



Cytogenetic

10th lecture

Another Type of Inheritance

OBJECTIVES



→ Introduction

→ Another Type of Inheritance



Introduction

Another type of inheritance refers to **Mendel's Laws exception (non Mendelian pattern of inheritance)**.

Non-Mendelian inheritance is any pattern of inheritance in which traits do not segregate in accordance with Mendel's laws.

These laws describe the inheritance of traits linked to single genes on chromosomes in the nucleus. In Mendelian inheritance, each parent contributes one of two possible alleles for a trait. If the genotypes of both parents in a genetic cross are known, Mendel's laws can be used to determine the distribution of phenotypes expected for the population of offspring.



Introduction

There are several situations in which the proportions of phenotypes observed in the progeny do not match the predicted values.

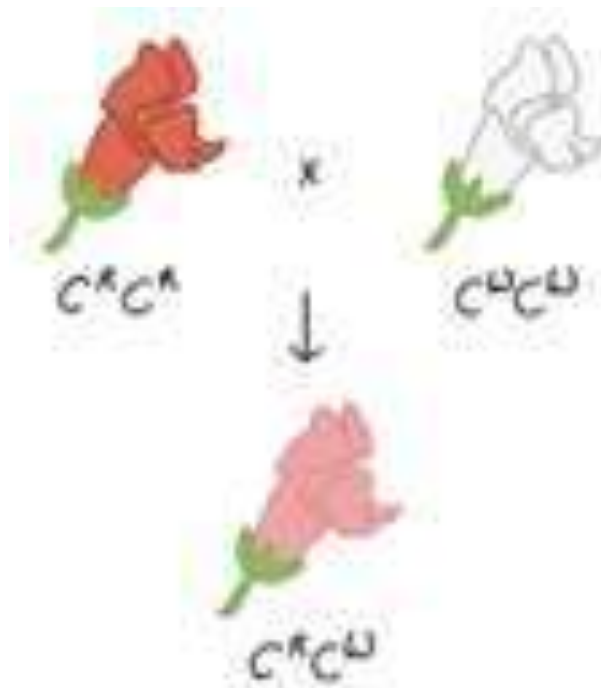
Nevertheless, Mendel's laws are very important for genetics and still applying . In the field of health, Mendel's laws are fulfilled in what is know as monogenic or Mendelian diseases - cystic fibrosis, color blindness.

Non-Mendelian inheritance plays a role in several disease processes.

Another Type of Inheritance

Today many phenomena are known that are not **governed by Mendel's laws**, among them are:-

1. **Intermediate dominance (incomplete dominance)**, there is no dominant allele or recessive allele. In heterozygous individuals the features corresponding to the two alleles are mixed. An example of intermediate dominance is carnation color. When we cross a red carnation (C^R) with a white carnation (C^W), the offspring are mix of the both parent colors.



Another Type of Inheritance

2. **Codominance**, in the heterozygous state there is no recessive allele, but both behave as dominant, such as in intermediate inheritance, but unlike the latter, both features are manifested without mixing. An example of codominance is the color of begonias or the ABO system. Begonia plant with two different colors do not mix and present simultaneously. Both alleles are being expressed in the heterozygote individual.

Gametes	R	R
W	RW	RW
W	RW	RW



Another Type of Inheritance

3. **New character**, it is possible that F1 individuals present a new phenotype that is not the result of an intermediate character between both parents. It means the appearance of a new character, as occurs for example in the Coleus plant.



4. **New mutations with a dominant effect**, sometimes a new allele with a dominant effect appears, breaking the dominance pattern that was known. Suppose we have an **A** (dominant) allele and **a** (recessive) allele for one locus. It is possible that at a certain moment in time a mutation **de novo** appears, causing a new allele **a** that dominates the allele **A** (previously dominant).

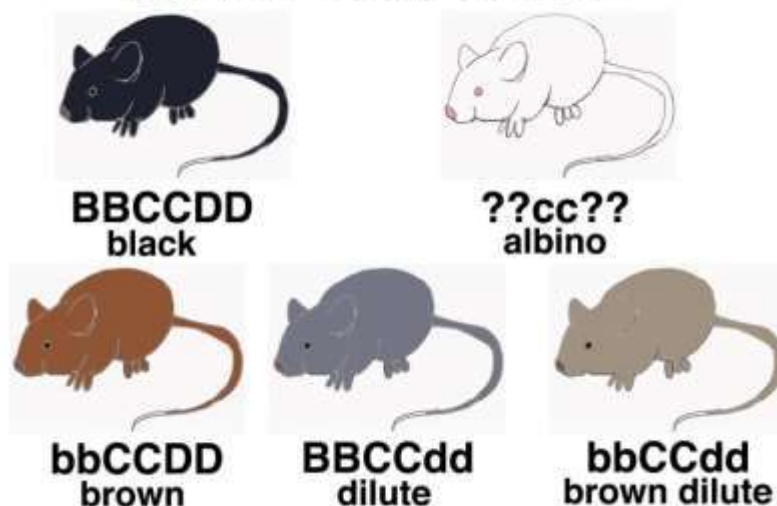
Another Type of Inheritance

5. **Epistasia**, phenomenon that involves the interaction between **different genes** when expressing a certain phenotypic character.

In other words, the expression of one or more genes depends on the expression of another gene. There is a gene - gene interaction when determining the phenotype of the individual.

For instance, animals that have the gene to produce **black pigmentation** will only be expressed black phenotype, if there is lack of the albinism mutation. In case they present the albinism gene mutation, the pigmentation gene will be masked by the albinism gene.

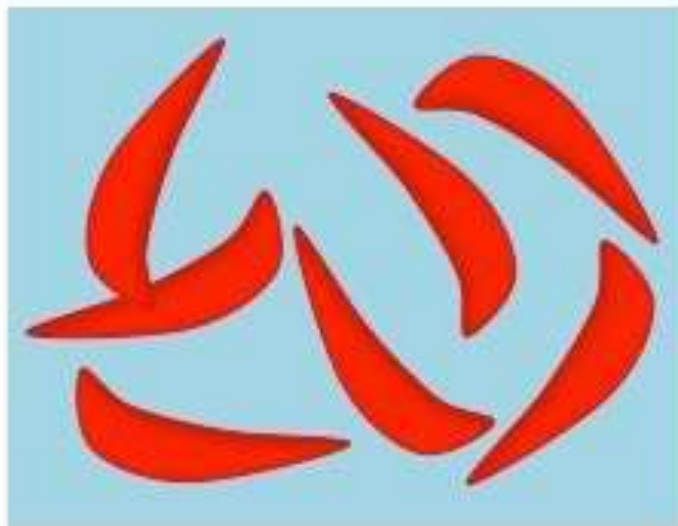
Mouse Coat Colors



Another Type of Inheritance

6. **Pleiotropy**, a single gene is responsible for various phenotypes that are not related to each other.

For instance, the gene mutation that causes sickle cell anemia affects red blood cells and also confers some resistance to malaria.



aa

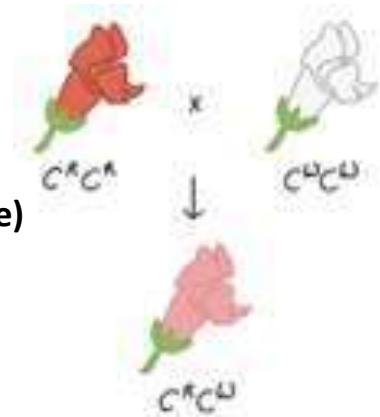
Resistant to malaria
but has fatal sickle cell disease



KEY POINTS

Non-Mendelian inheritