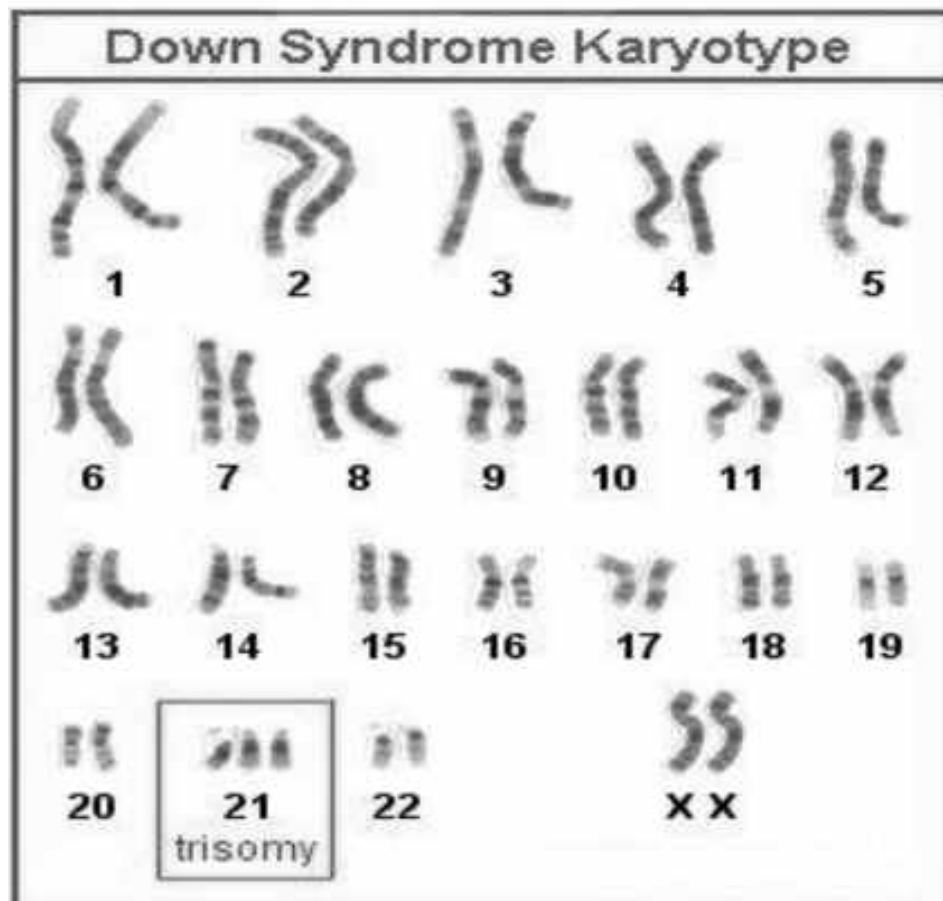
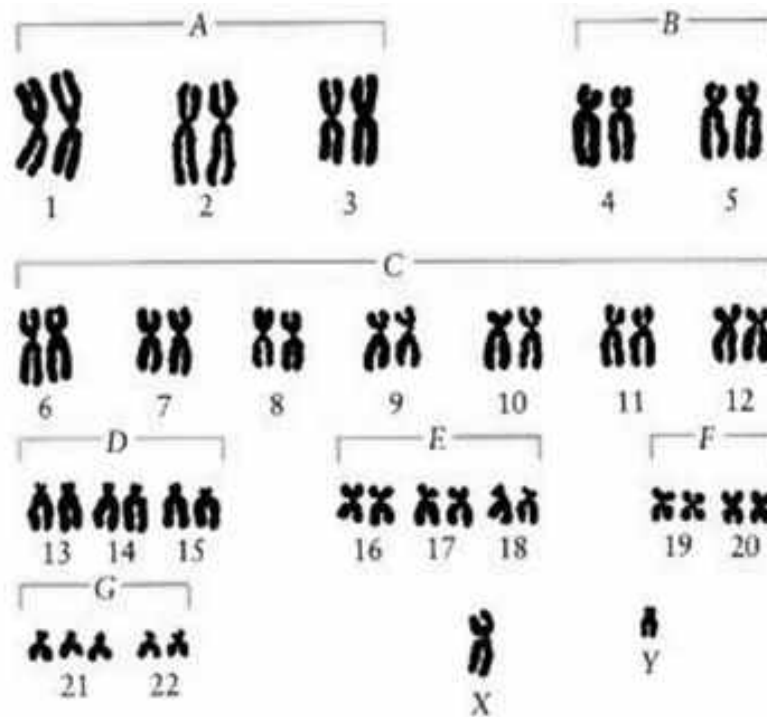
Chromosomes identified by:

- Their size
- Their shape (the position of the centromere)
- Banding patterns produced by specific stains (Giemsa)
- Chromosomes are analyzed by organizing them into a karyotype.
- Karyotype is the general morphology of the somatic chromosome.
- Generally, karyotypes represent by arranging in the descending order of size keeping their centromere in a straight line.

IDIOTYPE

Idiotypic: the karyotype of a species may be represented diagrammatically, showing all the morphological features of the chromosome; such a diagram is known as Idiotype.





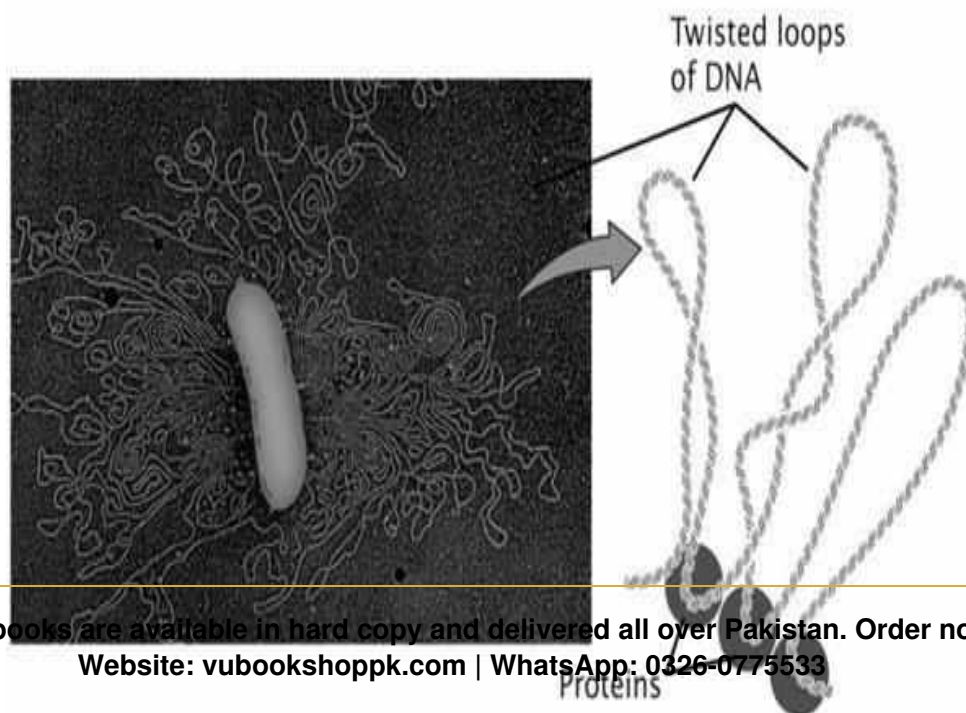
Lesson 26

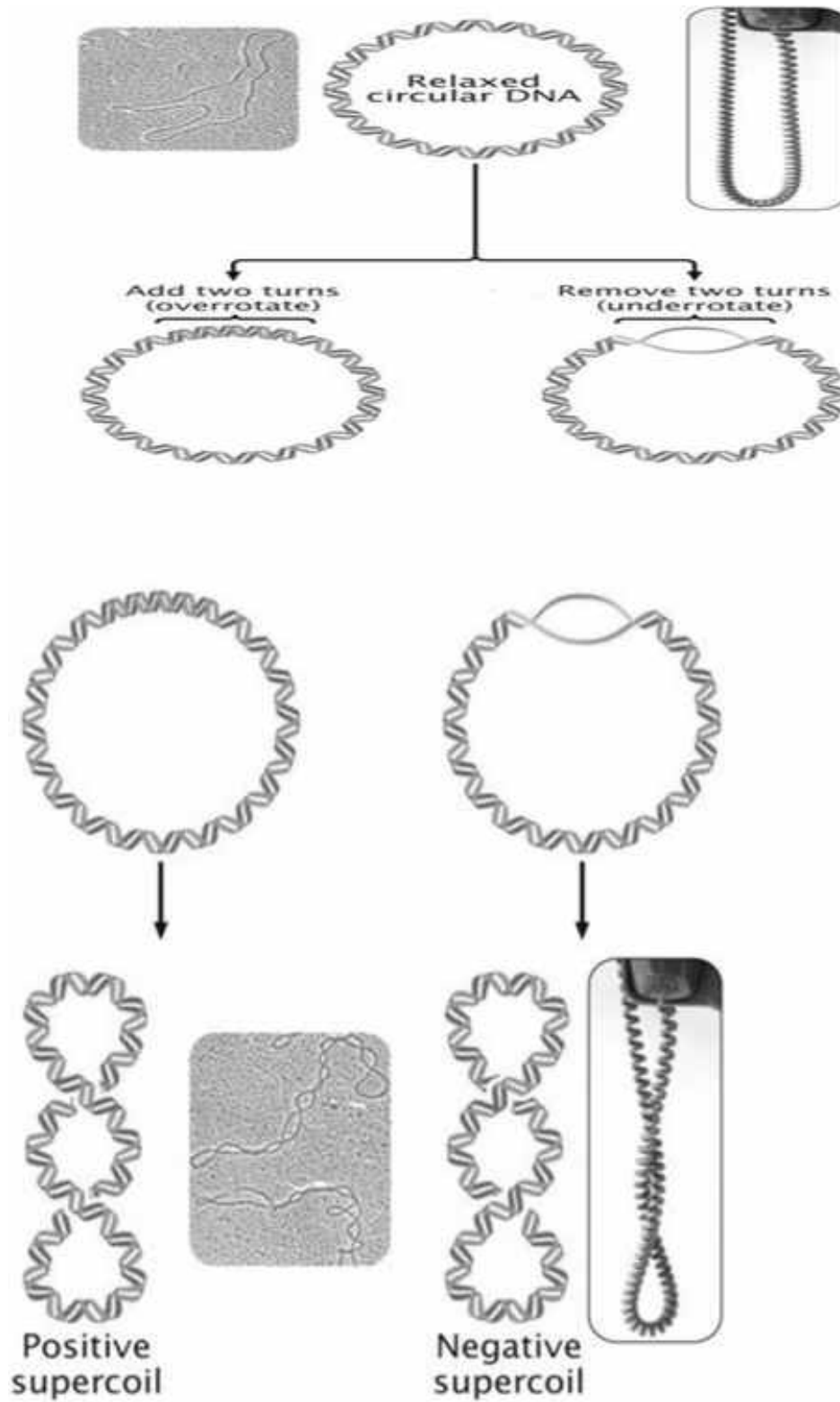
Prokaryotic Chromosomes

- The prokaryotes usually have only one chromosome, and it bears little morphological resemblance to eukaryotic chromosomes.
- The genome length is smallest in RNA viruses.
- The number of gene may be as high as 150 in some larger bacteriophage genome.
- In E.coli, about 3000 to 4000 genes are organized into its one circular chromosome.
- The chromosome exists as a highly folded and coiled structure dispersed throughout the cell.
- There are about 50 loops in the chromosome of E. coli.
- These loops are highly twisted or supercoiled structure with about four million nucleotide pairs.
- During replication of DNA, the coiling must be relaxed.
- DNA gyrase is necessary for the unwinding the coils.

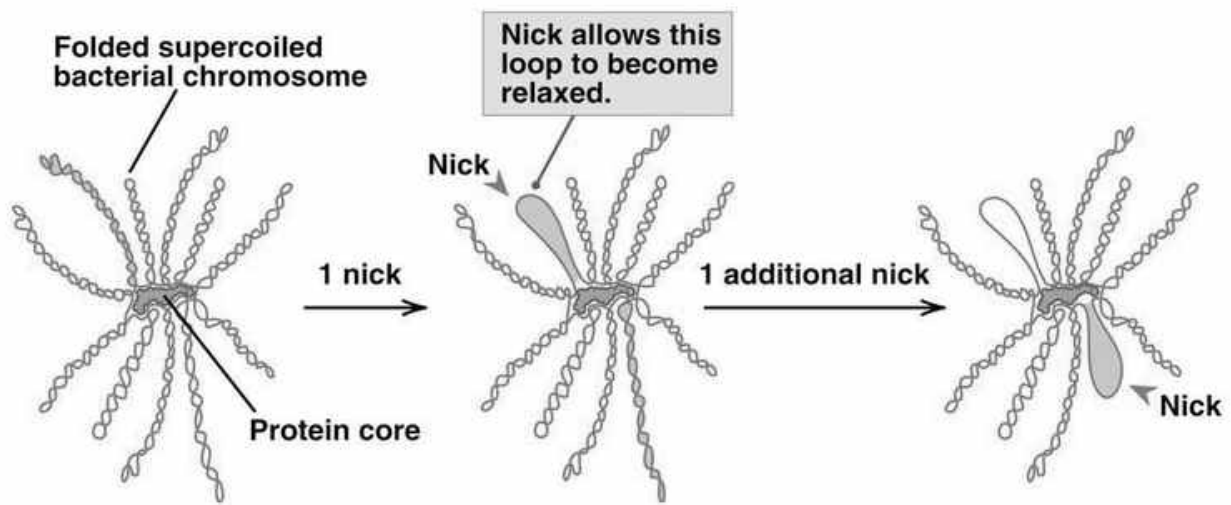
Bacterial Chromosome:

Single, circular DNA molecule located in the nucleoid region of cell.





Mechanism of folding of bacterial CHROMOSOME



Lesson 27

Sex chromosomes and sex determination

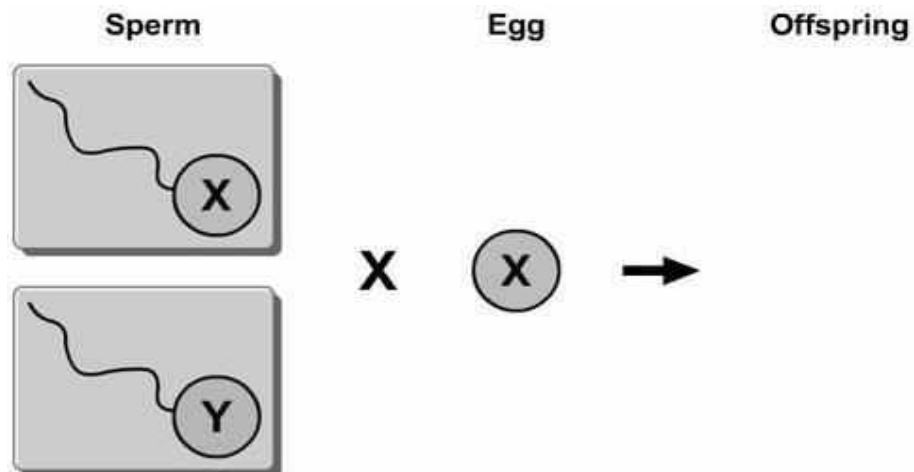
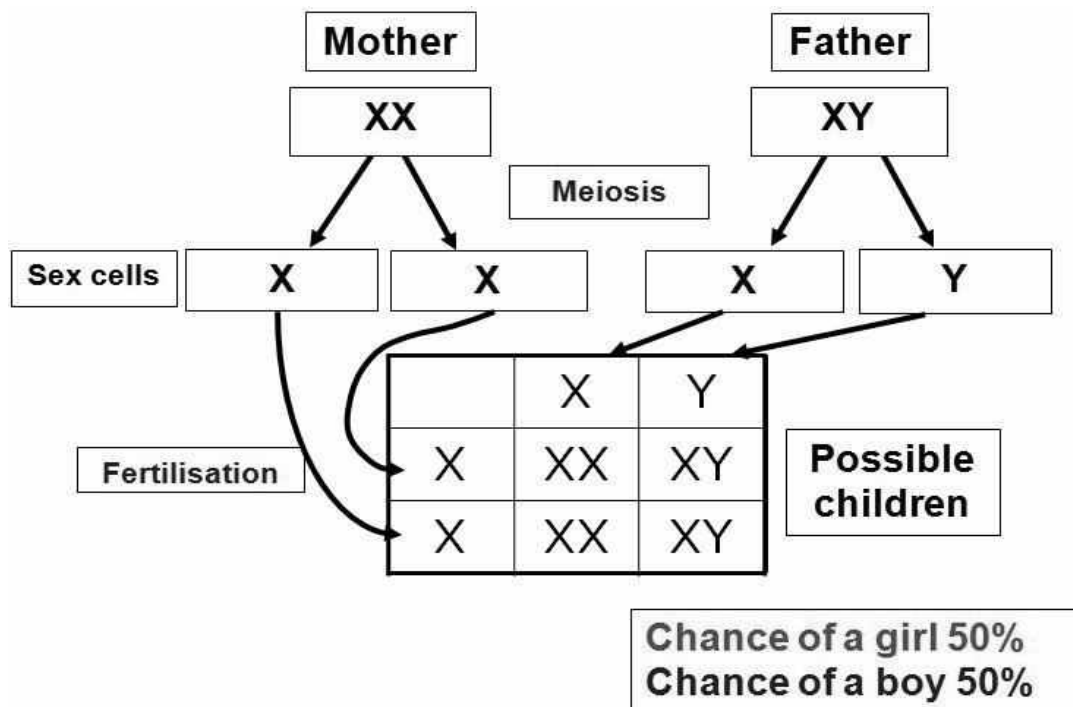
Sex Chromosomes

- Sex of many animals is determined by genes on chromosomes called sex chromosomes.
- Sex can be homogametic
- Sex can be heterogametic

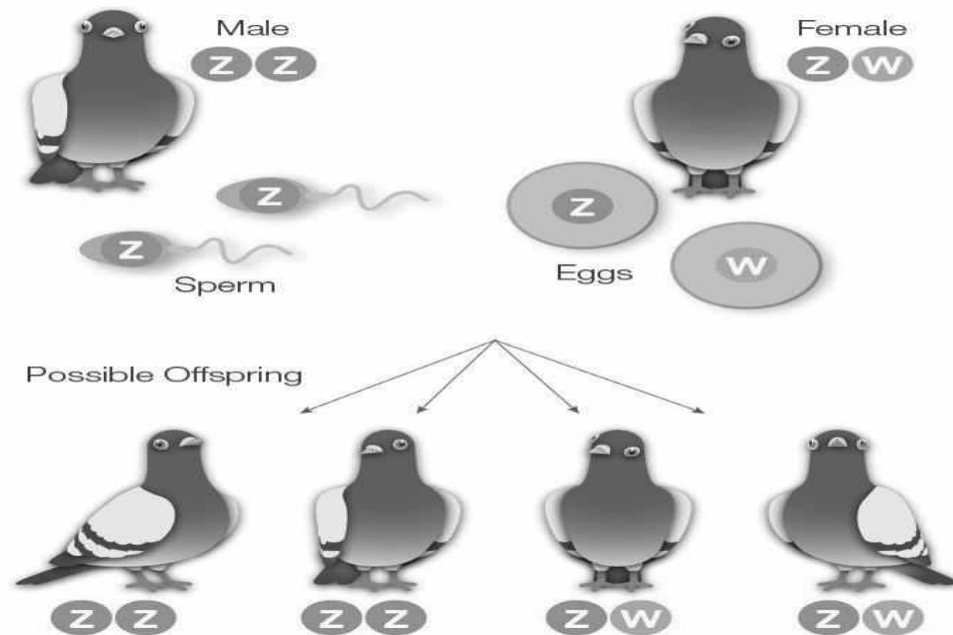
Sex determination in different animals

HOMOGAMETIC SEX	HETEROGAMETIC SEX	SEX DETERMINATION
Female XX	Male XY	Presence of Y-chromosome = maleness (mammals and fish) Presence of second X-chromosome = femaleness (Drosophila, the fruit fly)
Male ZZ	Female ZW	Birds, amphibians, reptiles, butterflies, moths.
Female XX	Male Xo	Grasshoppers

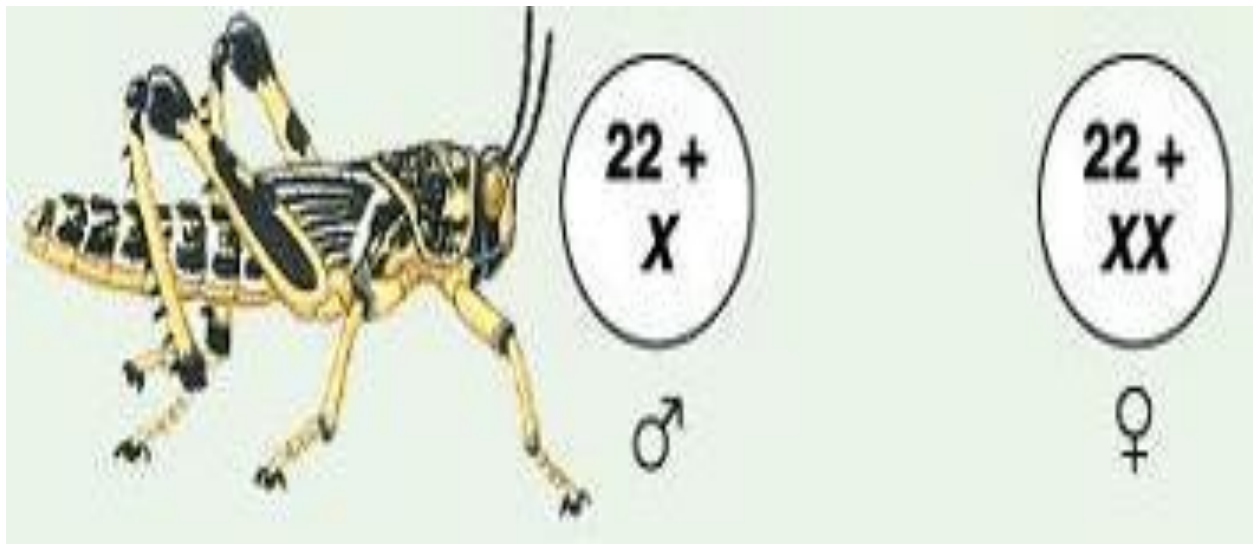
Inheritance of gender in humans



Sex system in birds



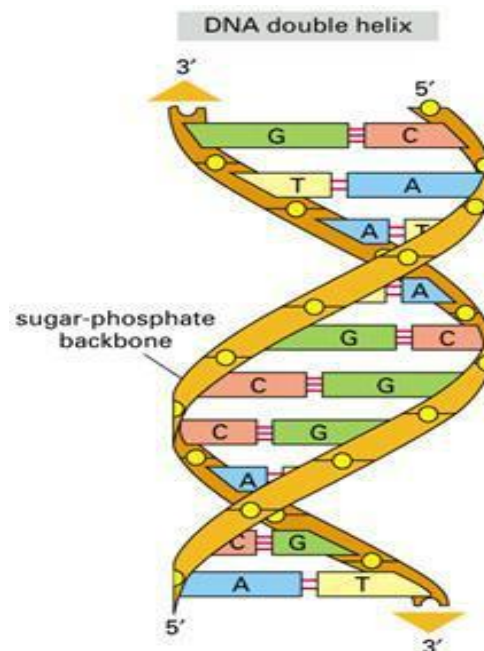
Xo system in grasshopper:



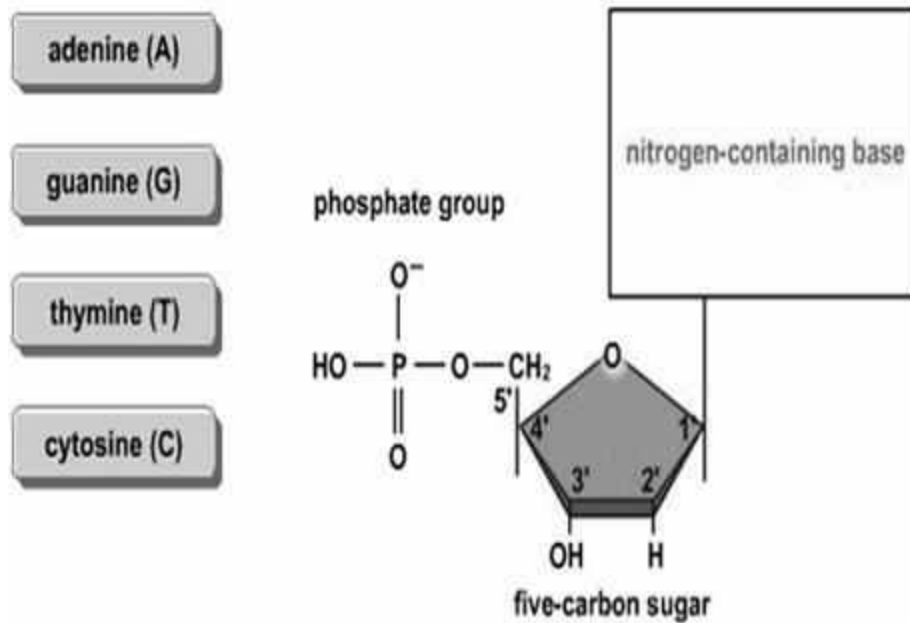
Lesson 28

Salient features of DNA

- Watson: X-rays diffraction pattern projected by DNA.
- Erwin Chargaff demonstrated ratio of A:T are 1:1, and G:C are 1:1
- Chemical structure of nucleotide identified.
- Composed of 2 polymers of nucleotides.
- Run antiparallel.
- Molecule structure resembles a spiral staircase.
- Complementary base pairing:
 - A-T, C-G
- Genetic information in the linear sequence of nucleotides.
- Genetic information is to synthesize proteins.
- DNA forms double helix with two complimentary strands holding - hydrogen bonds.
- DNA duplication occurs using one strand of parental DNA as template to form complimentary pairs with a new DNA strand.



The structure of Nucleotides includes: A phosphate sugar backbone, with one of the 5 nitrogenous bases (ATCG,U).



Lesson 44

NUCLEOTIDE

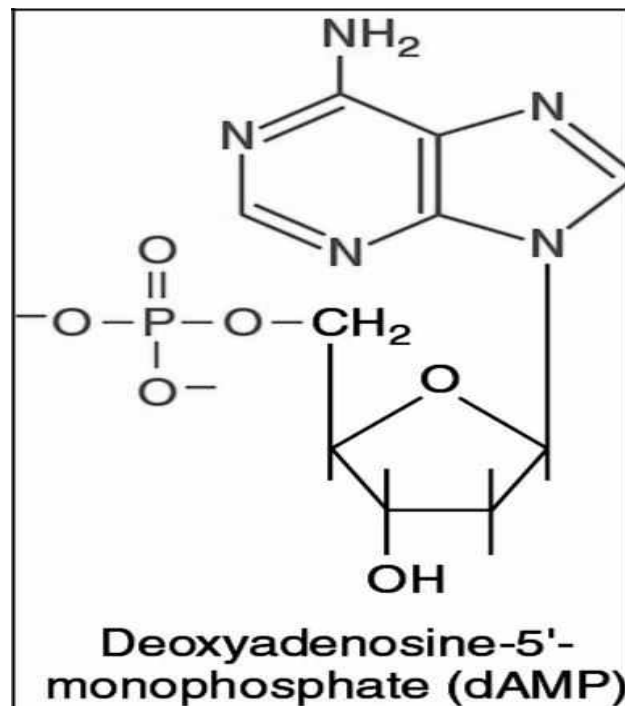
Made of three components:

- 5 carbon sugar (pentose)
- nitrogenous base
- phosphate group

NUCLEOTIDES

- Oligonucleotide – short polymer (<10)
- Polynucleotide – long polymer (>10)
- Nucleoside = monomer of sugar + base

NUCLEOTIDE MONOMER

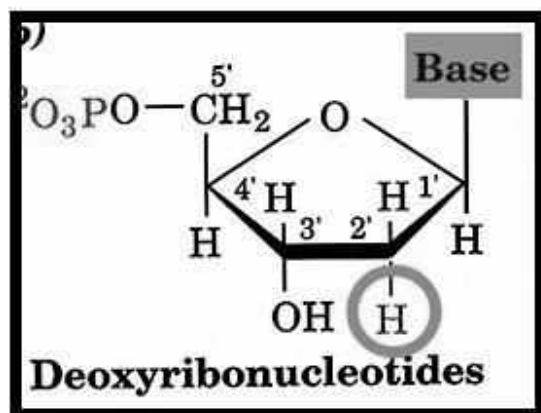


Sugar molecules

•

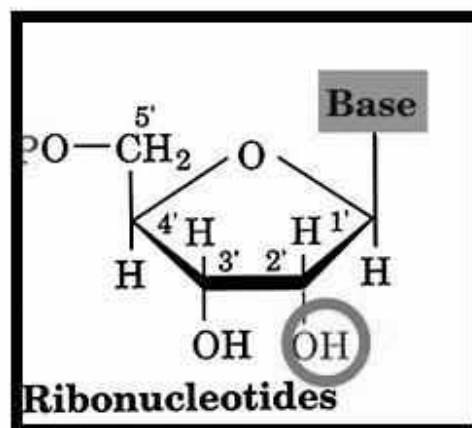
Two types of sugar molecules

DNA



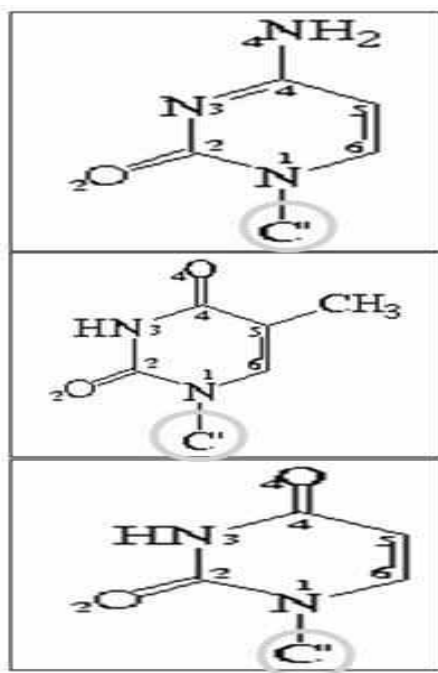
2'-deoxy-D-ribose

RNA



2'-D-ribose

Nitrogenous Bases pyrimidines

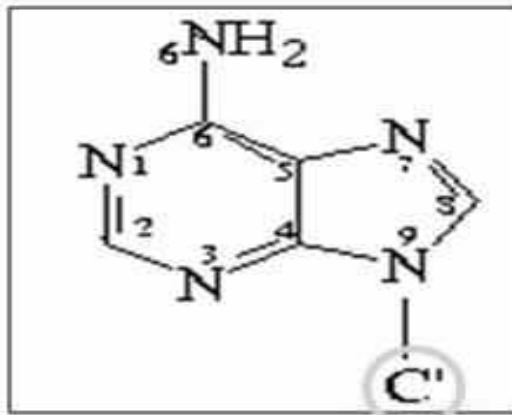
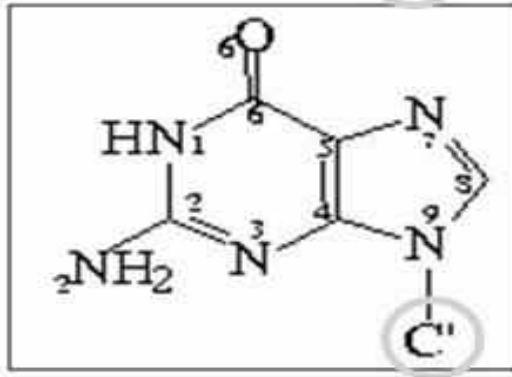


cytosine

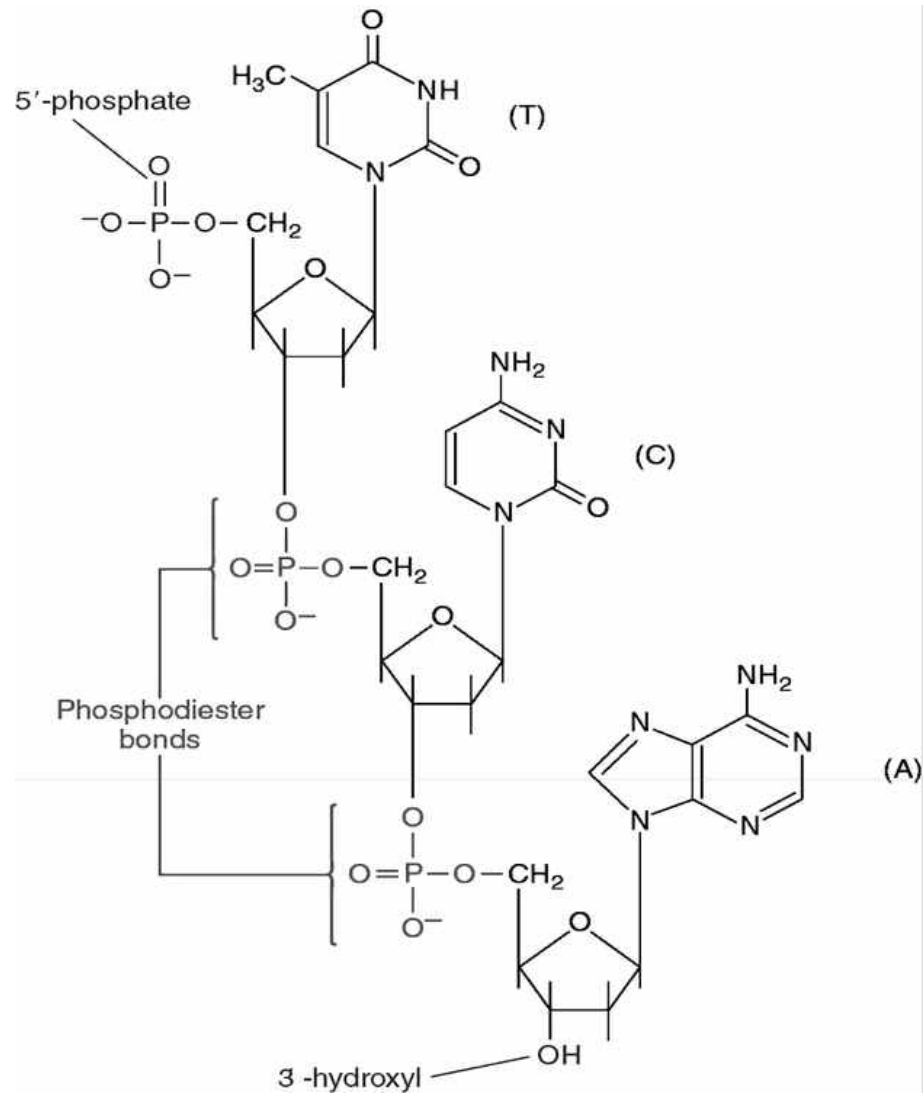
thymine

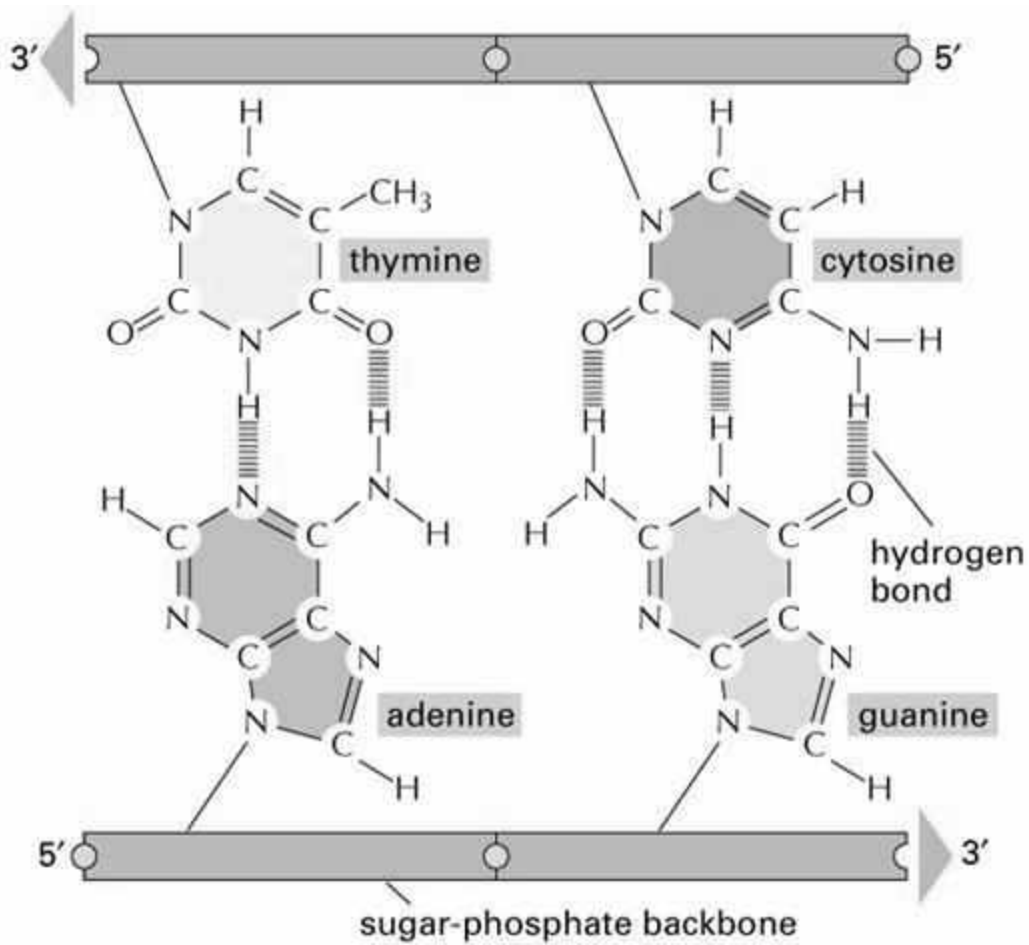
uracil

Nitrogenous bases purines

*adenine**guanine*

POLYNUCLEOTIDE LINKAGE



Pairing of A – T , c – G

Lesson 30

Conformations of DNA

B-DNA

Right-handed helix.

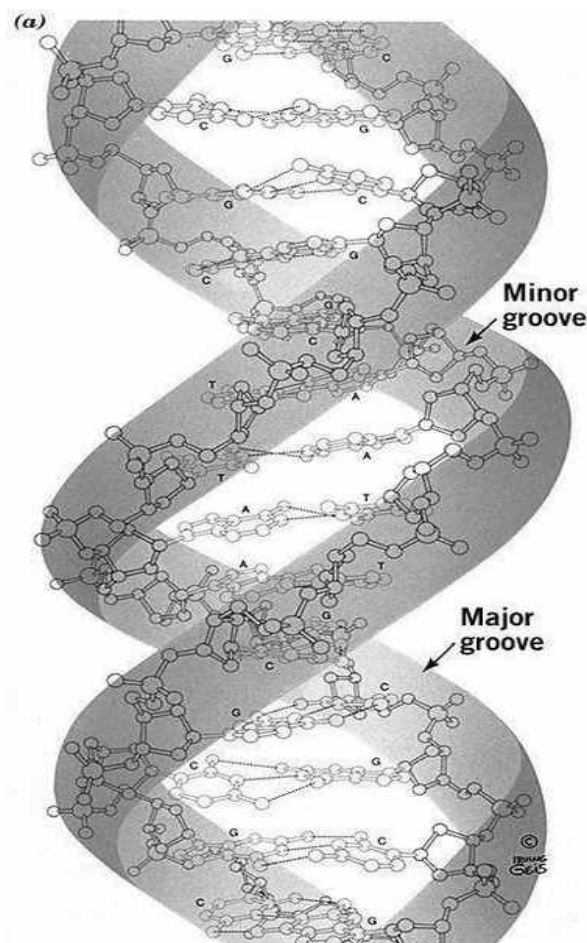
Intermediate.

Planes of the base pairs nearly perpendicular to the helix axis

Tiny central axis.

Wide + deep major groove.

Narrow + deep minor groove.



A-DNA

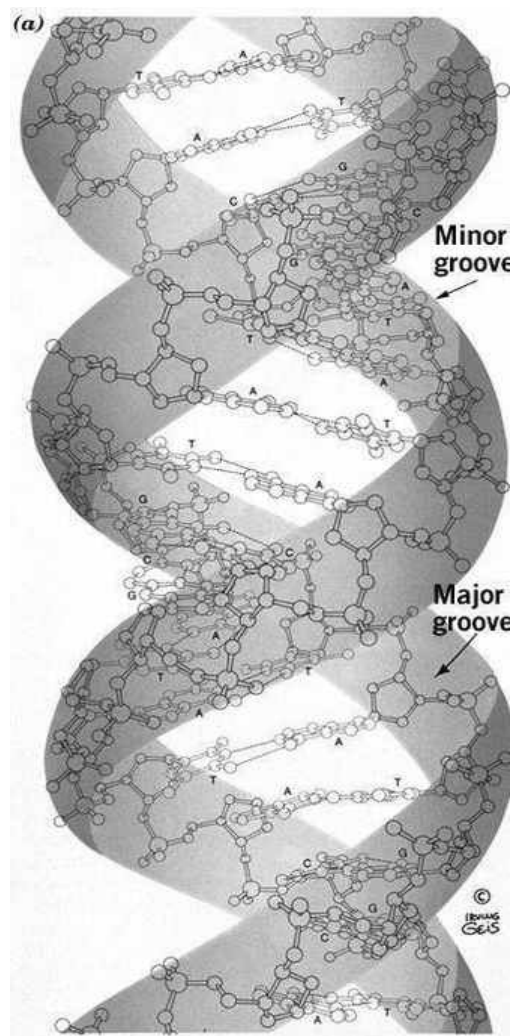
Right-handed helix.

Widest .

Planes of the base pairs inclined to the helix axis.

Narrow + deep major groove.

Wide + shallow minor groove.



Z-DNA

Left-handed helix.

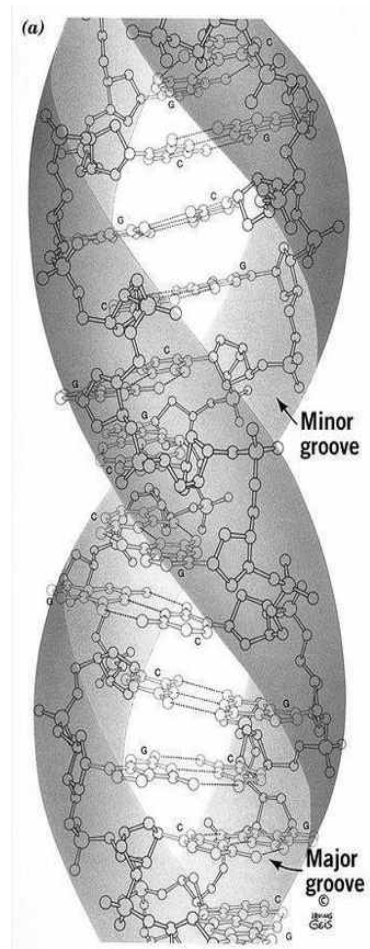
Narrowest .

Planes of the base pairs nearly perpendicular to the helix axis.

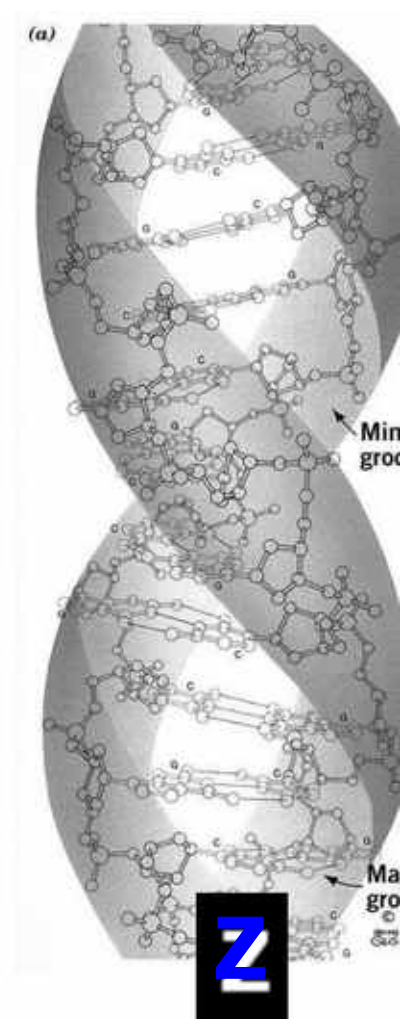
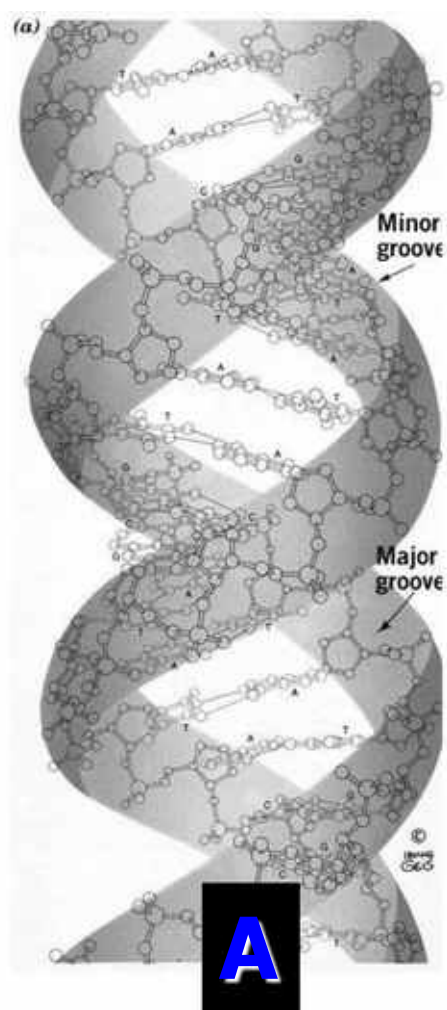
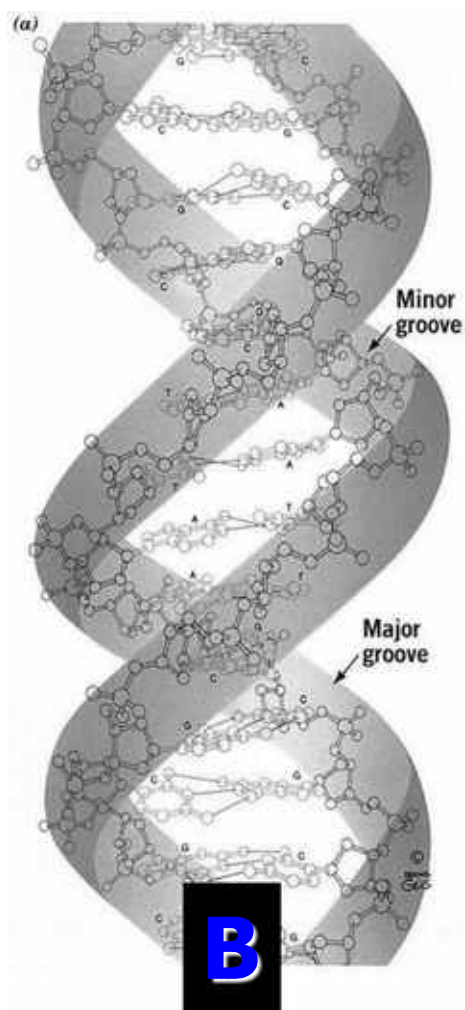
No internal spaces.

No major groove.

Narrow + deep minor groove.



	A-DNA	B-DNA	Z-DNA
<i>Helix</i>	Right-handed	Right-handed	Left-handed
<i>Width</i>	Widest	Intermediate	Narrowest
<i>Planes of bases</i>	planes of the base pairs inclined to the helix axis	planes of the base pairs nearly perpendicular to the helix axis	planes of the base pairs nearly perpendicular to the helix axis
<i>Central axis</i>	6Å hole along helix axis	tiny central axis	no internal spaces
<i>Major groove</i>	Narrow and deep	Wide and deep	No major groove
<i>Minor groove</i>	Wide and shallow	Narrow and deep	Narrow and deep



Lesson 31

Chargaff rule of base ratios

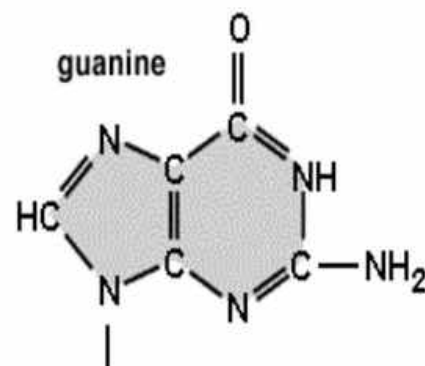
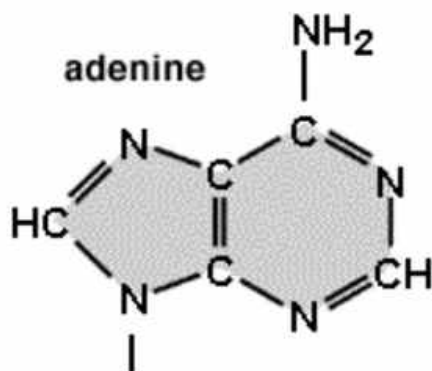
Chargaff

- 1944 - Study of DNA and its four chemical bases - adenine, cytosine, guanine and thymine.
- Discover amounts of adenine and thymine were equal, as were the amounts of cytosine and guanine.

Purines

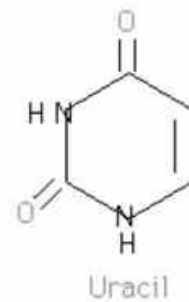
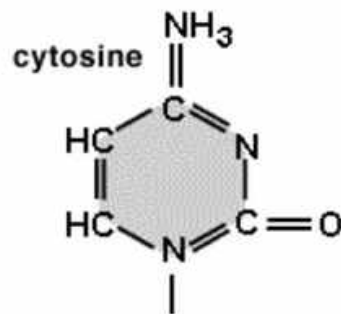
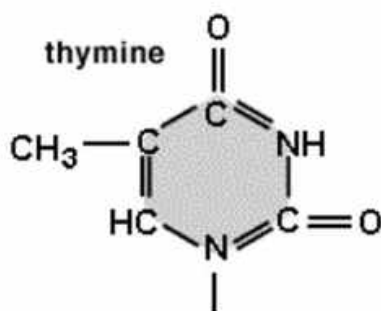
- Consist of a six-membered and a five-membered nitrogen-containing ring, fused together.
- Adenine = 6-amino purine

Guanine = 2-amino-6-oxy purine



Pyrimidines

- Have only a six-membered nitrogen-containing ring.
- Uracil = 2,4-dioxy pyrimidine
- Thymine = 2,4-dioxy-5-methyl pyrimidine
- Cytosine = 2-oxy-4-amino pyrimidine

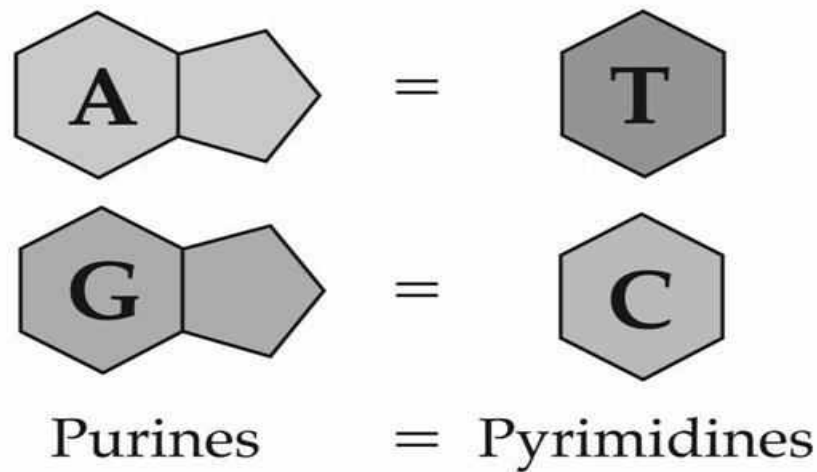


Chargaff's first parity rule

States that purines pair with pyrimidines, specifically A with T and C with G.

Chargaff's second parity rule

- % of A approximately equals % of T
- % of G approximately equals % of C

Chargaff's second parity rule**G-C rule**

States that (G+C) % is constant within a species, but often differs between species.

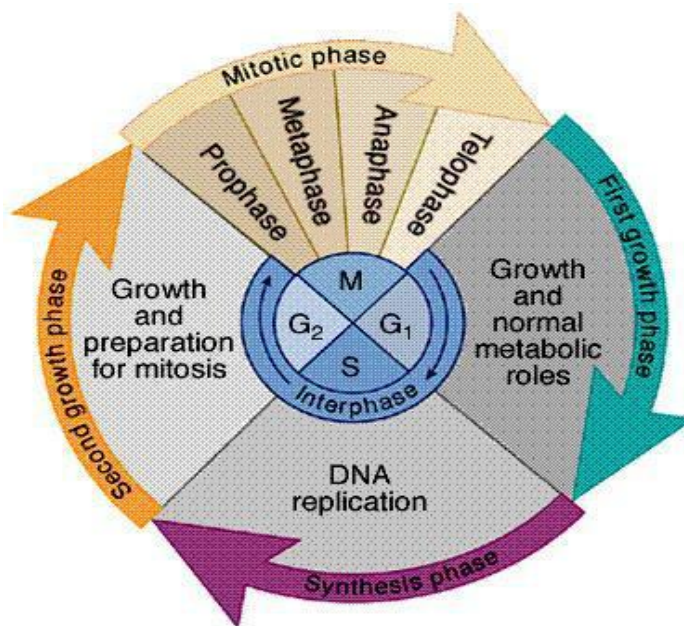
Cluster rule

States that pyrimidines often occur in clusters, and hence on the complementary strand purines do likewise.

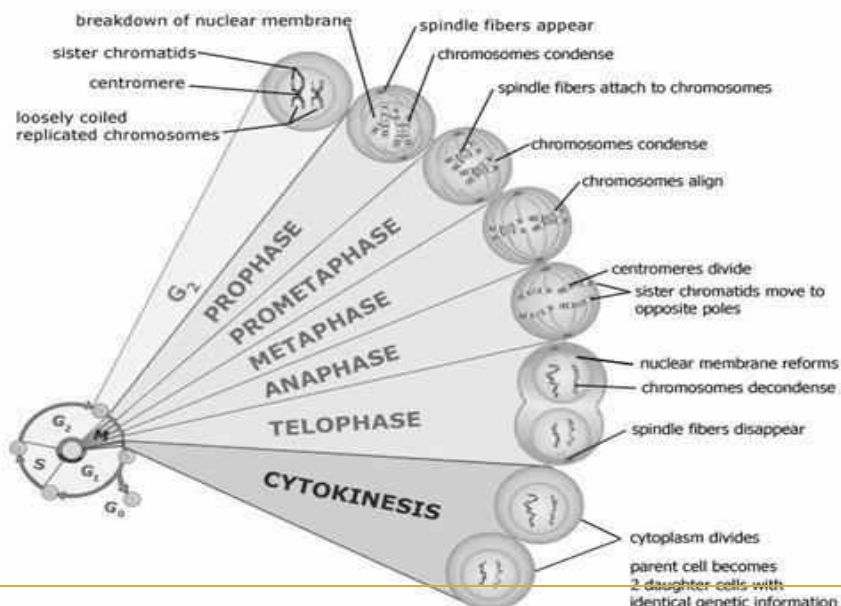
Lesson 32

Cell cycle: The cell cycle consists of;
Interphase
Mitotic phase

Phases of cell cycle



Mitotic phase



G0 phase

- G0 phase also called as post-mitotic phase.
- Eukaryotes cells generally enter into G0 state from G1.

Interphase

- Before a cell enters into cell division, it needs to take nutrients.
- Interphase is a series of changes that takes place in a newly formed cell.

Interphase proceeds in three stages;

- G1 stage
- S stage
- G2 stage

Function:

Functions of cell cycle include reproduction, growth and development after tissue renewal.

Lesson 33

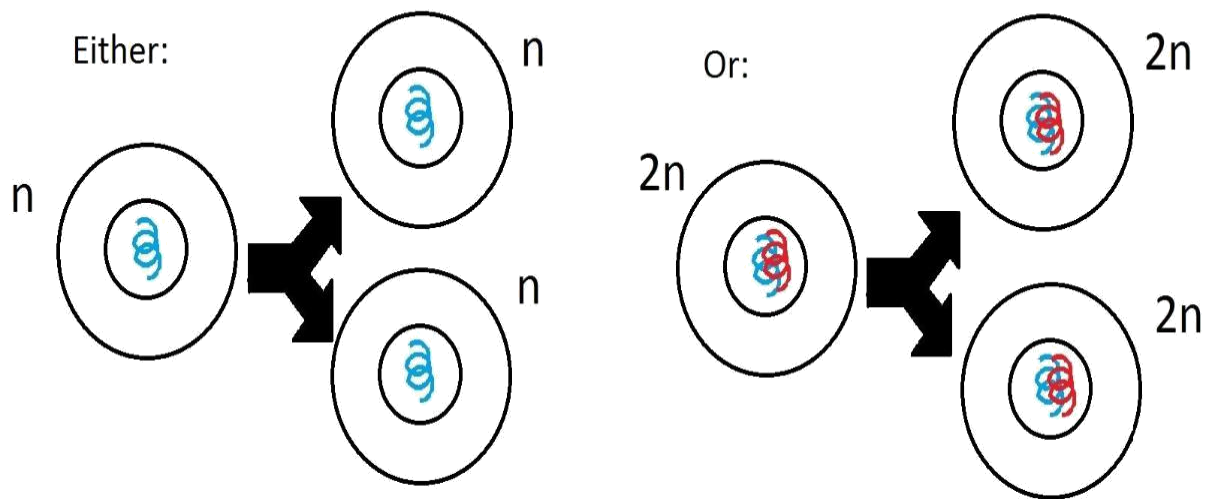
Mitosis and Meiosis

Mitosis: A single cell divides into two identical daughter cells. Some haploid & diploid cells divide by mitosis. It produces two new cells from a single cell. Both new cells are genetically identical to the original cell. Each cell has to have its own cytoplasm and DNA.



Chromosomes replicate before mitosis, DNA replicate to produce identical copies. Two sister chromatids have to break apart.

MITOSIS



A single cell divides into two identical daughter cell

Interphase: Interphase consists of

G1 phase

S phase

G2 phase

Interphase summary Interphase ~ 90% of the time.

G1: new cell absorbs nutrients and grows larger.

S phase: Synthesis of new DNA for daughter cells.

G2: Cell continues to grow, gets too large, needs to divide.

Prophase of mitosis:

Prophase is characterized by four events: Chromosomes condensed - more visible. Nuclear membrane disappears. Centrioles are separated and take positions on the opposite poles of the cell. Spindle fibers form and radiate toward the center of the cell.

Chromosomes condense at the start of mitosis.

DNA wraps around histones that condense it.

Prophase- chromosomes are condensed- Different levels of condensation/folding Chromosomes condense at the start of mitosis. DNA wraps around histones that condense it.

Prophase is the first stage of mitotic cell division.

Metaphase of mitosis

During metaphase, two events occurs; Chromosomes line up across the middle of the cell. Spindle fibres connect the centromere of each sister chromatid to the poles of the cell, where centrioles are present. Metaphase – chromosomes are aligned in the middle

Metaphase-Summary During metaphase, two events occurs; Chromosomes lined up in the middle line. Spindle fibres connect to centromere.

Anaphase of mitosis

Anaphase of mitosis During anaphase, three events occurs; Centromere split – as a result sister chromatids are separated. Sister chromatids become individual chromosomes. Separated chromatids move to opposite poles of the cell.

Anaphase Securin is a protein which inhibits a protease known as separase. Destruction of securin results in split of centromeres and the new daughter chromosomes are pulled toward the poles.

Cell in an oval shape Chromosomes are drawn to each side of the cell.

Non-kinetochore spindle fibers push against each other,that stretch the cell into an oval shape

Summary Centromere split and chromosomes are separated. Chromosomes arrived at poles. Cell stretches into an oval shape.

Telophase

It consists of four events: Chromosomes start to uncoil. Nuclear envelope forms around the chromosomes at each pole of the cell.

Telophase Spindle fibers break down and dissolve. Daughter nucleus is formed in each of the daughter cell. Telophase Nuclear membranes are formed around each set of chromatids. Nucleoli also reappear. Chromosomes unwind back into chromatin material.

Telophase – effects of prophase are reversed During telophase, the effects of prophase and pro-metaphase are reversed.

Telophase Summary Spindle fibers break down and nuclear members develops around each daughter nucleus.

Cytokinesis

Cytokinesis is the division of the cytoplasm into two individual cells. Process differs in plants and animal cells

Cytokinesis in animal cells Cell membrane forms a cleavage furrow that eventually pinches the cell into two equal parts. Each part containing its own nucleus and cytoplasmic organelles.

Cytokinesis in Plants cells a cell plate is formed in midway that divides the nuclei. Cell plate gradually develops into a separating membrane.

Plants cell- cytokinesis

Cytokinesis - comparison

Summary Cytokinesis differs in animal and plant cells. In animal cells, the membrane pinches and divides the cell. In plant cells, a cell plate forms that divides the cell.

Mitotic apparatus/ spindles include

- Centrosomes
- Spindle microtubules
- Asters

Mitotic apparatus/ spindles the apparatus of microtubules controls chromosome movement during mitosis. Centrosome replicates Centrosome replicates, forming two centrosomes that migrate to opposite poles. Assembly of spindle microtubules begins in the centrosome. Mitotic spindles – asters Asters are the radial array of short microtubules extends from each centrosome Spindles microtubules attach to kinetochores Spindle microtubules attach to the kinetochores of chromosomes and move the chromosomes to the metaphase plate.

Mitotic spindles in anaphase, sister chromatids separate and move along the kinetochore microtubules toward opposite ends of the cell.

Meiosis

Meiosis: Meiosis - diploid cells are reduced to haploid cells. This is a process by which gametes (sex cells) are produced.

Chromosome numbers would be doubled without meiosis. If meiosis did not occur, the chromosome number in each new generation would be doubled. The offspring would die.

Meiosis is a two cell divisions process. There is only one duplication of chromosomes during meiosis I.

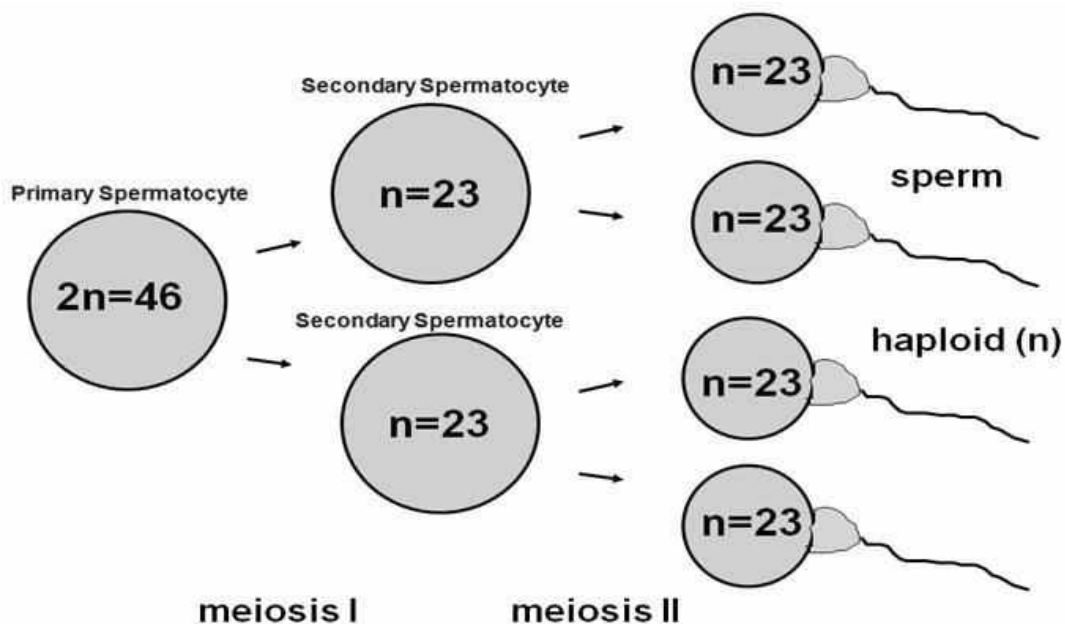
Meiosis I

Meiosis II

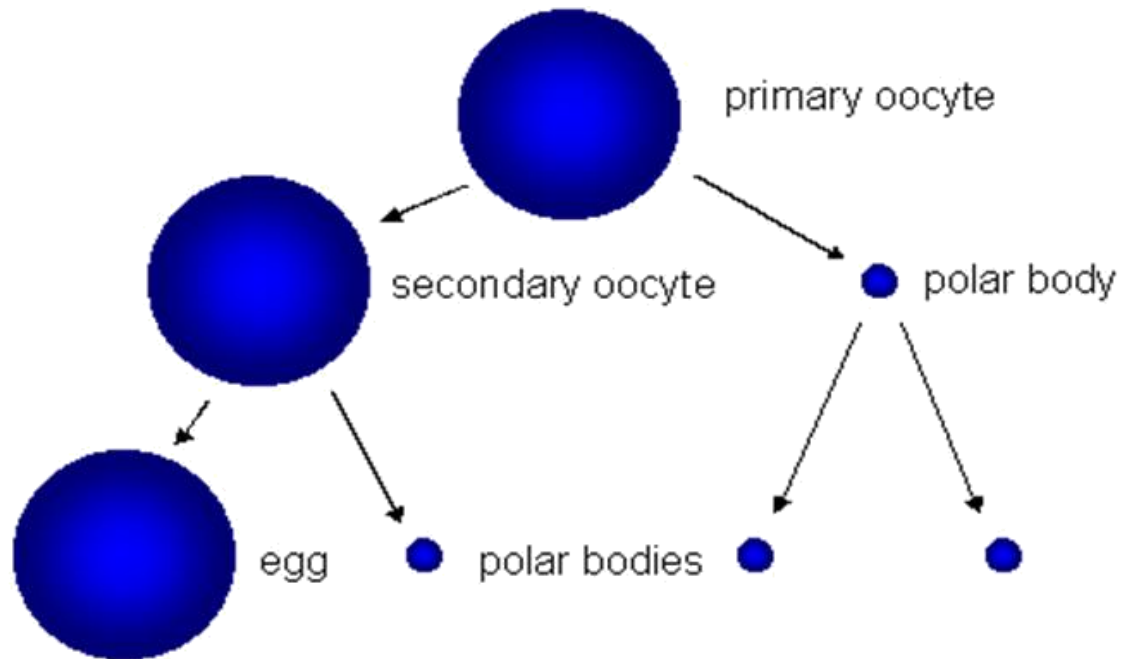
Spermatogenesis and oogenesis

Meiosis in males is called spermatogenesis and produces sperms.

Meiosis in females is called oogenesis and produces ova.



Spermatogenesis: Four sperm cells are produced from primary spermatocyte



Oogenesis: The polar bodies die. Only one ovum (egg) is produced from each primary oocyte.

Stages of meiosis: There are two stages of meiosis

Meiosis I

Meiosis II

During meiosis I, homologous chromosomes separate.

During meiosis II, sister chromatids separate.

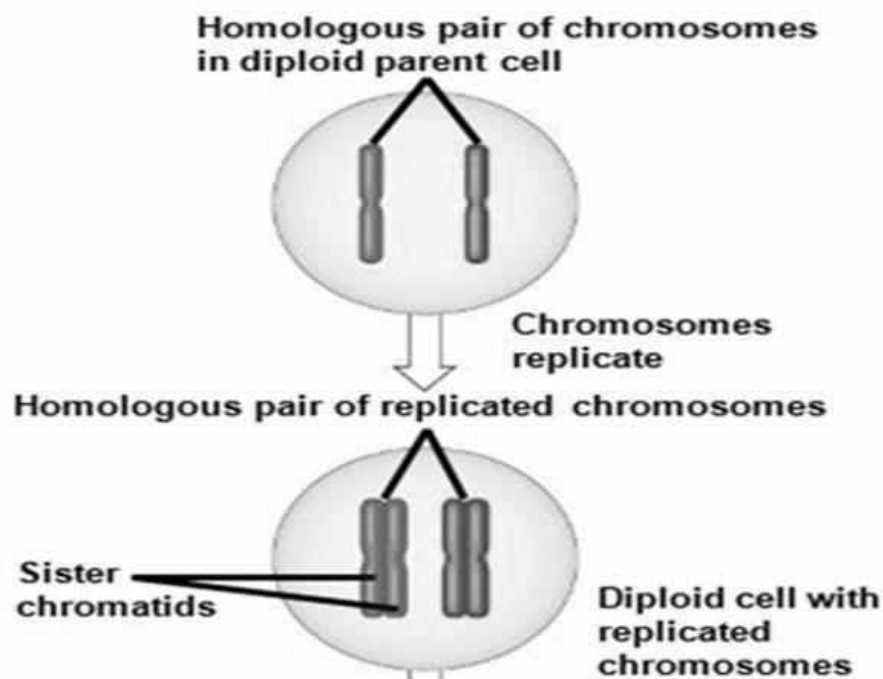
Meiosis I – Reductional division

Meiosis I results in two haploid daughter cells. It is called the reductional division. Homologous chromosomes separate.

Meiosis II: Second cell division where sister chromatids separate. As a result of meiosis II, two haploid cells become four haploid cells. Meiosis II behaves like mitosis, where no reduction in chromosomes number.

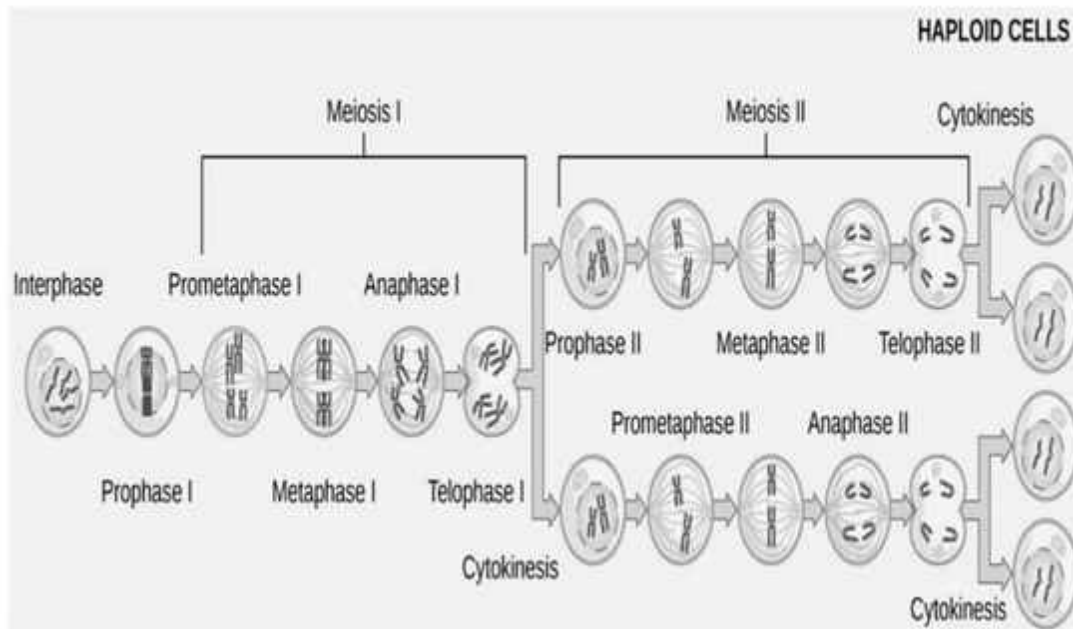
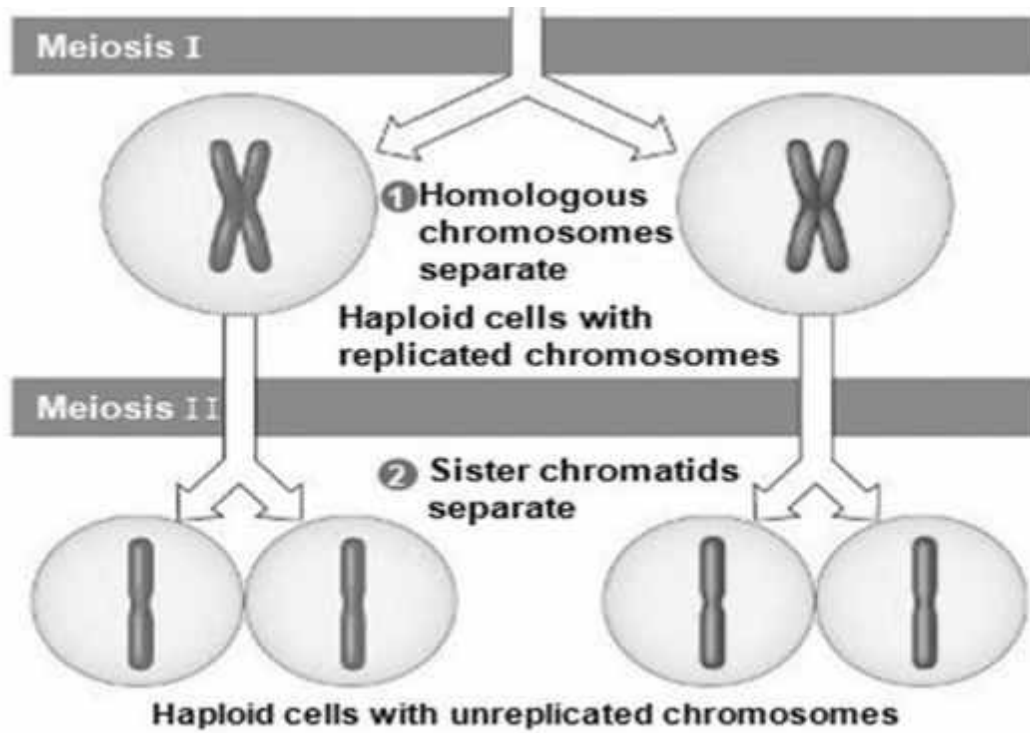
Meiosis II – Equational division: Meiosis II results in four haploid daughter cells with unreplicated chromosomes; it is called equational division.

Interphase chromosomes replicates



Meiosis I, Meiosis II

Meiosis - four haploid cells

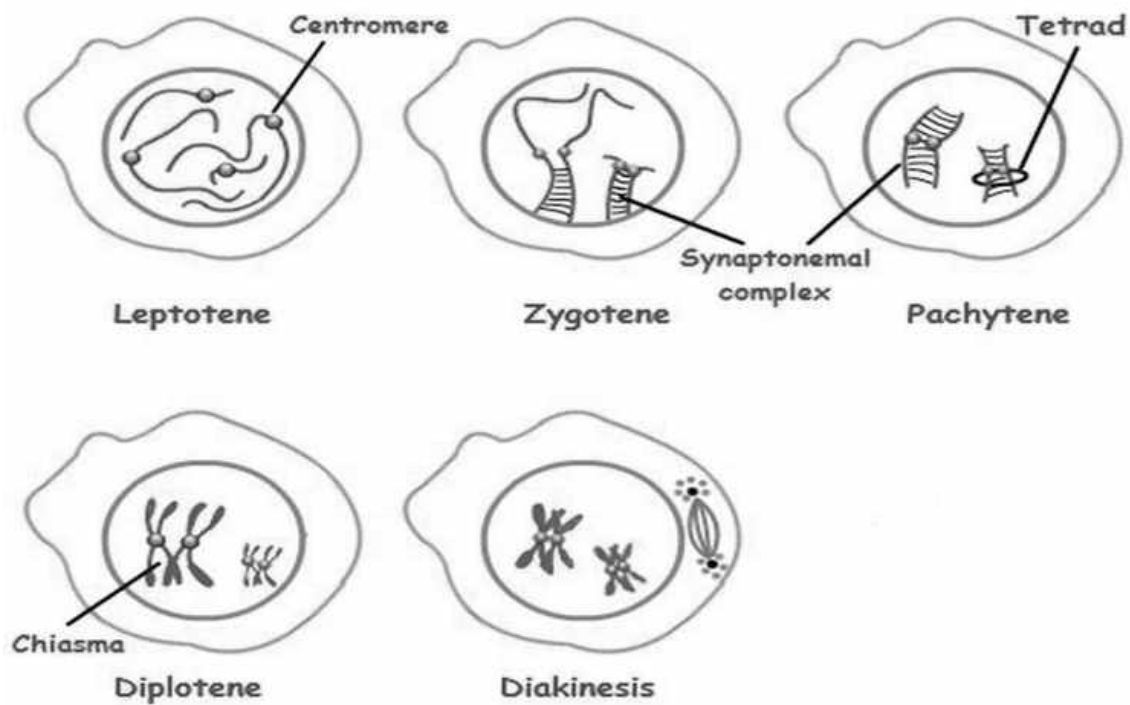


Prophase I of meiosis

Prophase I occupies more than 90% of the time required for meiosis. Five sub stages of prophase I.

Sub stages of prophase I

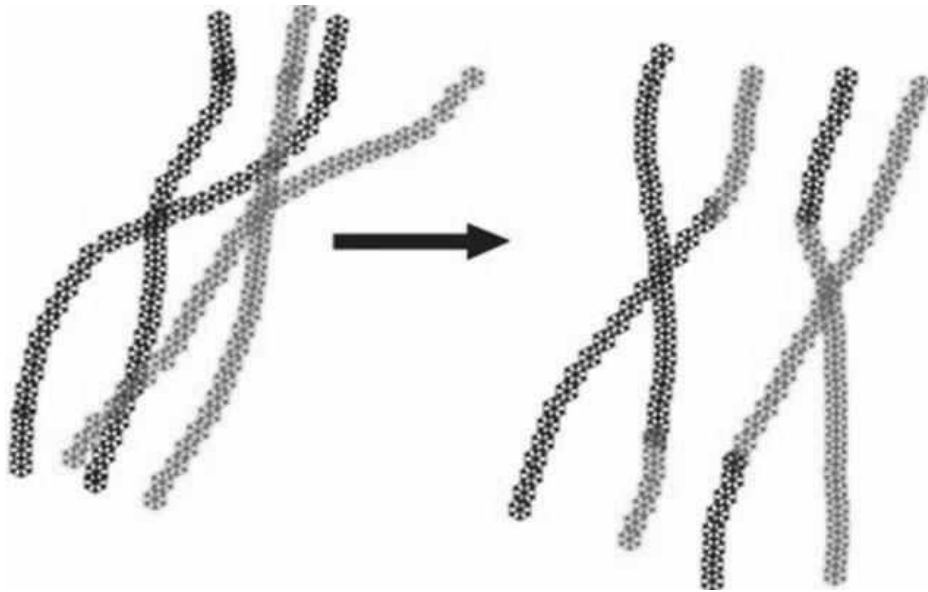
- Leptotene
- Zygotene
- Pachytene
- Diplotene
- Diakinesis



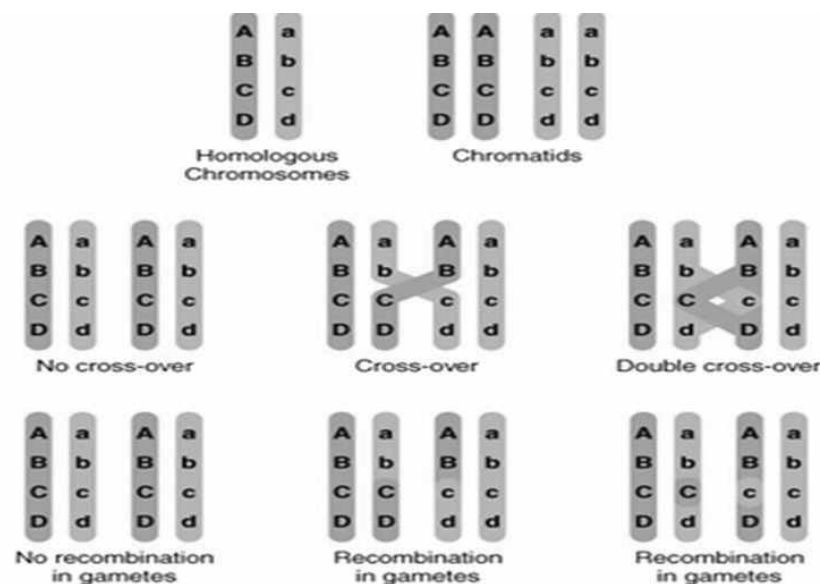
Events of prophase I: The duplicated homologous chromosomes pair. The nucleolus disappears. Centrioles migrate to opposite poles of the cell. Meiotic spindle forms between the two pairs of centrioles. Nuclear membrane disappears.

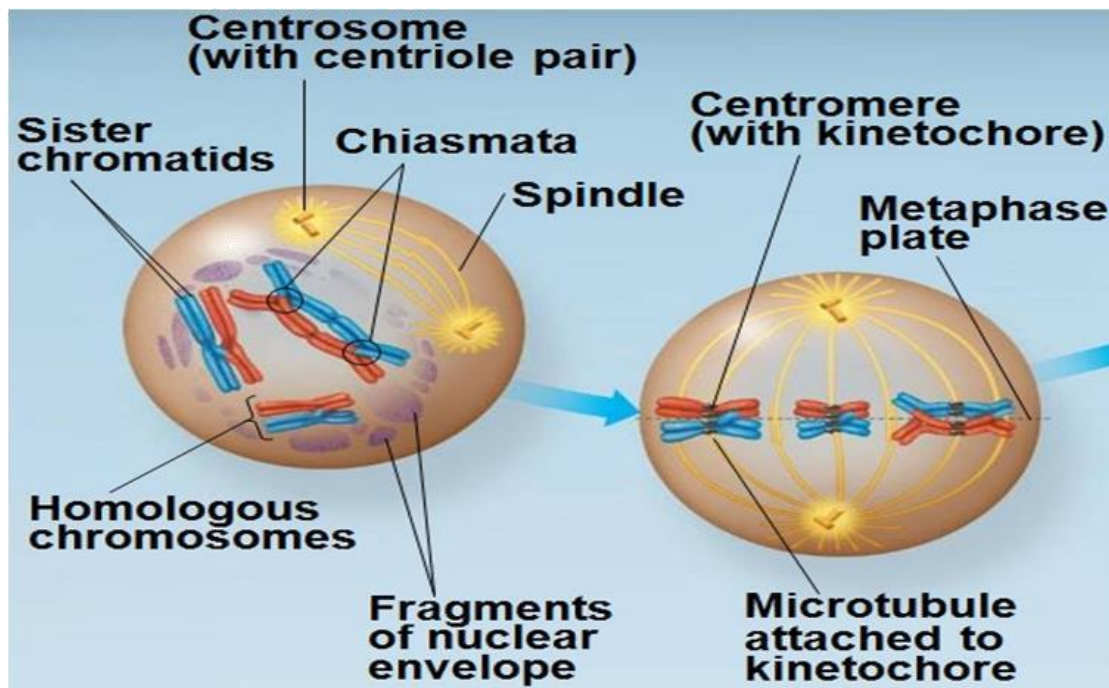
Chiasmata formation during prophase I During pairing up of chromosomes, nonsister chromatids exchange DNA segments. Each pair of chromosomes forms a tetrad, a group of four chromatids.

Pairing and exchange of chromosome fragments



Prophase I – Chiasmata



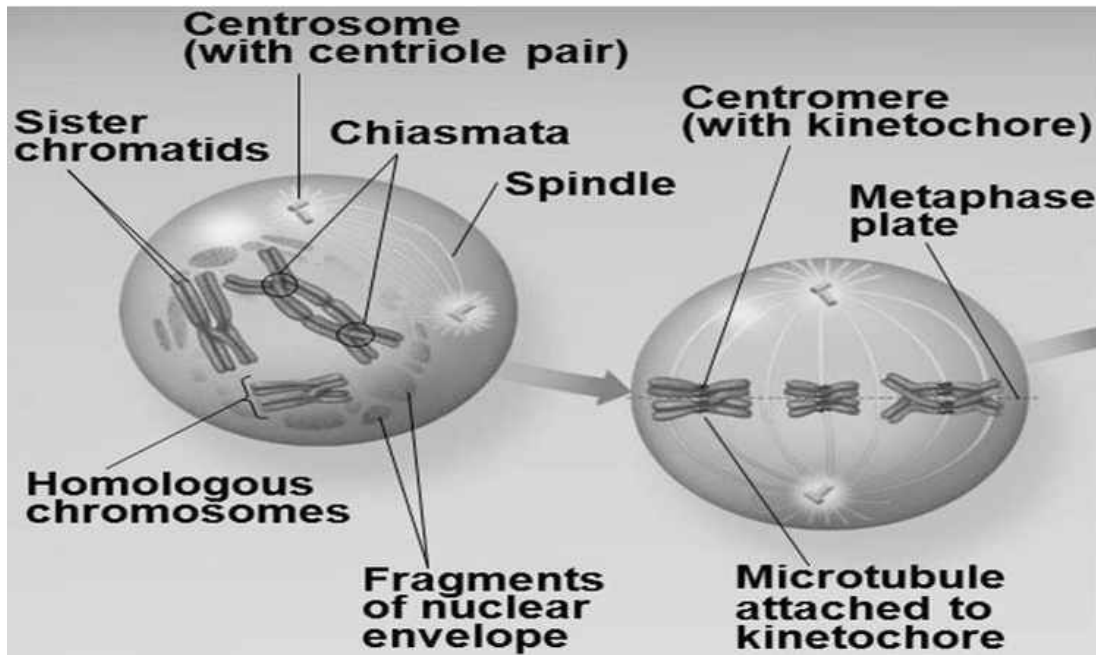


Summary - Prophase I

- Homologous chromosomes pairs.
- Nucleolus disappears.
- Meiotic spindle forms.
- Nuclear membrane disappears.

Metaphase I of meiosis:

In metaphase I, tetrads line up at the metaphase plate, with one chromosome facing each pole. Microtubules from one pole are attached to kinetochore of one chromosome of each tetrad. Microtubules from the other pole are attached to the kinetochore of the other chromosome.

Metaphase I

Anaphase I of meiosis Pairs of homologous chromosomes separate. One chromosome moves toward each pole, guided by the spindle apparatus.

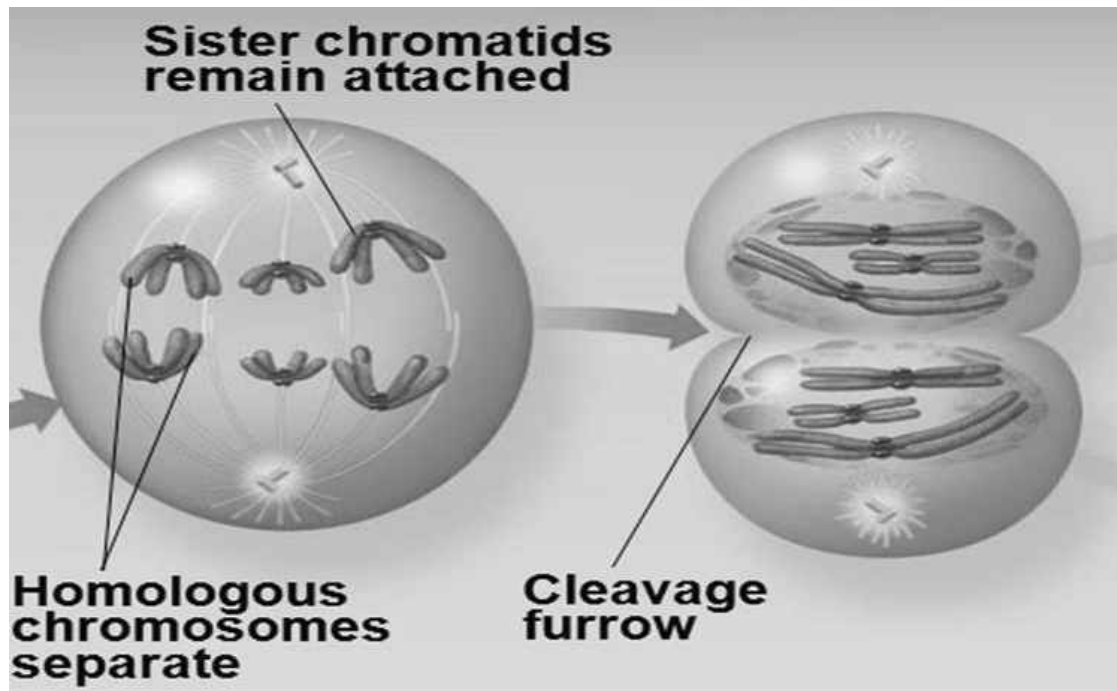
Anaphase I – sister chromatids attached at centromere Sister Chromatids remain attached at the centromere of each of the homologue chromosome and move as one unit toward the pole.

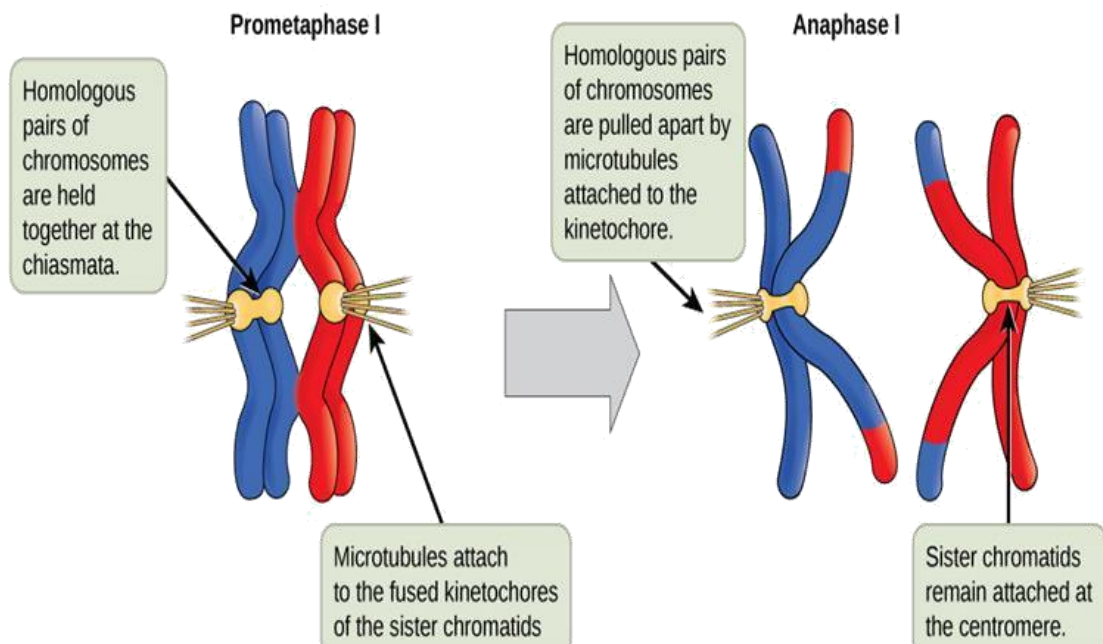
Difference between anaphase of mitosis and meiosis I

Sister chromatids remained joined in meiosis I, whereas in mitosis they separate.

In mitosis, centromere splits into two parts while in meiosis it do not splits.

Anaphase I





Summary - Anaphase I

Pairs of homologous chromosomes separate.

One chromosome moves toward one pole while other chromosome moves to other pole of the cell.

Telophase I of meiosis:

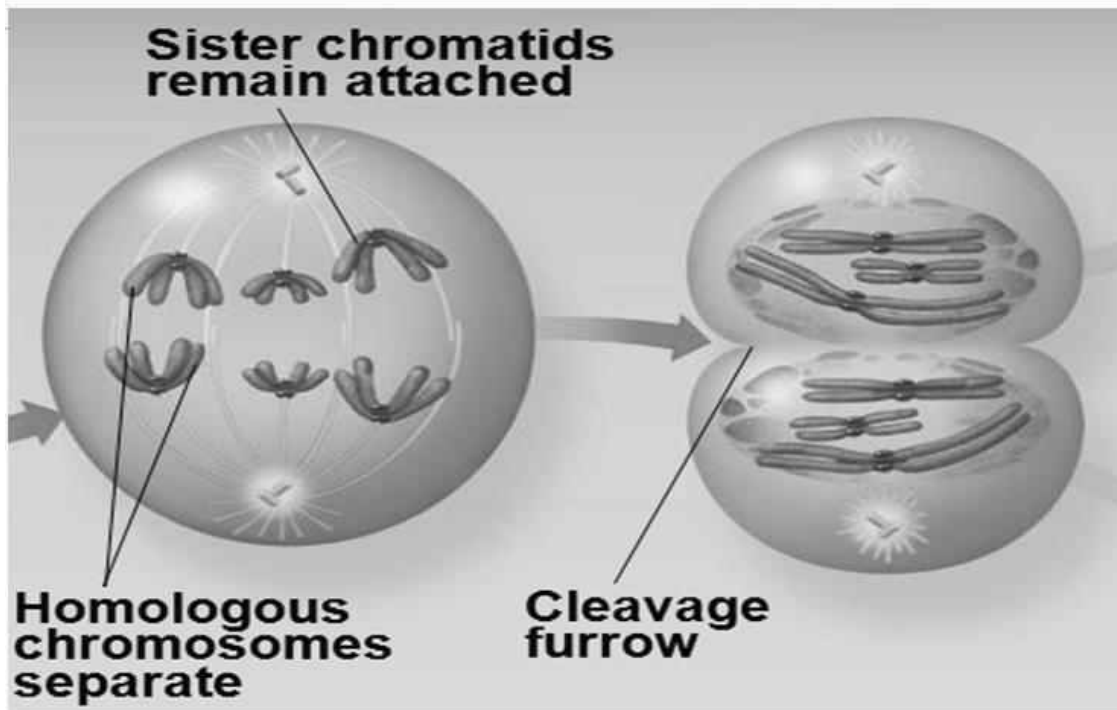
Haploid set of chromosomes arrived at each of the pole. Each chromosome still consists of two sister chromatids. Cytokinesis usually occurs simultaneously, forming two haploid daughter cells.

Cytokinesis – Animal cell and plants cell

In animal cells, a cleavage furrow is formed.

In plant cells, a cell plate formed.

No replication between Meiosis I and meiosis II: There is no chromosome replication between the end of meiosis I and beginning of meiosis II. Chromosomes are already replicated.

Telophase I

Haploid set of chromosomes arrived at each of the pole.

Meiosis I results, a diploid cell produced two haploid cells.

Prophase II of meiosis

Meiosis II similar to mitosis

Meiosis II also occurs in four phases:

Prophase II

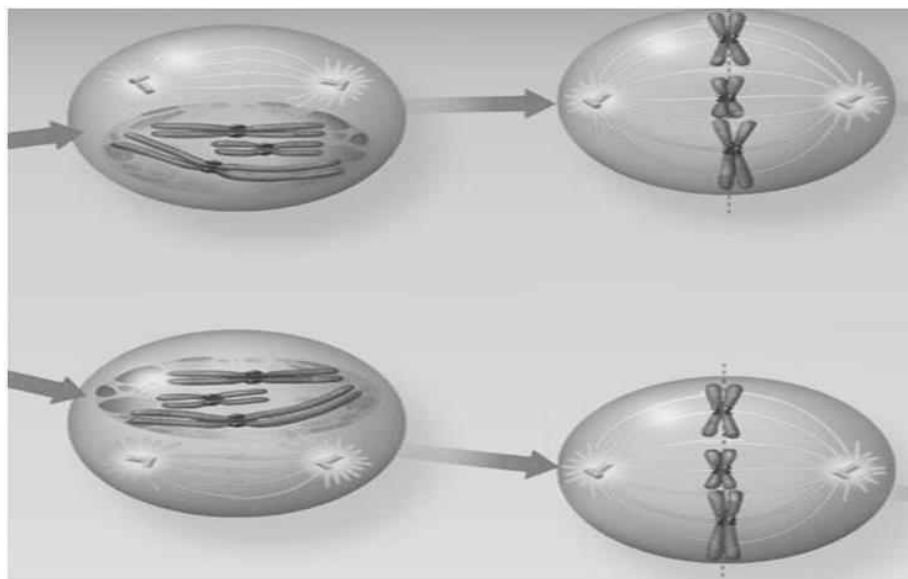
Metaphase II

Anaphase II

Telophase II and cytokinesis

Prophase II: No replication of Chromosomes as they are already replicated. Centrioles are separated and take positions on the opposite poles of the cell. Nuclear membrane disappears. Spindle fibers form and radiate toward the center of the cell.

Prophase II



Summary - Prophase II

Nuclear membrane disappears.

Spindle fibers form and radiate toward the center of the cell.

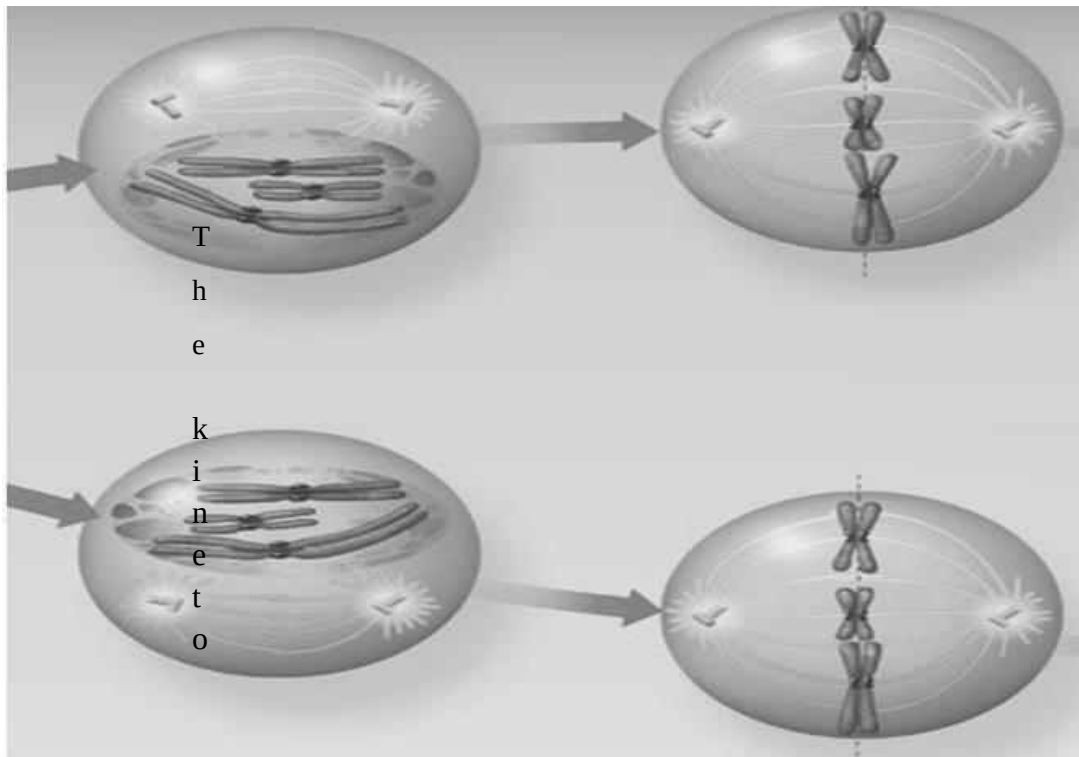
Centrioles take the position on poles.

Metaphase II of meiosis: In metaphase II, sister chromatids are arranged at the metaphase plate.

The kinetochores of sister chromatids attach to microtubules extending from opposite poles.

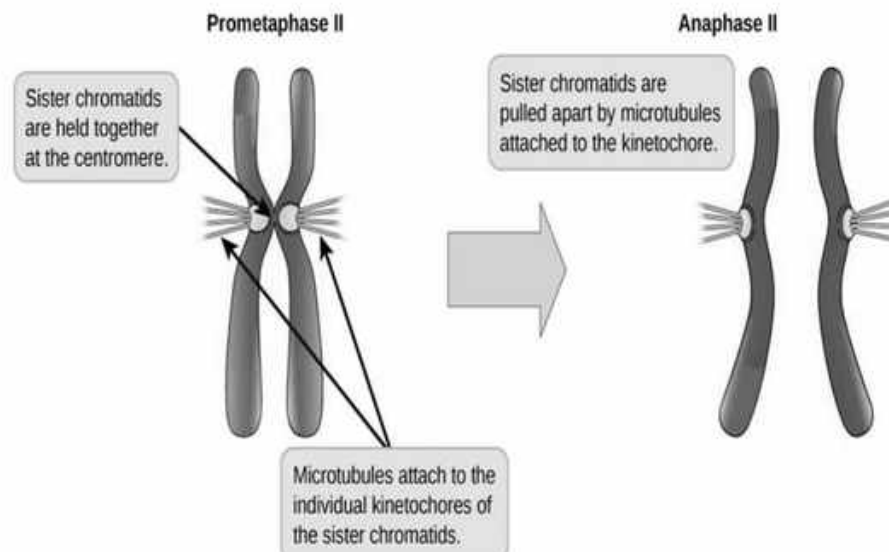
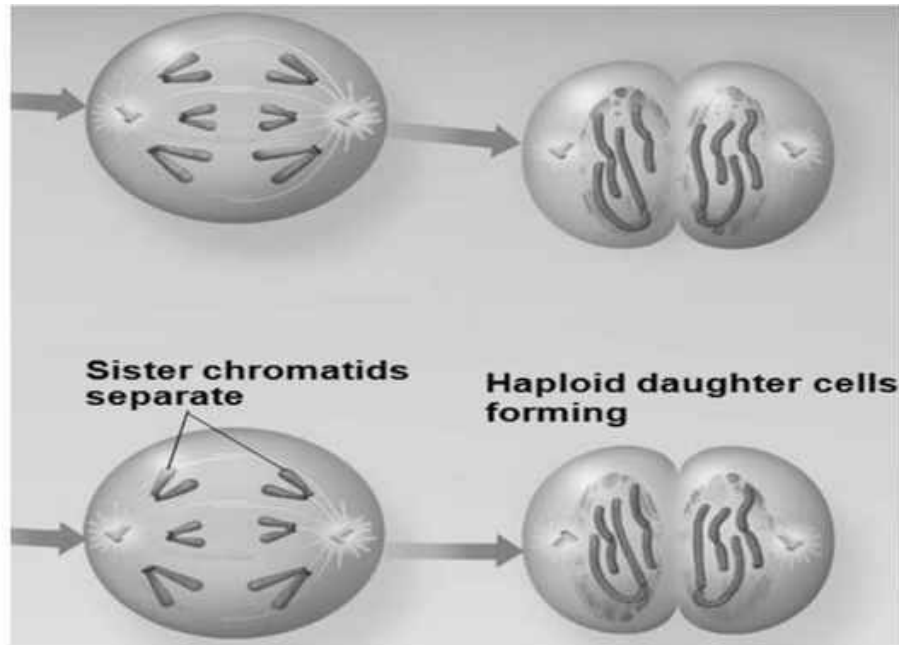
Chromosomes lined up across the middle of the cell. Due to crossing over during meiosis I, the two sister chromatids of each chromosome are no longer genetically identical.

Metaphase II



Kinetochores of sister chromatids attach to microtubules extending from opposite poles. Chromosomes lined up across the middle of the cell.

Anaphase II of meiosis: Centromere split – as a result sister chromatids are separated. Sister chromatids become individual chromosomes. Separated chromatids move to opposite poles of the cell.

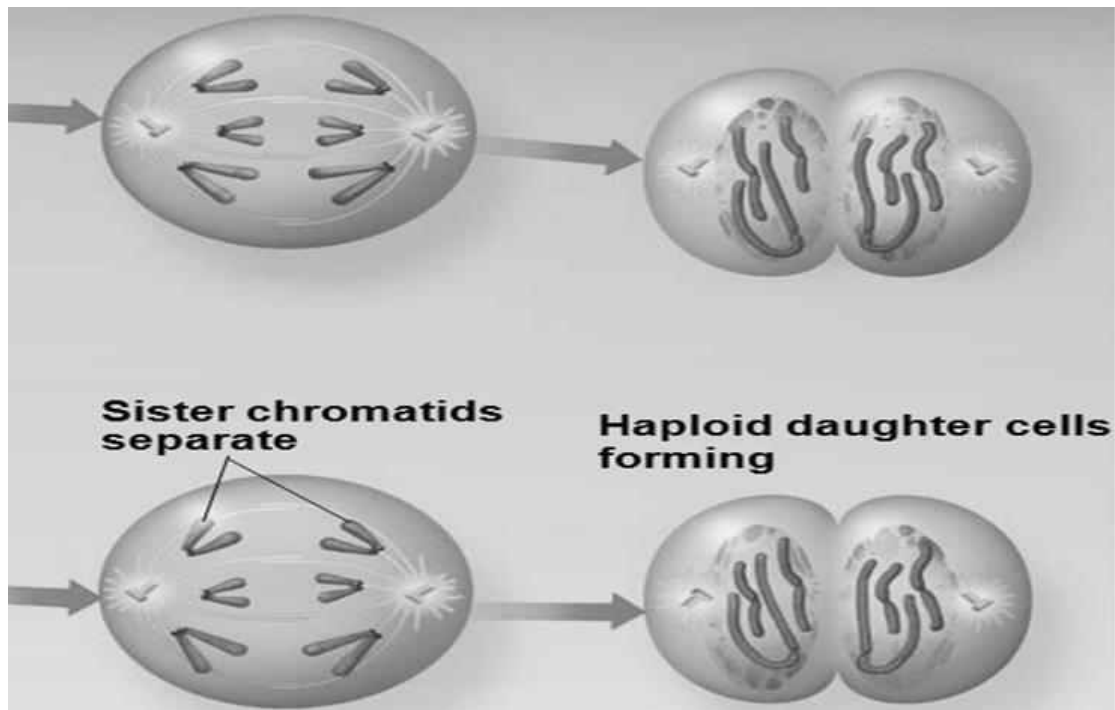


Summary - Anaphase II

Sister chromatids become individual chromosomes.

Separated chromatids move to opposite poles of the cell.

Telophase II of meiosis: In Telophase II, the chromosomes arrive at opposite poles. Nuclear membrane forms and the chromosomes begin de-condensing. Cytokinesis occurs. Now, there are four daughter cells, each with a haploid set of chromosomes. Each daughter cell is genetically distinct from the others and from the parent cell.



Telophase II

Summary - Telophase II

Four daughter cells are produced each with a haploid set of chromosomes.

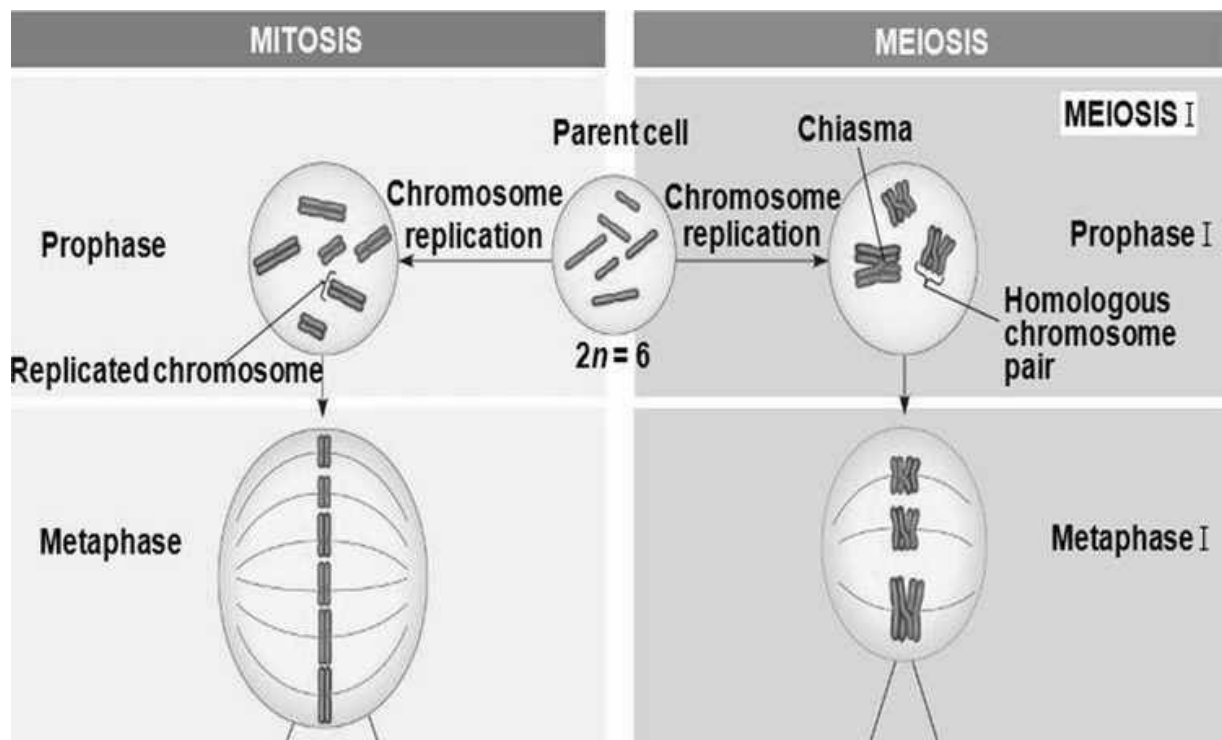
Each daughter cell is genetically distinct from the others and from the parent cell.

Mitosis and meiosis

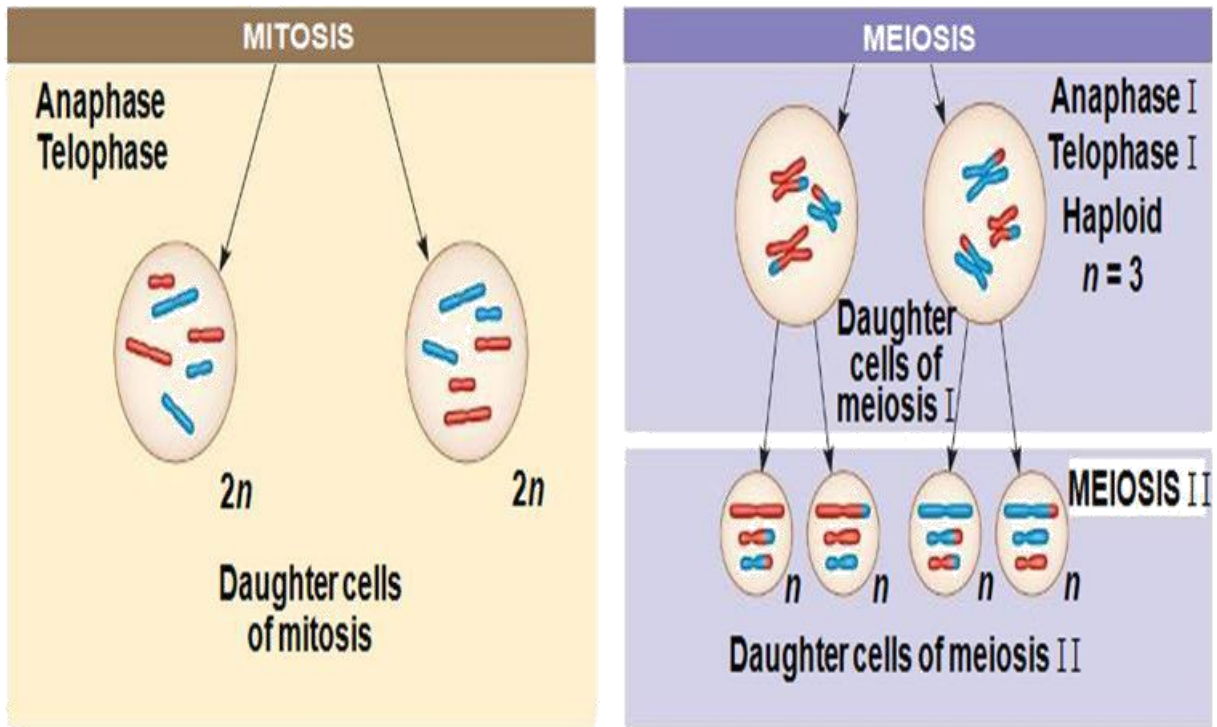
Mitosis: Mitosis conserves the number of chromosome sets, producing cells that are genetically identical to the parent cell.

Meiosis: Meiosis reduces the number of chromosomes sets from two (diploid) to one (haploid), producing cells that differ genetically from each other and from the parent cell.

Comparison



The mechanism for separating sister chromatids is virtually identical in meiosis II and mitosis.



Comparison

Meiosis reduces the number of chromosomes sets from diploid to one haploid and produced four daughter cells which not identical to each other and parent cell.

Mitosis – produces two daughter cells which are identical to parent cell.

Summary - Mitosis and meiosis

SUMMARY		
Property	Mitosis	Meiosis
DNA replication	Occurs during interphase before mitosis begins	Occurs during interphase before meiosis I begins
Number of divisions	One, including prophase, metaphase, anaphase, and telophase	Two, each including prophase, metaphase, anaphase, and telophase
Synapsis of homologous chromosomes	Does not occur	Occurs during prophase I along with crossing over between nonsister chromatids; resulting chiasmata hold pairs together due to sister chromatid cohesion
Number of daughter cells and genetic composition	Two, each diploid ($2n$) and genetically identical to the parent cell	Four, each haploid (n), containing half as many chromosomes as the parent cell; genetically different from the parent cell and from each other
Role in the animal body	Enables multicellular adult to arise from zygote; produces cells for growth, repair, and, in some species, asexual reproduction	Produces gametes; reduces number of chromosomes by half and introduces genetic variability among the gametes

Lesson 34

Multiple alleles

Three or more alternative forms of a gene (alleles) that can occupy the same locus/position on a chromosome.

Genes have specific loci on chromosomes

According to chromosomal theory of inheritance, genes have specific loci/position on chromosomes.

Diploid individuals have two alleles

Diploid individuals have two alleles, one on each of the homologous chromosome.

All genes do not have two forms

All genes do not have two forms; many have multiple alleles or multiple forms.

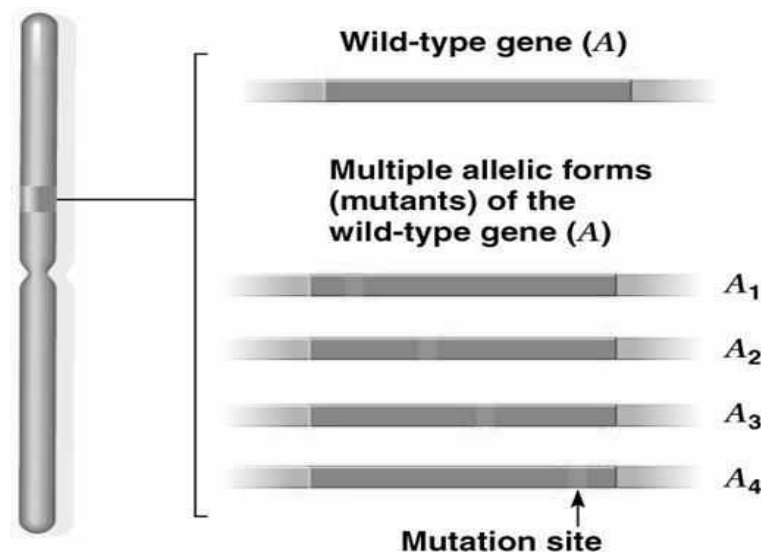
ABO blood groups

Mono-allelic, di-allelic and poly-allelic

30% genes in humans are di-allelic - they exist in two forms.

70% are mono-allelic; they exist only in one form.

Few are poly-allelic.



Multiple alleles

Poly-allelic genes are tissue specific

Poly-allelic genes are usually associated with tissue types.

These genes are so varied that they provide us with our genetic finger print.

Number of alleles - number of genotypes

Di-allelic genes can generate 3 genotypes.

Genes with 3 alleles can generate 6 genotypes.

Genes with 4 alleles can generate 10 genotypes.

Multiple alleles - conclusion

Three or more alternative forms of a gene (alleles) that can occupy the same locus/position on a chromosome.

Lesson 35

Multiple alleles - blood groups

Abo blood system

Controlled by a tri-allelic gene.

Allele A, Allele B, Allele i

Generate 6 genotypes.

Two of the alleles are co-dominant to each other

Two of the alleles are codominant to one another.

Both are dominant over the third allele.

Allele A and Allele B when exist together will be co- dominant.

Alleles control the production of antigens

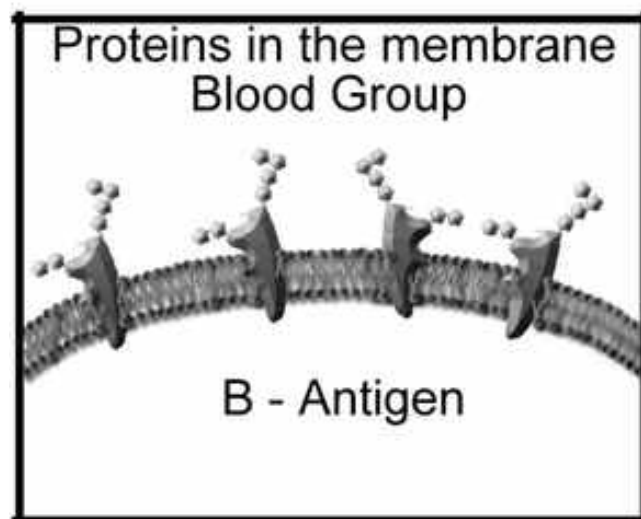
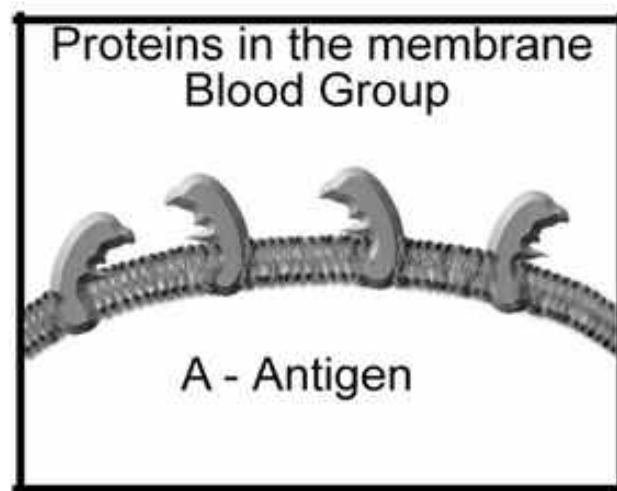
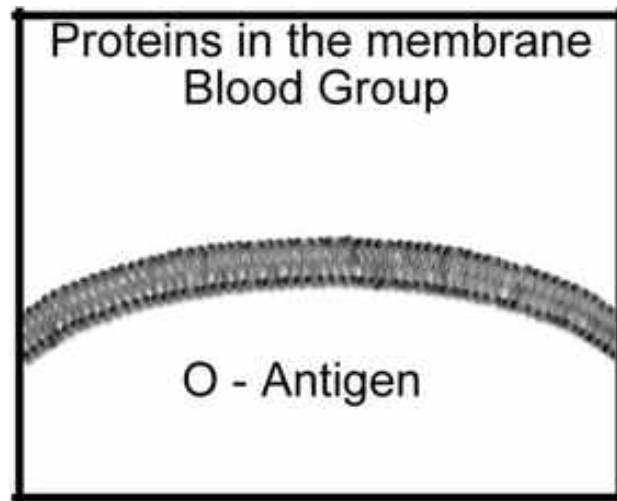
The alleles control the production of antigens on the surface of the red blood cells.

Alleles and antigens

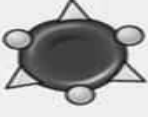
Allele I^A produces antigen A

Allele I^B produces antigen B

Allele "i" produces no antigen



Alleles and antigens

$I^A I^A$ or $I^A i$	A	
$I^B I^B$ or $I^B i$	B	
$I^A I^B$	AB	
ii	O	

Blood group

6 Genotypes	4 Phenotypes (blood group types)
$I^A I^A$	A
$I^A I^B$	AB
$I^A i$	A
$I^B I^B$	B
$I^B i$	B
ii	O

Blood groups exists in homo and hetero forms

Blood type A - homozygous and heterozygous.

Blood type B - homozygous and heterozygous.

Blood types AB and O have only one genotype each.

Blood groups system – conclusion

Controlled by a tri-allelic gene.

Four major blood groups – can be positive – negative based on Rh factor.

Lesson 36

Blood groups and Transfusions

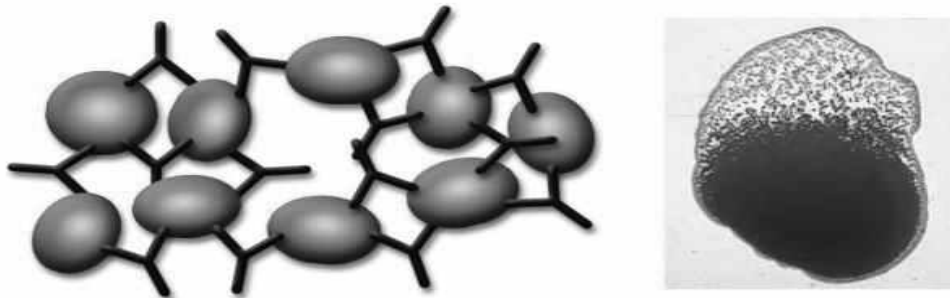
Immune system– self and non-self

Blood types vary and your immune system recognizes your own blood type as being self.

Other blood group types are recognized as non-self.

Type A produce antibodies to agglutinate cells which carry Type B antigens. They recognize them as non-self

The opposite is true for Type B.



Blood group type o, do not carry any antigens

Neither of these people will agglutinate blood cells which are Type O.

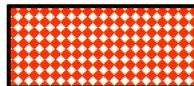
Type O cells do not carry any antigens for the ABO system.

Universal – donor and recipient

Type O blood may be transfused into all the other types = the universal donor.

Type AB blood can receive blood from all the other blood types = the universal recipient.

		Recipient			
Type		A	B	AB	O
Donor	A				
	B				
	AB				
	O				



= Agglutination



= Safe transfusion

Donor-recipient compatibility

Person with Type A (Heterozygous) married a person Type B (Heterozygous) blood. genotypes and phenotypes ?

$I^A i$ X $I^B i$

Genotypic Ratio:

$I^A I^B$ $I^A i$ $I^B i$ ii

Phenotypic Ratio:

AB: A: B: O

	I^A	i
I^B	$I^A I^B$	$I^B i$
i	$I^A i$	ii

If a cross between a person with type O with heterozygous type B, what would be genotypic and phenotypic ratio

$$ii \times I^B i$$

GENOTYPIC RATIO

$$I^B i : ii$$

Phenotypic Ratio

$$B : O$$

	i	i
I^B	I^Bi	I^Bi
i	ii	ii

Blood groups- conclusion

Immune system recognized the blood as self and non-self.

Lesson 37

Multiple alleles- rabbits

Multiple alleles In rabbits

Traits controlled by more than two alleles – multiple alleles.

Fur color of rabbits – example of multiple alleles.

Fur color in rabbits

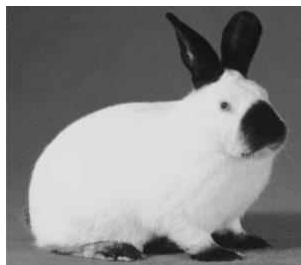
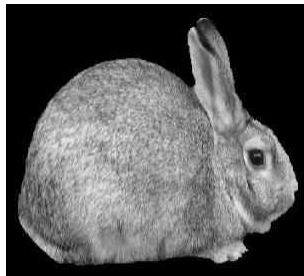
Fur color in rabbits

C = Agouti (dark gray)

c^{ch} = Chinchilla (light gray)

c^h = Himalayan (white with black points)

c = White



Allele			
C	c^{ch}	c^h	c
Genotype			
C^+C^+	$c^{ch}c^{ch}$	c^hc^h	cc
Phenotype			
WILD TYPE: Brown fur	CHINCHILLA: Black-tipped white fur	HIMALAYAN: White fur with black paws, nose, ears, tail	ALBINO: White fur
			

Genotypes of Fur color

- White cc
Himalayan c^hc^h, c^hc
- Chinchilla $c^{ch}c^{ch}, c^{ch}c^h, c^{ch}c$
Gray CC, Cc^{ch}, Cc^h, Cc

Dominance of alleles

Allele C dominant to allele c^{ch}

Allele c^{ch} dominant to allele c^h

Allele c^h dominant to allele c

Multiple alleles conclusion

Traits controlled by more than two alleles.

Lesson 38

Alleles and genotypes

Number of alleles and number of genotypes

$$\text{Genotypes} = n(n + 1)/2$$

$$\text{Homozygotes} = n$$

$$\text{Heterozygotes} = n(n - 1)/2$$

# alleles	# genotypes	Homozygotes	Heterozygotes
1	1	1	0
2	3	2	1
3	6	3	3
4	10	4	6
5	15	5	10

Number of alleles and number of genotypes

$$\text{Genotypes} = n(n + 1)/2$$

$$\text{Homozygotes} = n$$

$$\text{Heterozygotes} = n(n - 1)/2$$

Calculate genotypes for fur color of rabbits, if Four (4) alleles for fur color.

$$\text{Genotypes} = n(n + 1)/2$$

$$\text{Homozygotes} = n$$

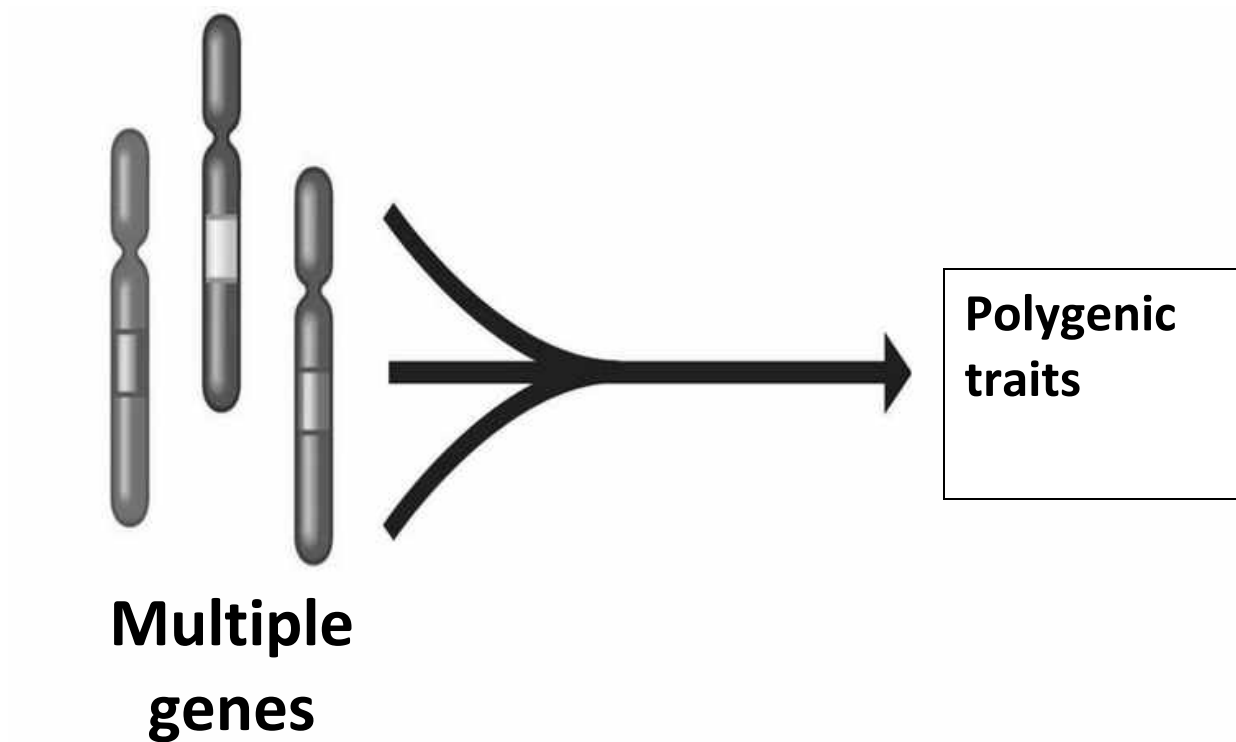
$$\text{Heterozygotes} = n(n - 1)/2$$

Number of alleles and number of genotypes

Based on number of alleles, number of genotypes can be calculated.

Lesson 39

Polygenic inheritance: Condition when two or more genes influence the expression of one trait. Polygenic inheritance is controlled by multiple genes



Multiple genes produce a spectrum of resulting phenotypes.

Skin color, height etc.

Pepper color

Gene 1: R= red r = yellow

Gene 2: Y= absence of chlorophyll; y = presence of chlorophyll



Possible genotypes

R-/Y- : red (red/no chlorophyll)



R-/yy : brown/orange (red/chlorophyll)



rr/Y- : yellow (yellow/no chlorophyll)



rr/yy : green (yellow/chlorophyll)

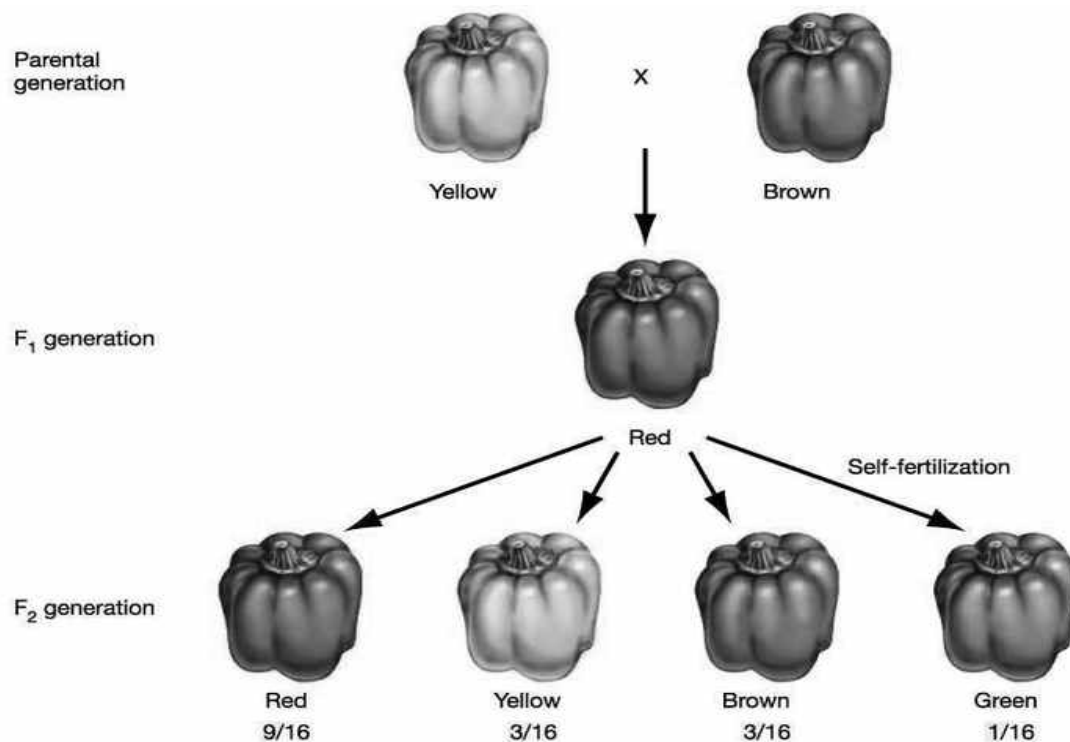


Test cross: Try crossing a brown pepper ($RRyy$) with a yellow pepper ($rrYY$). Which trait will your offspring (F_1 generation) produce?

What traits are produced when you cross two of the peppers found in the F_1 generation?

Brown Pepper $RRyy$, Yellow pepper $rrYY$

Polygenic inheritance is a condition when two or more genes influence the expression of one trait.

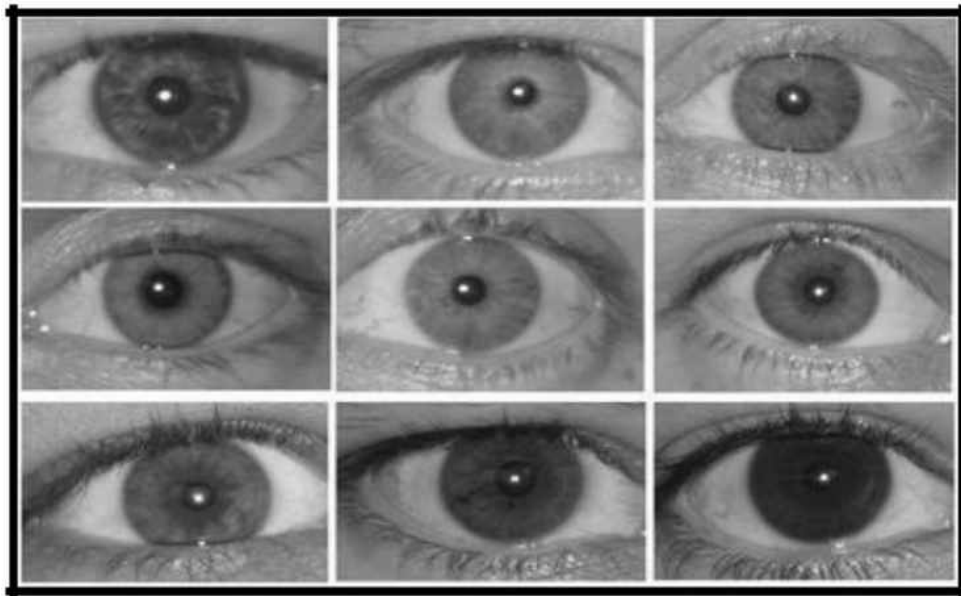


Lesson 40

Examples of polygenic traits Eye color, height, body shape and intelligence. Many of these traits are also affected by the person's environment, so they are called multifactorial.

Polygenic traits, or continuous traits, are governed by alleles at two or more loci, and each locus has some influence on the phenotype. Hair, eye and skin color are polygenic traits.

Polygenic trait – eye color



Stature, shape of face, finger prints

Stature

Shape of face

Fingerprint patterns

Chicken Combs Four different comb shapes. Comb shape is controlled by two genes found on two different chromosomes.

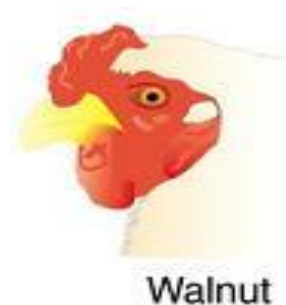
- Gene 1: R
- Gene 2: P

Four different phenotypes result

- Rose Combs (R-pp)



- Walnut Combs (R-P-)



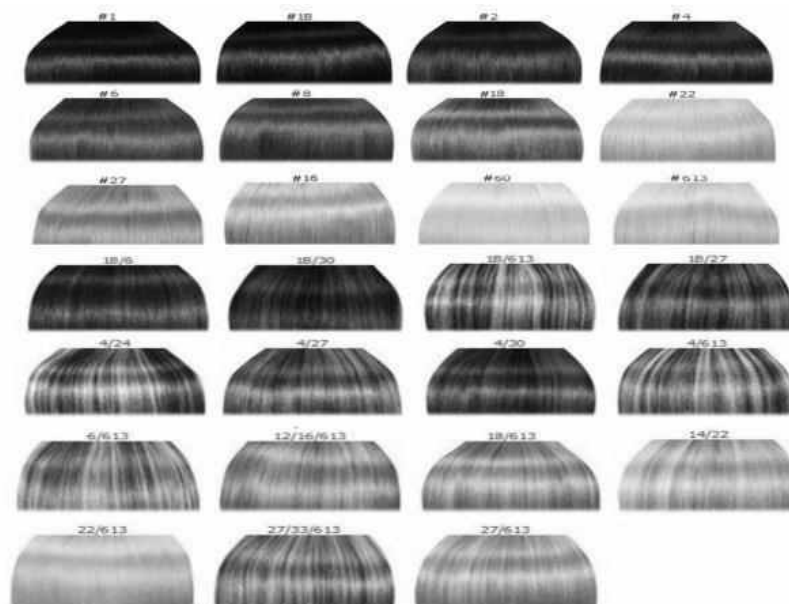
- Pea Combs (rrP-)



- Single Combs (rrpp)



Hair color Hair color is controlled by alleles on chromosomes 3, 6, 10, and 18. When more dominant alleles appear in the genotype; the darker will be the hair.



Lesson 41

Epistasis and modifier genes

Epistasis is a phenomenon that consists of the effect of one gene being dependent on the presence of one or more modifier genes. Type of polygenic inheritance where alleles at one gene locus can hide or prevent expression of alleles at second gene locus.

Positive epistasis – double mutation

Double mutation has a fitter phenotype than either single mutation.

Positive epistasis between beneficial mutations generates improvements in function.

Negative epistasis – two mutations have smaller effect

When two mutations together have a smaller effect than expected from their effects when alone, it is called negative epistasis.

Sign epistasis occurs when one mutation has the opposite effect when in the presence of another mutation.

Reciprocal epistasis occurs when two deleterious genes are beneficial when together.

Epistasis between genes

Epistasis within the genomes of organisms occurs due to interactions between the genes within the genome.

This interaction may be direct if the genes encode for proteins.

Interaction may be indirect, where the genes encode components of a metabolic pathway or network, developmental pathway.

Epistasis within genes when one deleterious mutation can be compensated for by a second mutation within that gene.

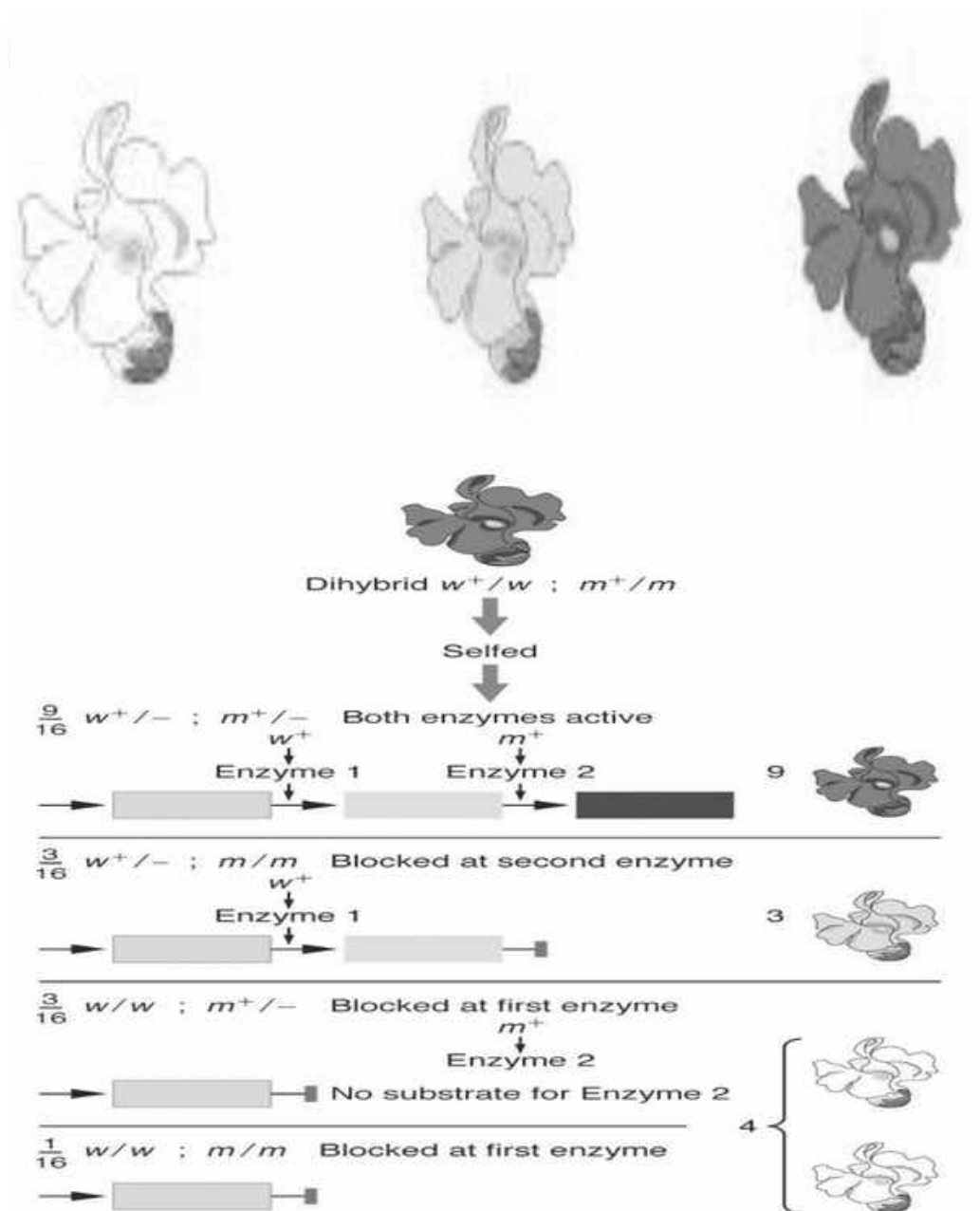
Epistasis Type of polygenic inheritance where alleles at one gene locus can hide or prevent expression of alleles at second gene locus. There are several types of epistasis.

Lesson 42

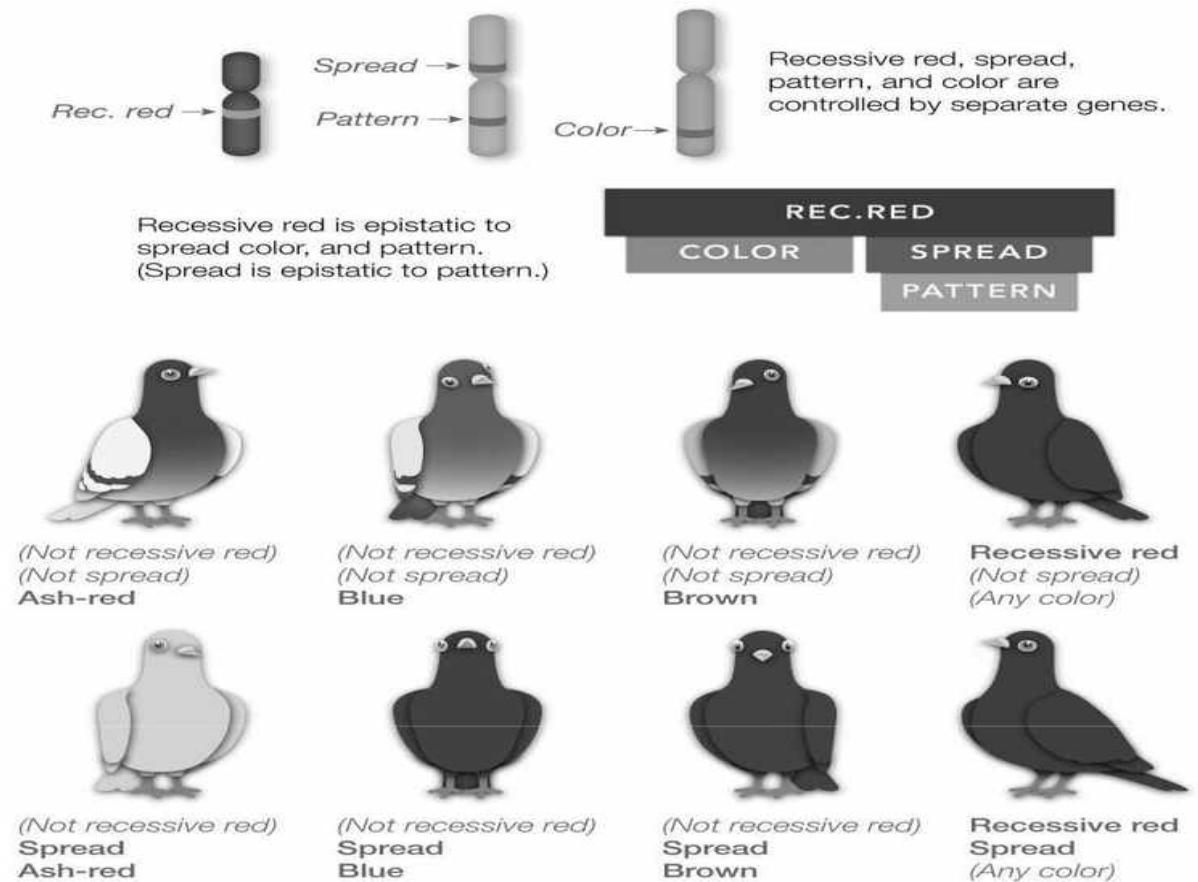
Recessive Epistasis Epistatic gene exerts its affect with homozygous recessive genotype.

Petal color in blue-eyed Mary plants Both enzymes active blue; Enzyme 1 active magenta

Precursor 1 → Precursor 2 → Blue anthocyanin
colorless magenta



Recessive Epistasis Epistatic gene exerts its affect with homozygous recessive genotype.



Dominant epistasis

Epistatic gene exerts its effect with the presence of a dominant allele.

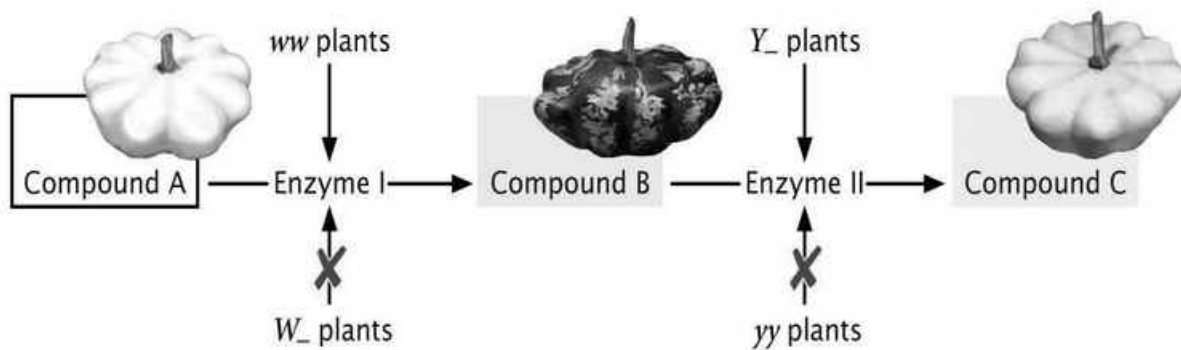
Dominant epistasis is fruit color in summer squash

Y = Yellow

yy = Green

W inhibits either color = color will be white (dominant)

w has no effect on color



Dominant Epistasis- ratios

Fruit color in summer squash

W w Y y x W w Y y

9/16 W _ Y _

3/16 W _ yy

3/16 w w Y _

1/16 w w yy

Duplicate dominant Epistasis

Fruit shape in Shepherd's purse

$A_ \text{ or } B_ = \text{heart shape}$

$aa \text{ and } bb = \text{narrow shape}$

Duplicate dominant Epistasis

Fruit shape in Shepherd's purse

$A_ \text{ or } B_ = \text{heart}$ $aa \text{ and } bb = \text{narrow}$

$A a B b \quad \times A a B b$

$9/16 A_ B_$

$3/16 \quad A_ b b$

$3/16 \quad a a B_$

$1/16 \quad a a b b$

Epistatic gene exerts its affect with the presence of a dominant allele.

Example of Epistasis

Fur color in dogs Fur color in Labrador Retrievers is controlled by two separate genes.

Gene 1: Represented by B; which controls color.

Gene 2: Represented by E which controls expression of gene B.

Epistasis

If a Labrador retriever has a dominant B allele, they will have black fur.

If they have two recessive alleles (bb) they will have brown fur.



BBEE and BbEe --> Black

bbEE and bbEe --> Brown

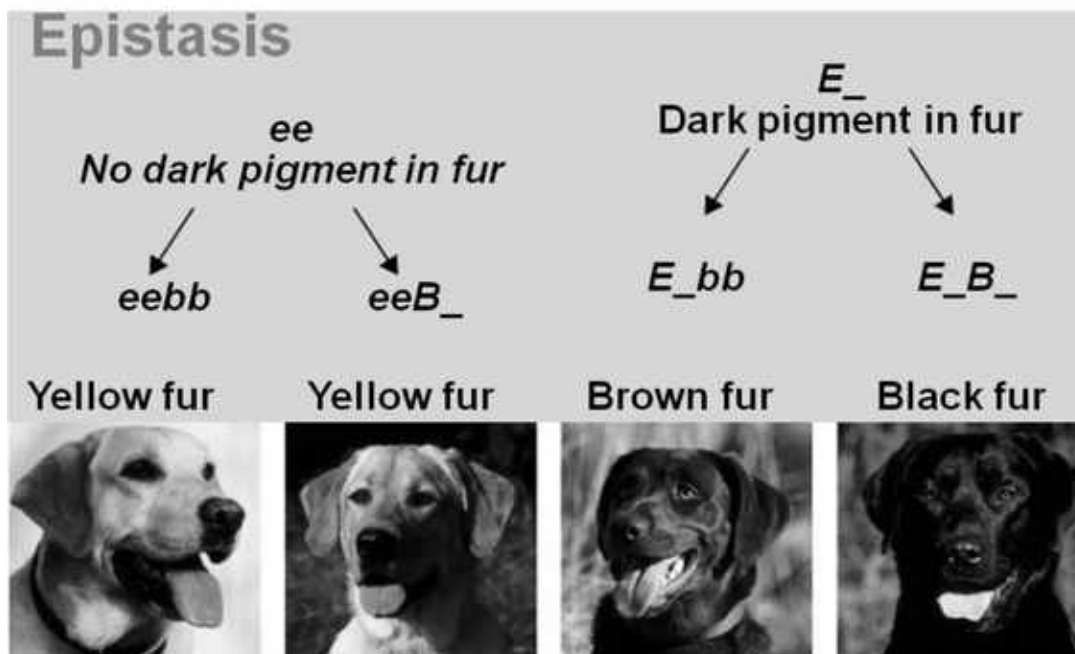
BBee, Bbee, or bbee --> Golden retrievers



Epistasis-genotypes/phenotype

Epistasis In dogs when a gene in recessive form has effect on expression of other genes.

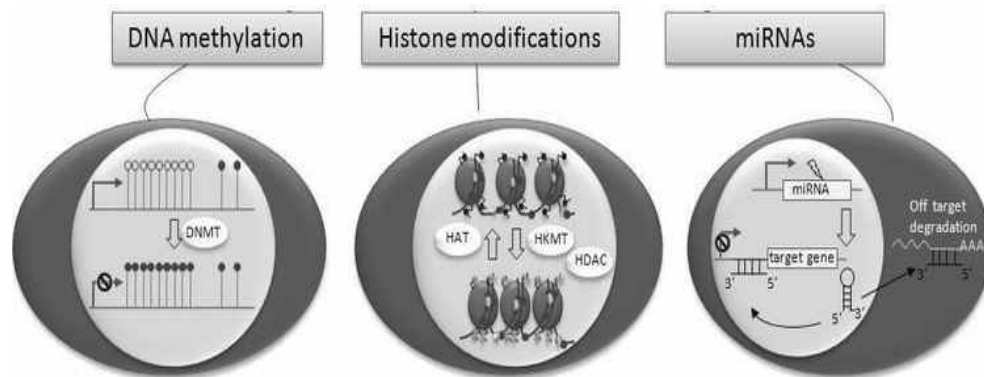
	EE	Ee	ee
BB			
Bb			
bb			



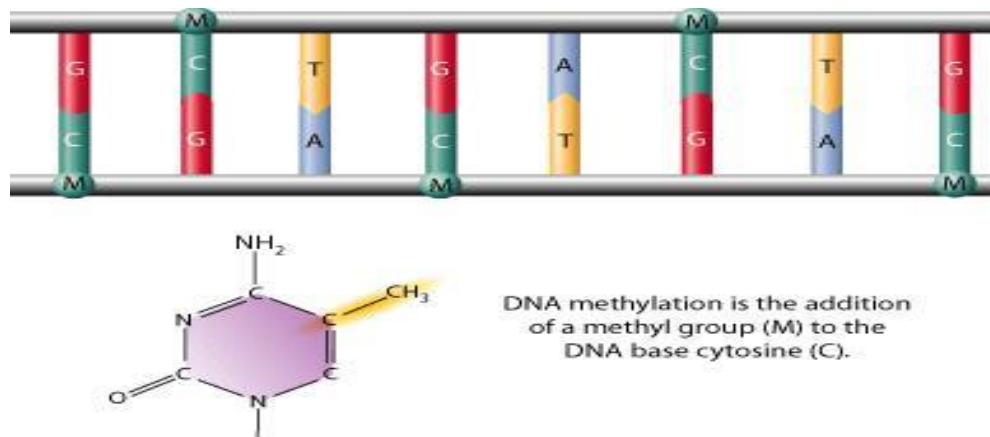
Lesson 43

Epigenetics literally means ‘above’ the genetics. Epigenetic trait is a stable and heritable phenotype resulting from changes in chromosome without alterations in the DNA sequence.

Causes of Epigenetics



Cytosine methylation: Methyl group to carbon-5 of cytosine residues.

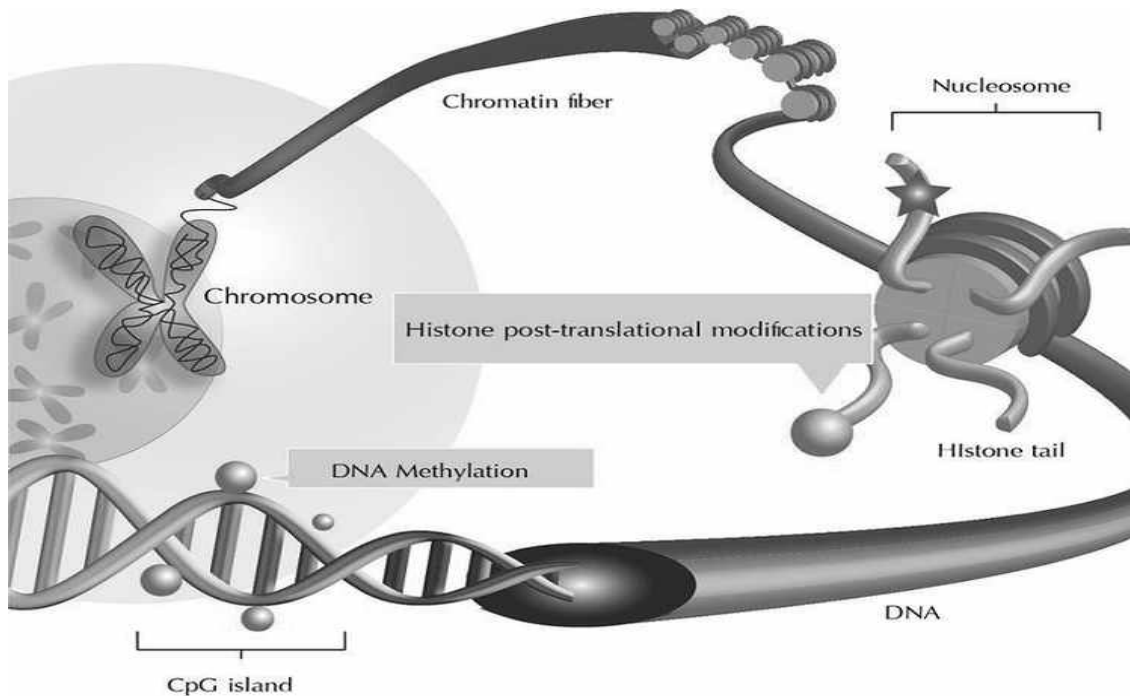


DNA Methylation is epigenetics, not changes in DNA sequence

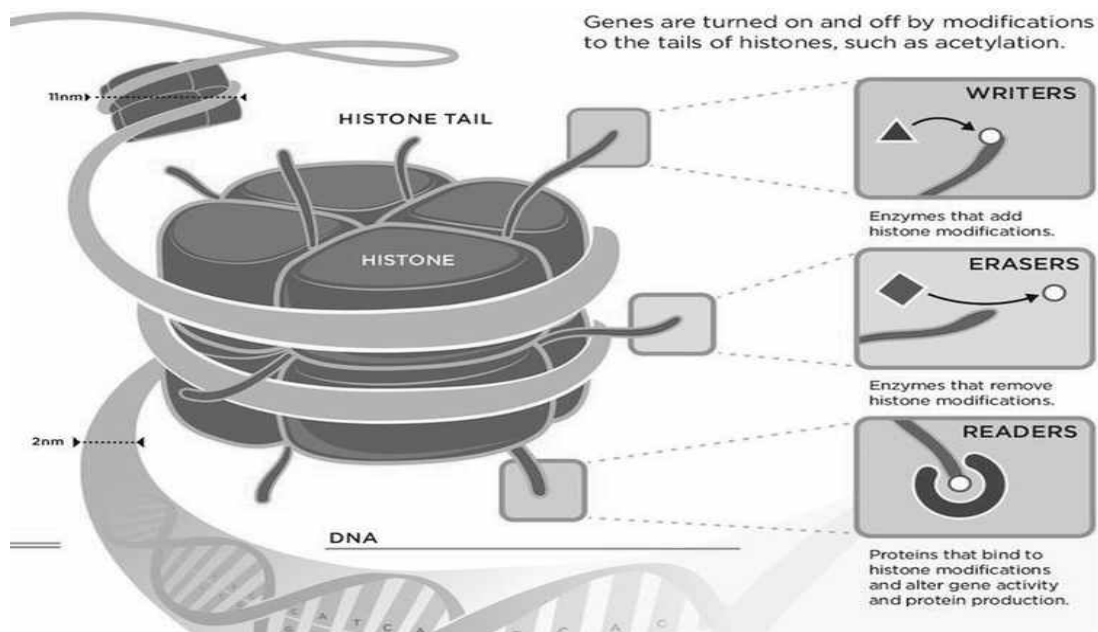
DNA methylations are regarded as epigenetics and not genetic changes in sequence of DNA.

Molecular Mechanism of Epigenetics Two primary mechanisms identified. Methylation of cytosine Posttranslational modification to histone proteins; includes acetylation, phosphorylation etc.

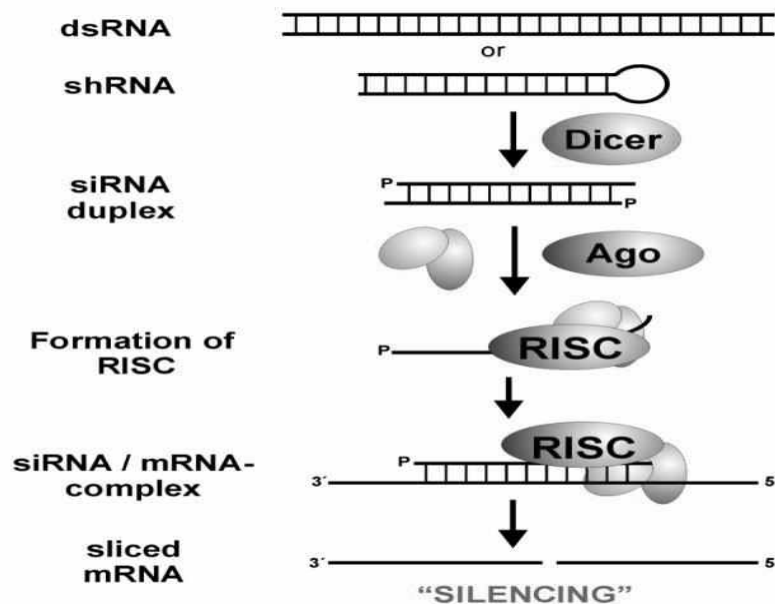
Molecular Mechanisms



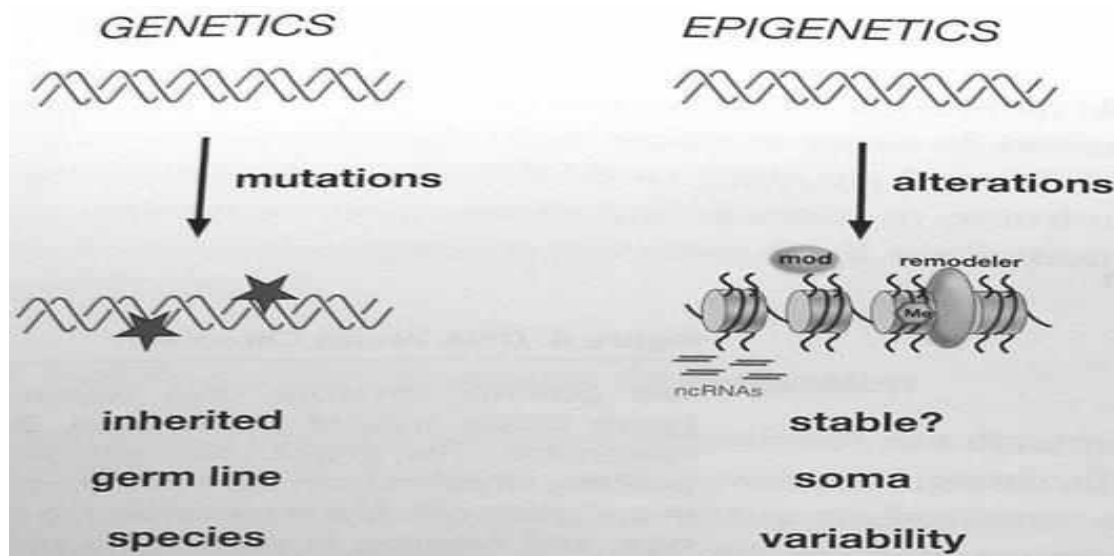
Histones modifications



Small interfering RNA – mechanism causing epigenetics A third mechanism involves expression of small interfering RNAs (siRNA).



Genetics vs Epigenetics



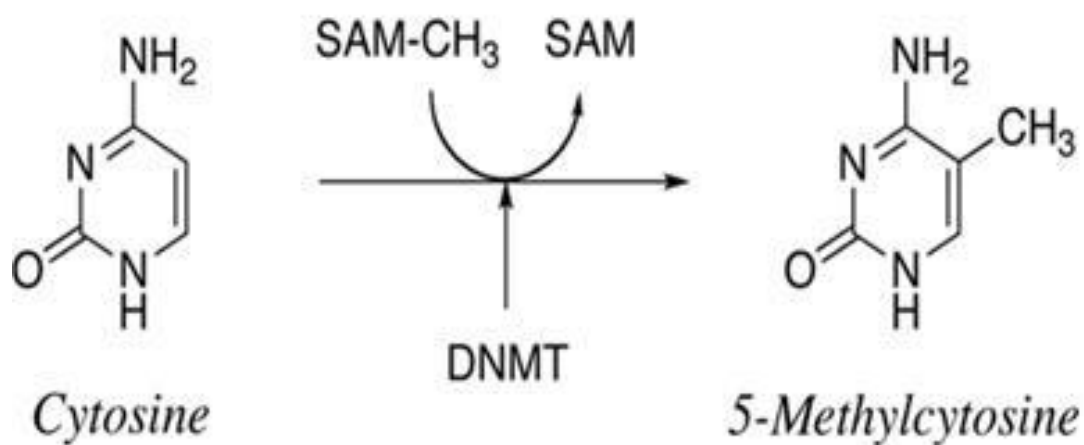
Epigenetics An epigenetic trait is a stable heritable phenotype resulting from changes in chromosome without alterations in the DNA sequence.

Lesson 44

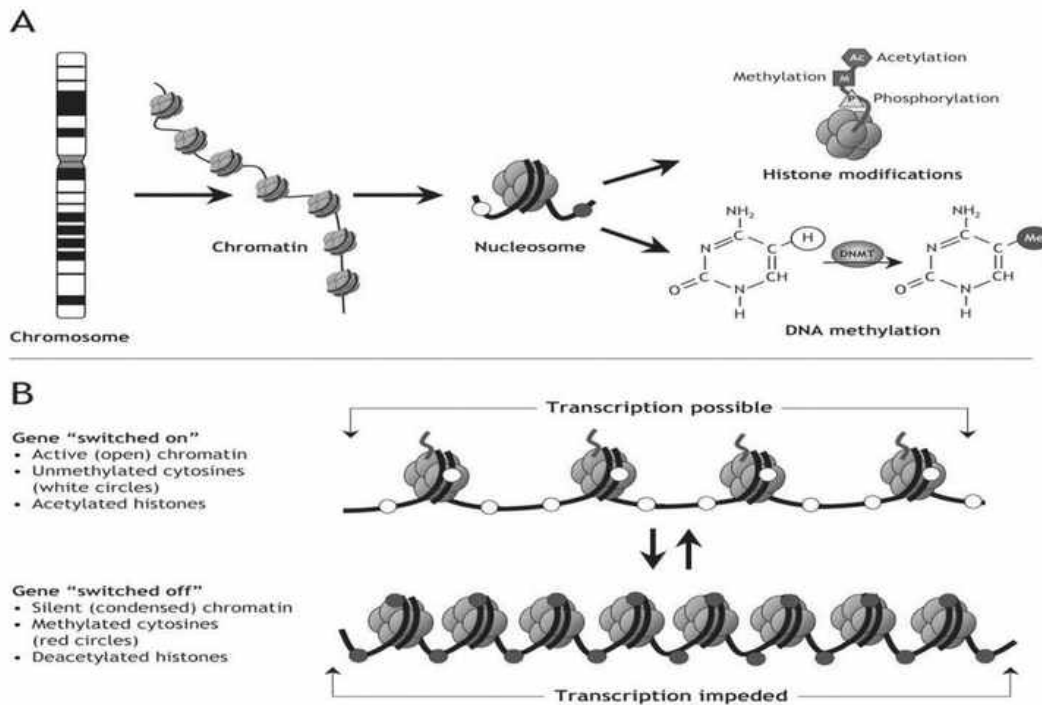
Epigenetic Modifications: Followings are the steps of epigenetics modifications

- Cytosine methylation
- Histones modification
- Non-coding RNAs (siRNAs)
- All above regulate gene expression.

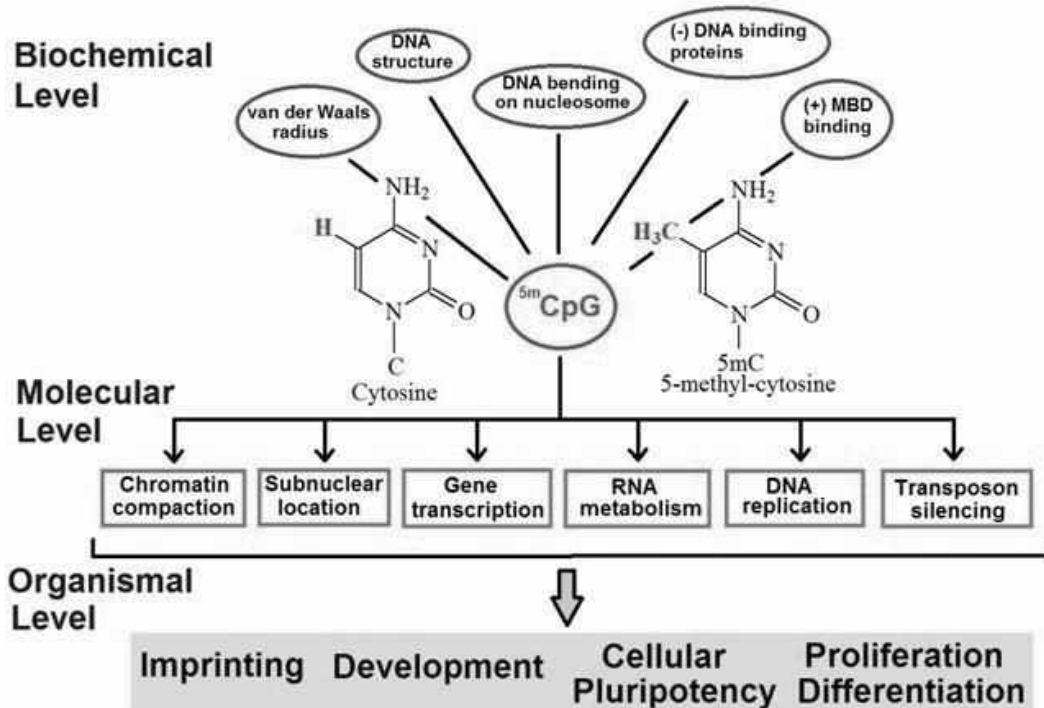
Cytosine Methylation – methyl transferase



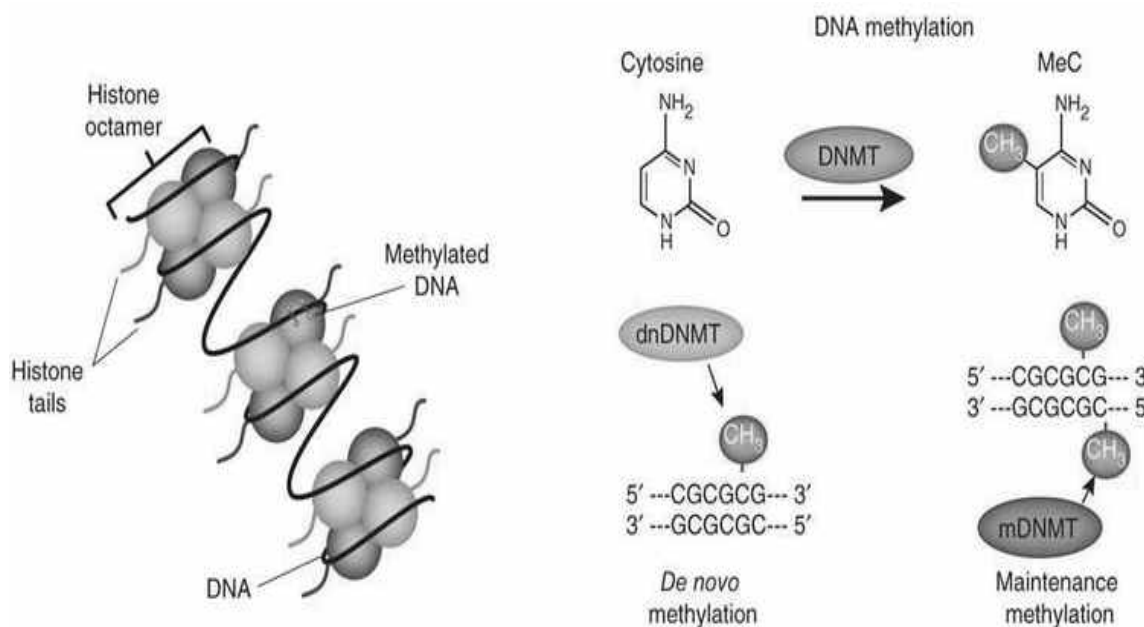
Genes-switched on & off



Methylated cytosine in cPg



Cytosine Methylation

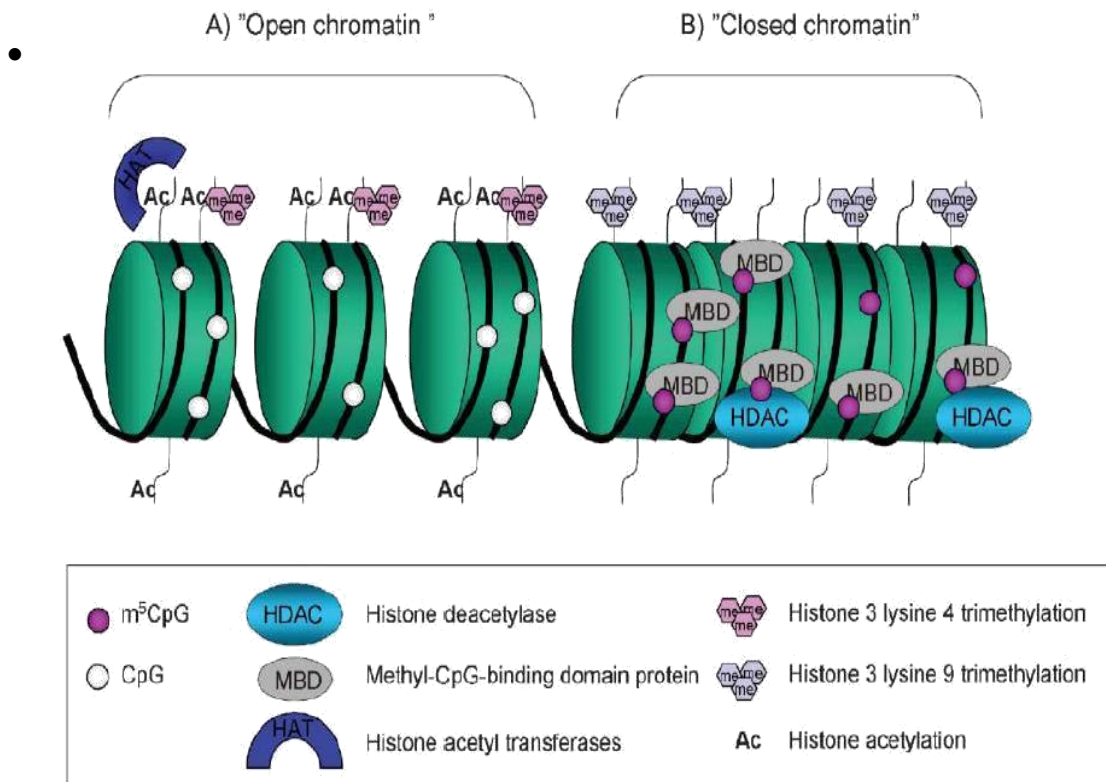


Cytosine Methylation occurs at upstream regions of genes Often located just upstream of genes (promoter regions). Associated with attenuation of expression of nearby genes.

Histones modifications Histones are the proteins that organize the genetic material. Have a high percentage of basic amino acids, which gives histones an overall positive charge, while DNA is negative charged.

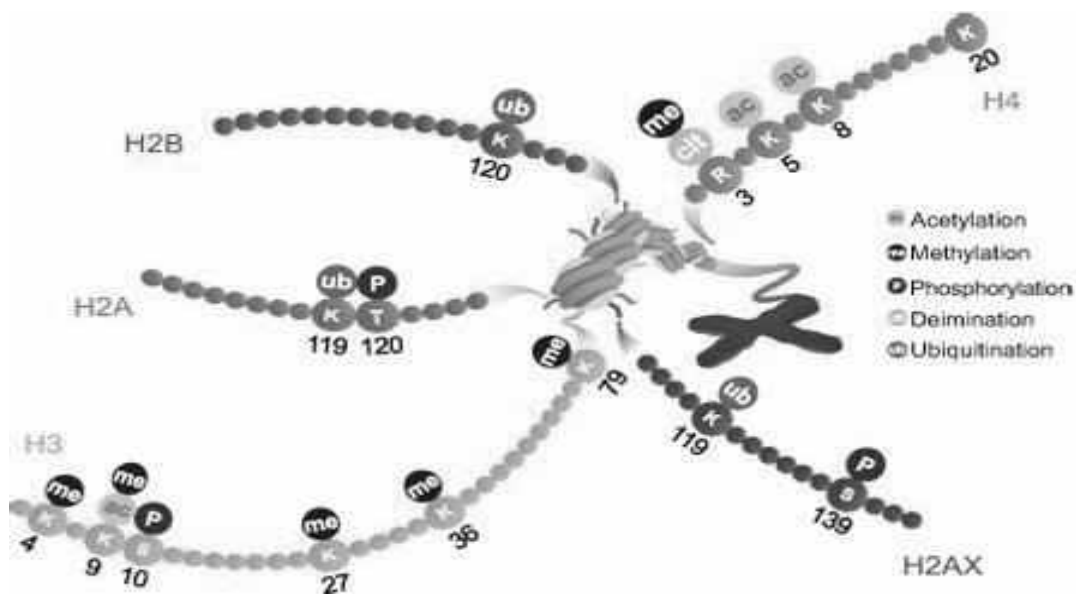
Acetylated Histones-genes are active when histones are acetylated, chromatin is open and genes are potentially active. When histones not tagged, deacetylated, the chromatin condenses and genes silenced.

Histones modifications



Most histones modifications occurs on the extended tails of histone proteins

Histones tails - acetylation



Histones acetylation two enzyme types involved in histone acetylation

HAT: Histone acetyltransferase

HDAC: Histone deacetylase.

Higher acetylation, higher gene expression Chromatin conformations changes to a form which is more open to transcription.

Acetylation = ↑ gene expression

Epigenetic modification - non coding RNA is a new mechanism for gene regulation. RNA which is not used for making proteins can be cleaved and used to inhibit protein-coding RNAs (siRNAs, microRNAs).

Three common types of modification

Cytosine methylation

Histones modifications

siRNAs

Lesson 45

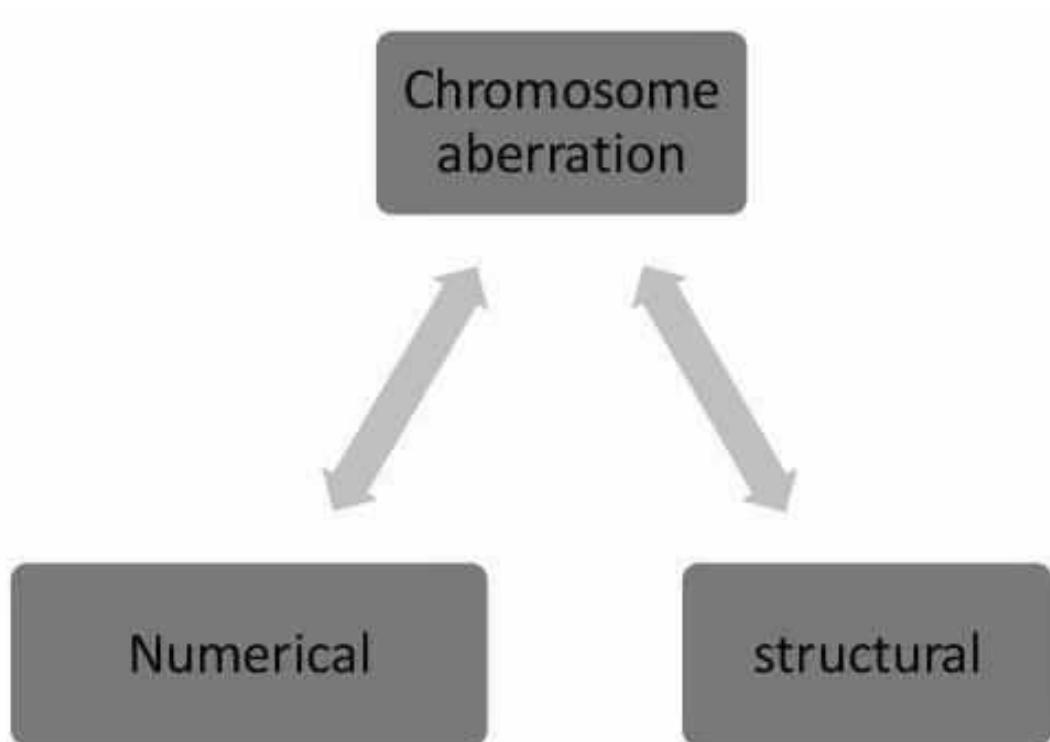
Chromosomal Aberrations: any change in normal number or structure of chromosomes. Affects individuals may be due altering the amounts of products of the genes involved. Altered amounts may cause anomalies directly or may alter the balance of genes

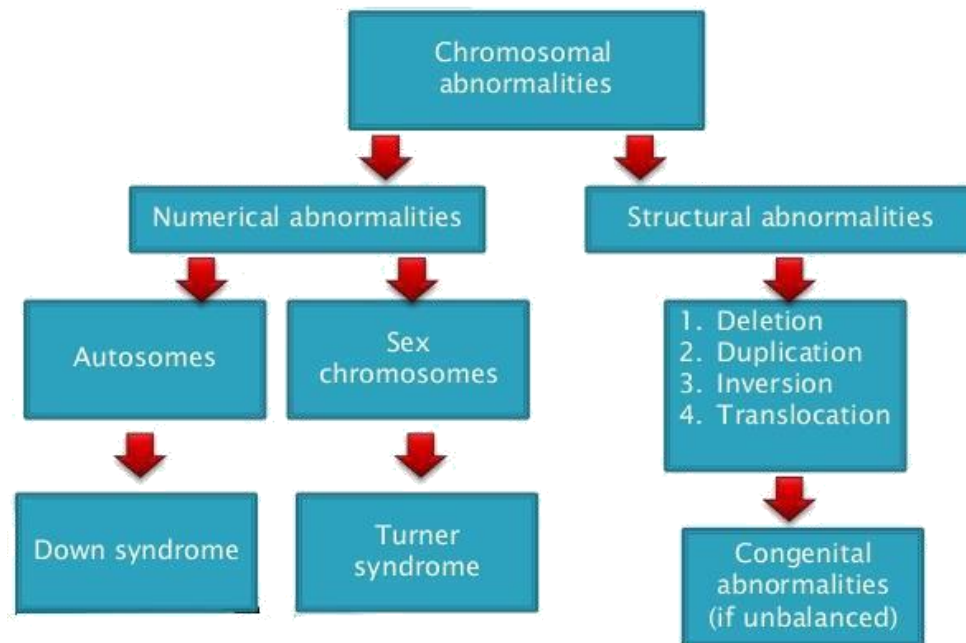
Classification

Numerical (usually due to de novo error in meiosis).

Structural (may be due to de novo error in meiosis or inherited).

Different cell lines (occurs post-zygotically).





Numerical changes

1. Aneuploidy

Hypoploidy

Hyperploidy

2. Euploidy

Monoploidy

Diploidy

Polyploidy

Structural

- Translocations
- Deletions
- Duplications
- Inversions

Different cell lines

Mosaicism

Lesson 46

Karyotyping- Nomenclature

Karyotype A normal male chromosome pattern would be described as: 46, XY.

46 = total number of chromosomes

XY = sex chromosome constitution

Description of anomaly any further description would refer to any abnormalities or variants found.

46,XY

47,XX,+21 Trisomy 21 (Down syndrome)

47,XXX Triple X syndrome

69,XXY Triploidy

45,XX,der(13;14)(p11;q11) Robertsonian translocation

46,XY,t(2;4)(p12;q12) Reciprocal translocation

46,XX,del(5)(p25) Deletion tip of chromosome 5

46,XX,dup(2)(p13p22) Duplication of part of short arm Chr 2

46,XY,inv(11)(p15q14) Pericentric inversion chromosome 11

46,XY,fra(X)(q27.3) Fragile X syndrome

46,XY/47,XXY Mosaicism normal/Klinefelter syndrome

47,XX,+21

47,XXX

69,XXY

45,XX,der(13;14)(q10;q10)

46,XY,t(2;4)(p12;q12)

46,XX,del(5)(p25)

46,XX,dup(2)(p13p22)

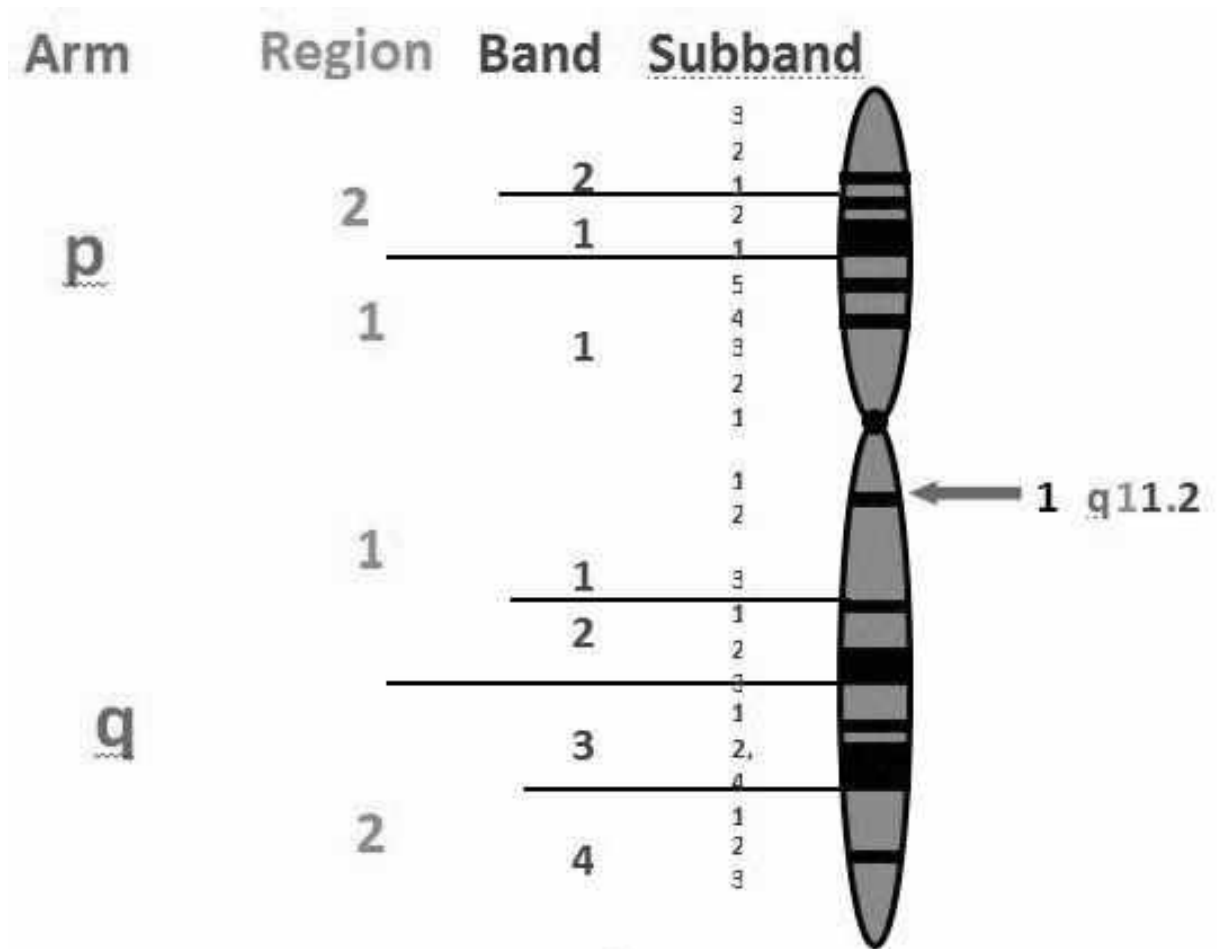
46,XY,inv(11)(p15q14)

46,XY,fra(X)(q27.3)

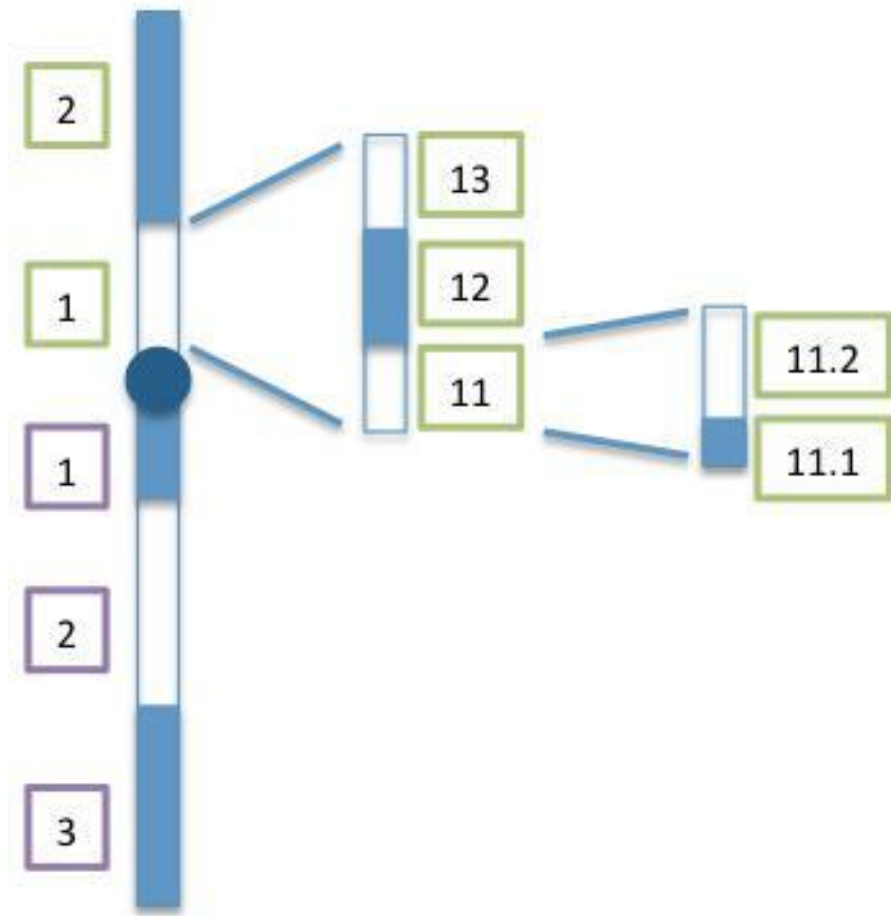
46,XY/47,XXY

Lesson 47

Defining chromosome regions



Bands within bands

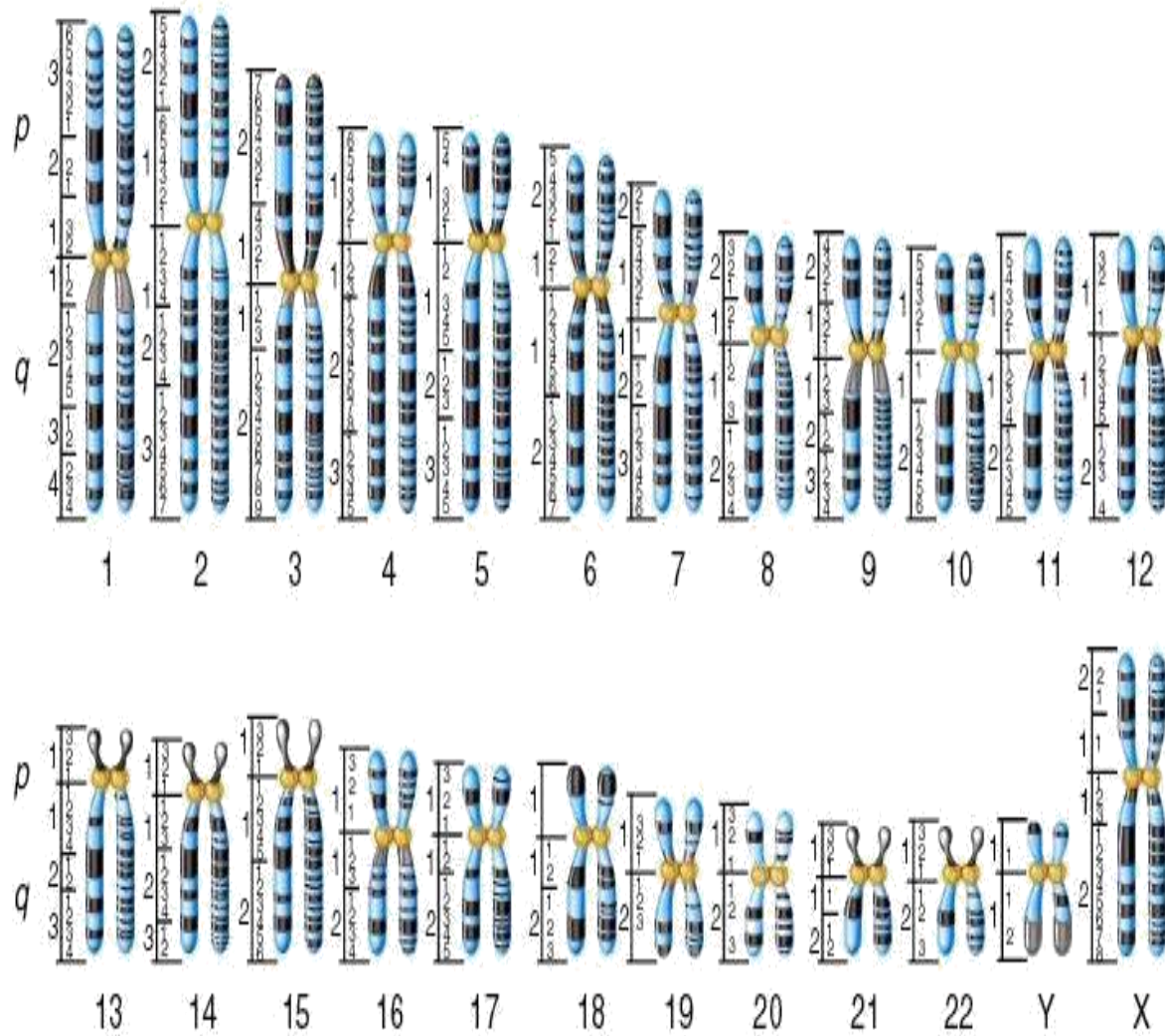


Chromosome identification Microscopic examination of chromosomes - Karyotype To identify and classify

Size

Location of the centromere

Banding patterns



Lesson 48

Common numerical abnormalities

Down syndrome (trisomy 21: 47,XX,+21)

Edwards syndrome (trisomy 18: 47,XX,+18)

Patau syndrome (trisomy 13: 47,XX+13)

Sex chromosome abnormalities

Turner syndrome 45,X

Klinefelter syndrome 47,XXY

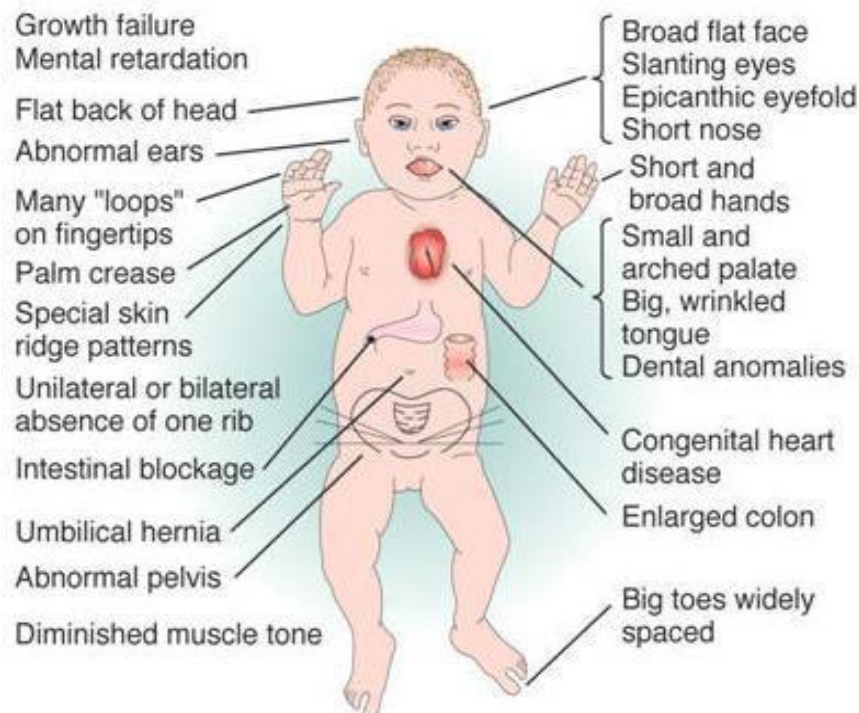
All chromosomes abnormalities

Triploidy (69 chromosomes)

Down syndrome this is a Trisomy 21 (47+21). The frequency of trisomy increases with increasing maternal age.

Sometimes, Robertsonian translocation involving chromosome 21

3-4 % not related to maternal age.



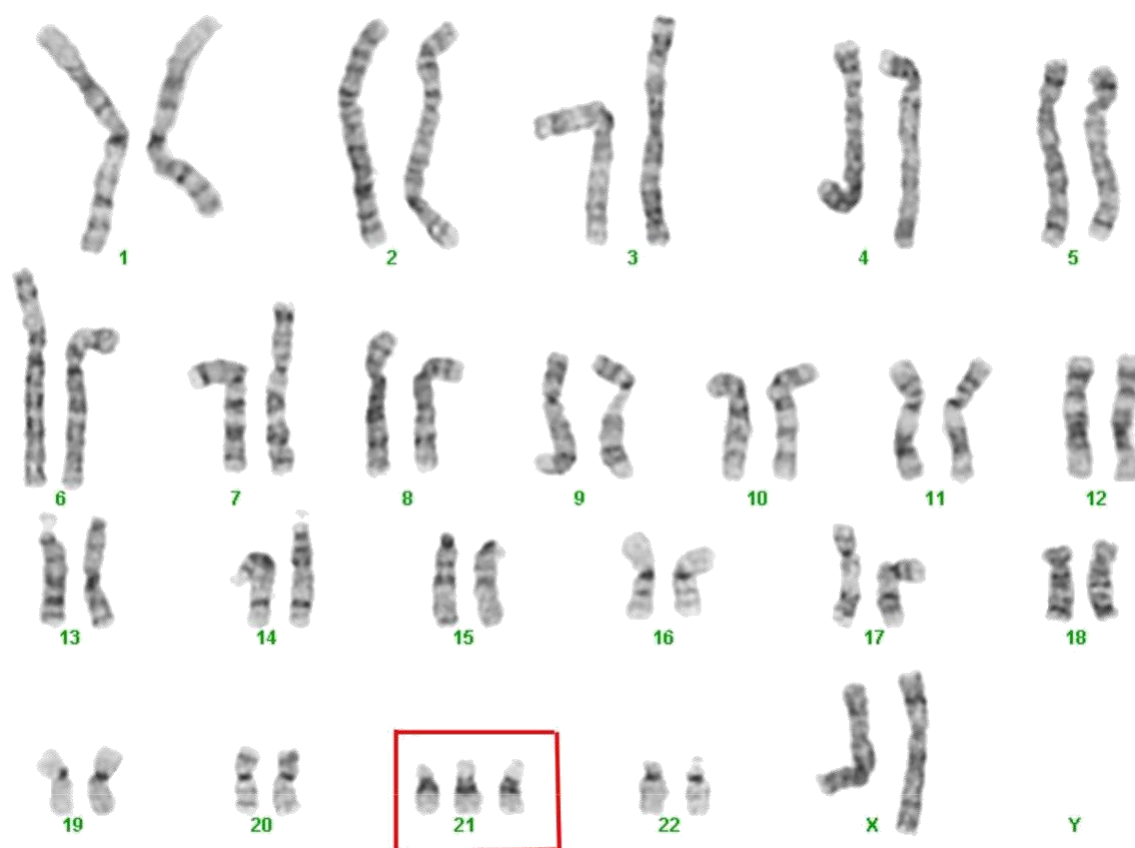
Down syndrome clinical features

Head and neck

- Brachycephaly
- Epicanthal folds
- Brushfield spots
- Flat nasal bridge
- Folded ears
- Open mouth
- Protruding tongue
- Short neck

Extremities

- Short fifth finger
- Short broad hands
- Incurved fifth finger
- Space between first and second toe
- Hyperflexibility of joints



Turner syndrome relatively common disorder caused by the loss of genetic material from one of the sex chromosomes.

Affects only females

Turner syndrome - clinical features

Short stature (143-145cm tall)

Loss of ovarian function

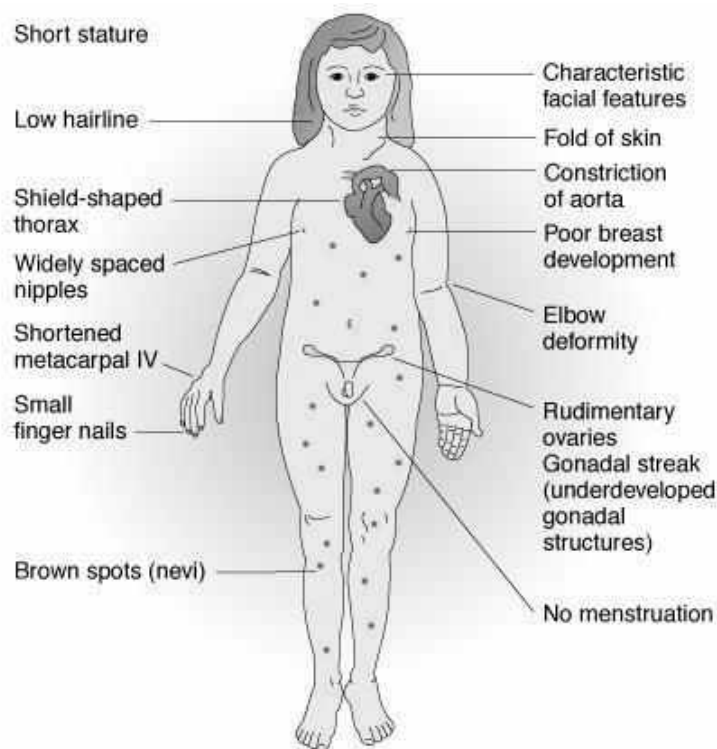
Hormone imbalances(thyroid, diabetes)

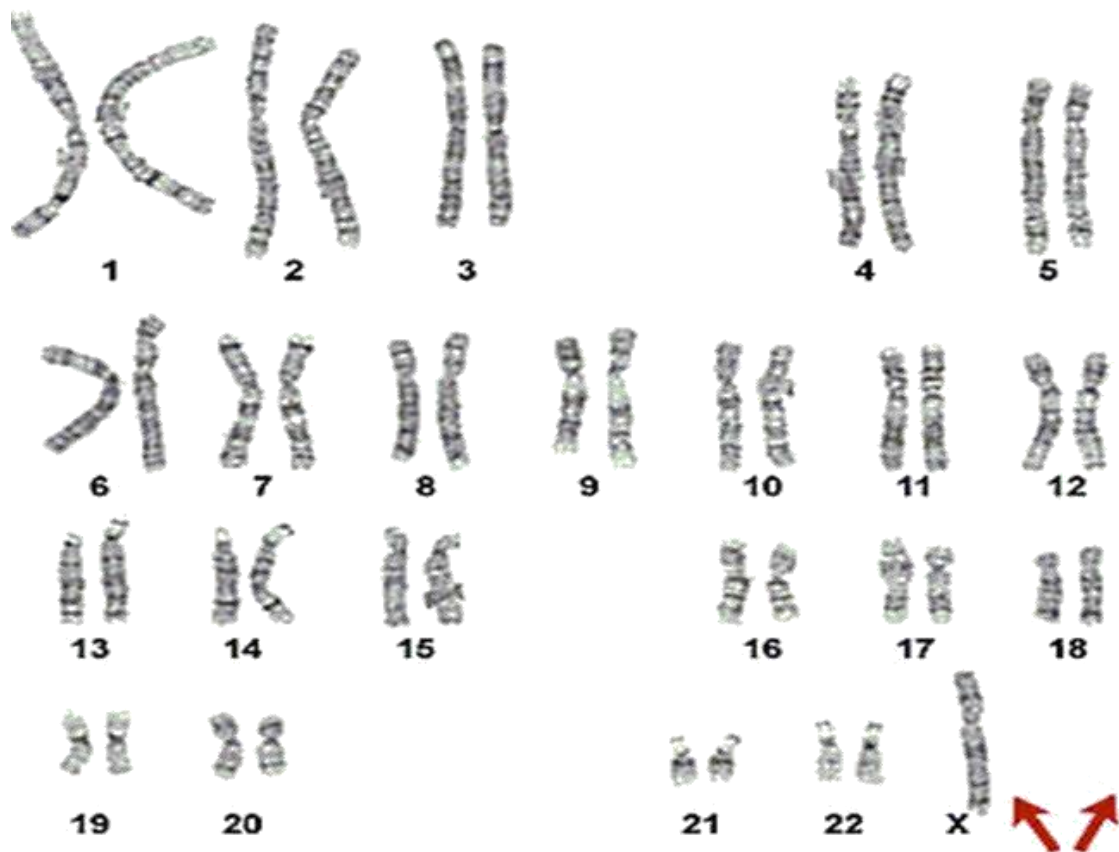
Stress and emotional deprivation

Diseases affecting the kidneys, heart, lungs or intestines

Bone diseases

Learning problems(esp. in math)





Although it is a genetic disorder, it is not usually hereditary.

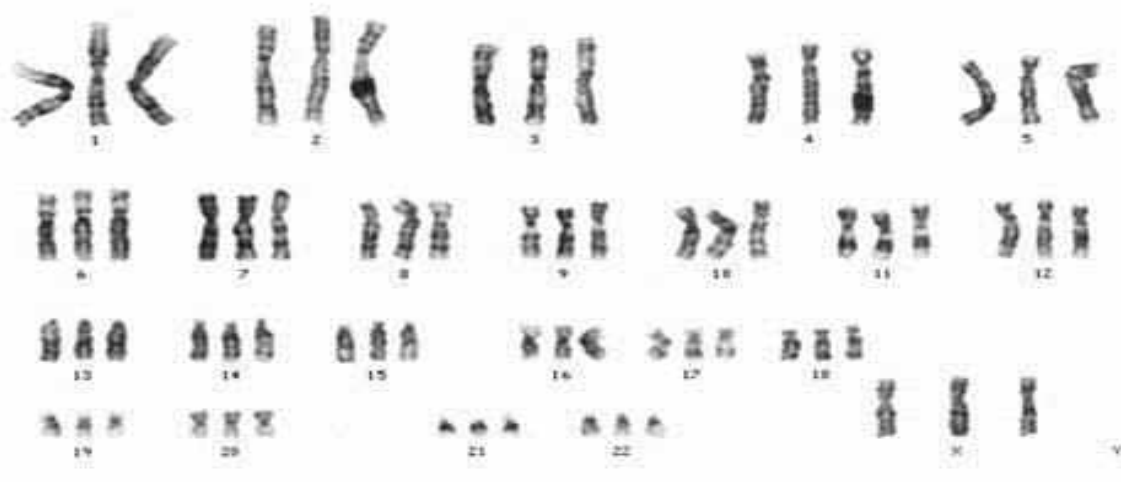
There are no known environmental causes of the syndrome.

Women with Turner Syndrome are usually infertile.

Triploidy- 69 chromosomes

Numerical abnormalities

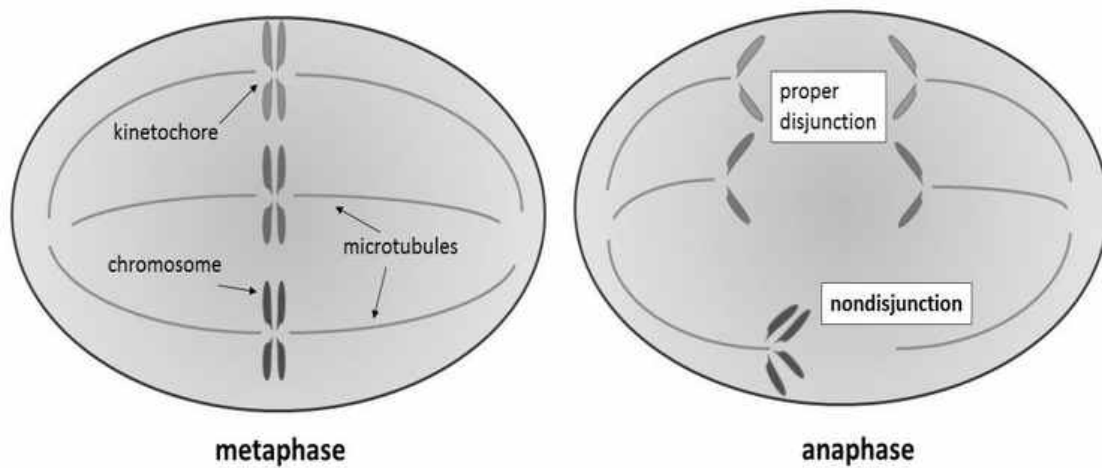
Due to chromosomes numbers.



Lesson 49

Non-disjunction:

When two homologous chromosomes or sister chromatids fail to separate during cell division, such a phenomenon is called as Non-disjunction



Types of Non-disjunction

Meiotic non-disjunction

Mitotic non-disjunction

Meiotic Non-disjunction If non-disjunction occurs during 1st meiotic division then all the sperms/ova derived from primary spermatocyte/oocytes will be abnormal.

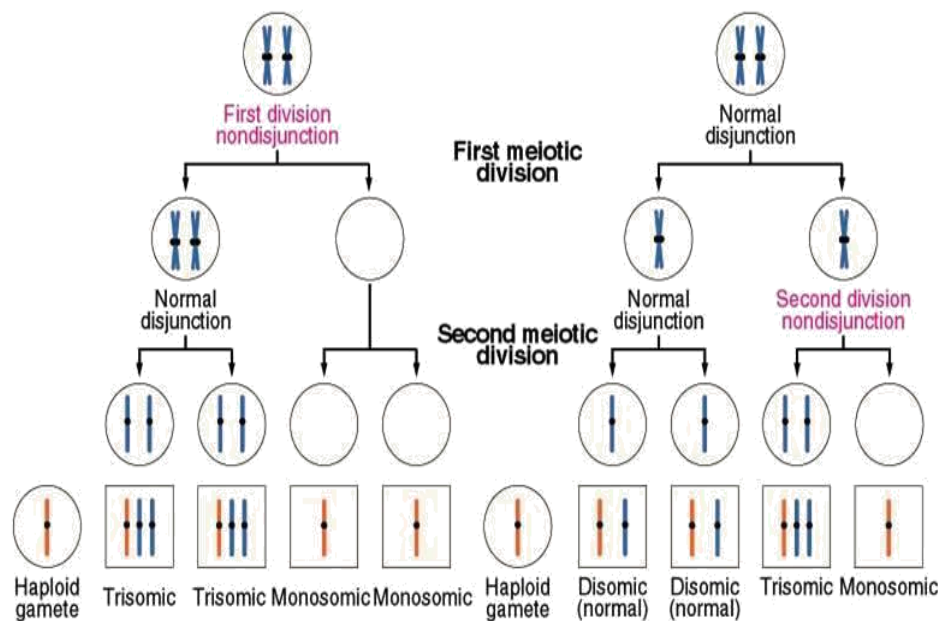
Failure of chromosomes separation

Failure of a pair of homologous chromosomes to separate in meiosis I.

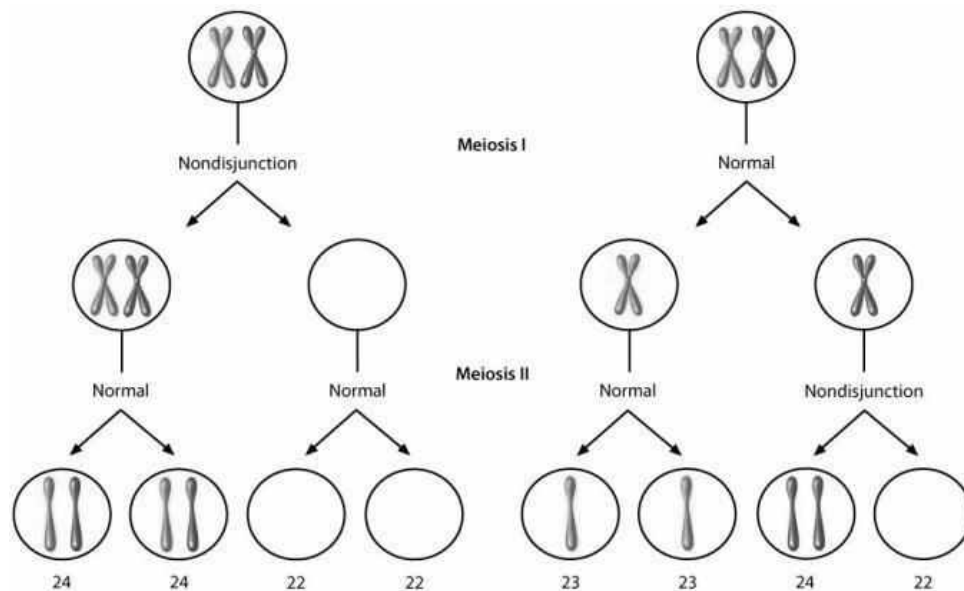
Failure of sister chromatids to separate during meiosis II.

Failure of sister chromatids to separate during mitosis.

Mitotic Non-disjunction Mitotic non-disjunction results in cells with different number of chromosomes. Breaking of the spindle fibers during metaphase or anaphase. If spindle fibers do not form for one of the chromosomes, then during anaphase it will not separate into two chromatids and one cell will have an extra chromatid and the other will be lacking one. Mitotic nondisjunction causes trisomic and monosomic daughter cells to be formed.



Cell with 46 chromosomes



Causes of non-disjunction

Aging effect on primary oocyte

Radiation

Delayed fertilization after ovulation

Lesson 50

Trisomy is a type of polysomy in which there are three copies of a particular chromosome, instead of the normal two. Trisomy is a type of aneuploidy (an abnormal number of chromosomes).

Trisomy -Autosomes and sex chromosome

Autosomal trisomy

Sex-chromosome trisomy

Trisomy of chromosome 21, which is found in Down syndrome, is called trisomy 21.

Trisomy Types

Primary trisomy - an entire extra chromosome has been copied.

Partial trisomy - an extra copy of part of a chromosome.

Secondary trisomy - the extra chromosome has duplicated arms.

Tertiary trisomy - extra chromosome is made up of copies of arms from two other chromosomes.

Common trisomy in humans

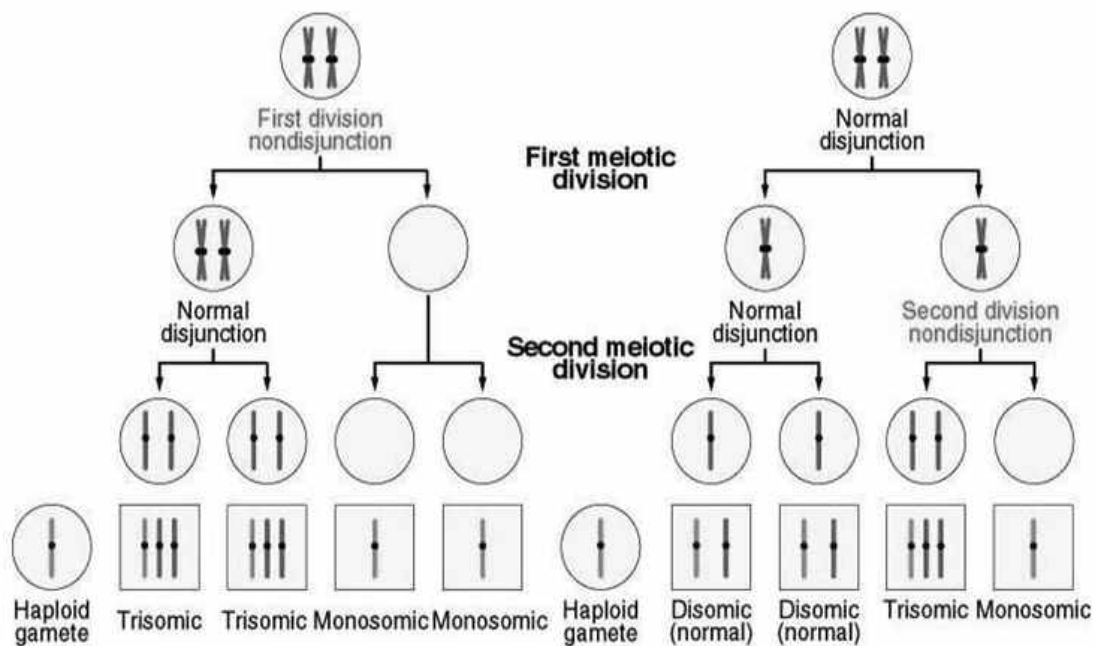
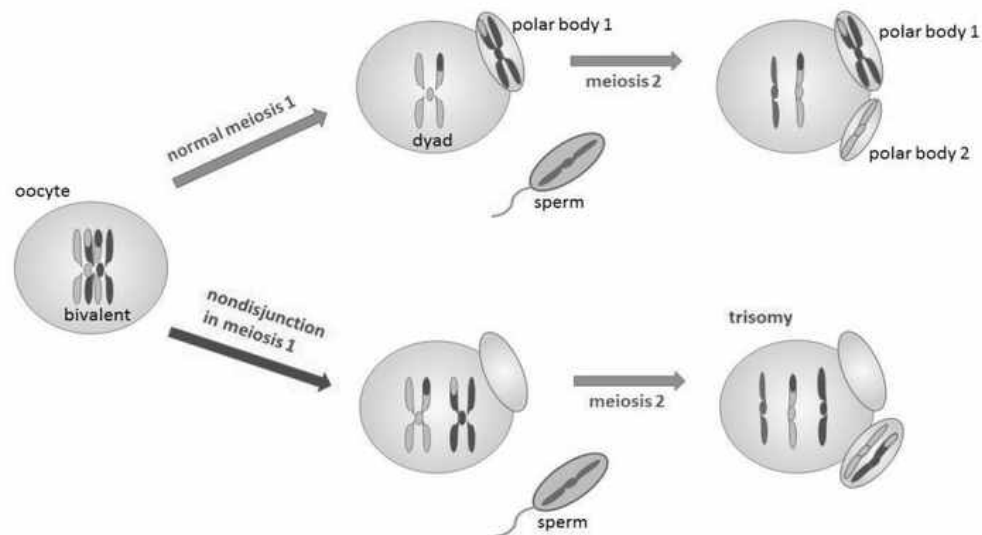
Trisomy 21

Trisomy 18

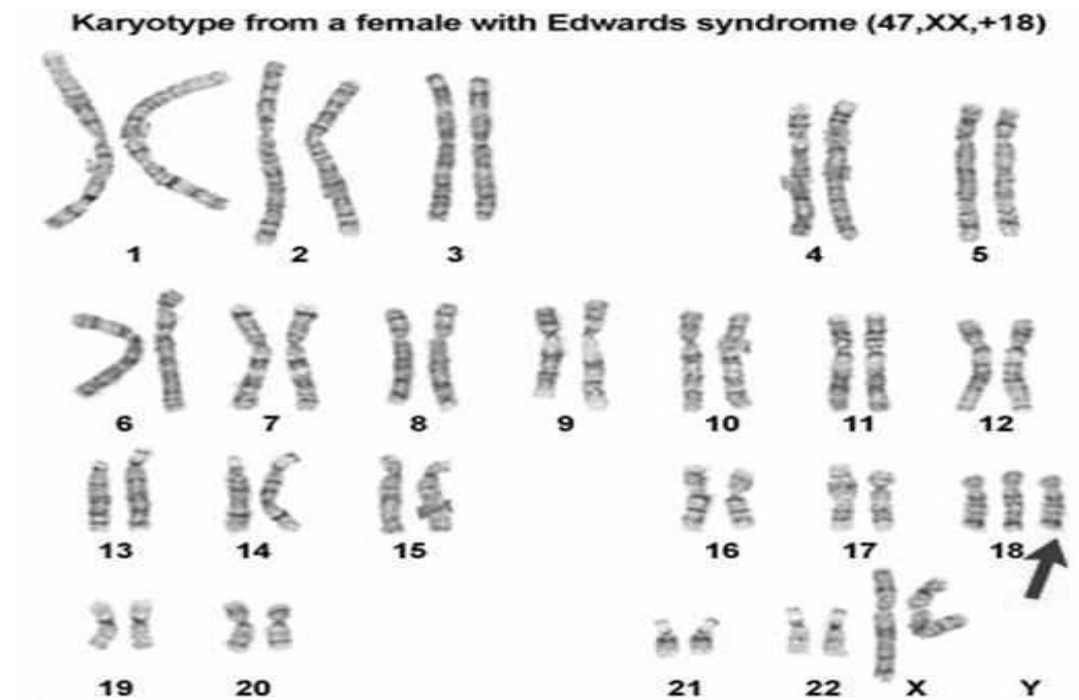
Trisomy 13

Klinefelter's syndrome (47 XXY)

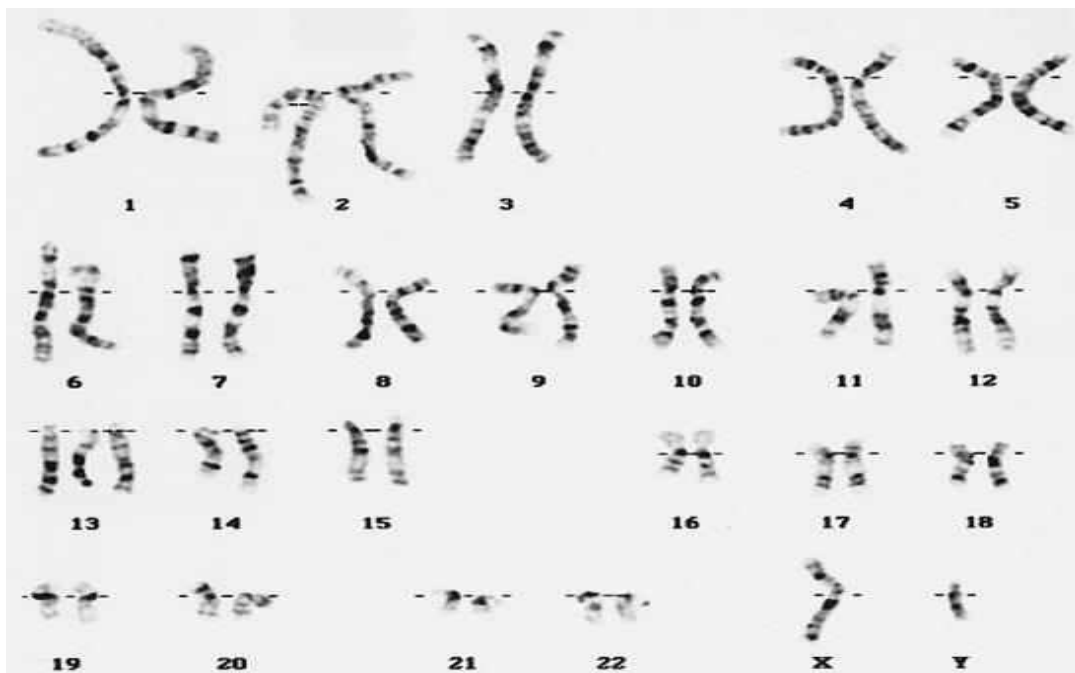
Trisomy 21 Down syndrome Trisomy 21 1 in 700 live births Associated with increased maternal age



Trisomy 18 Edwards' syndrome



Trisomy 13 Patau's syndrome



Trisomy is a type of polysomy in which there are three copies of a particular chromosome, instead of the normal two.

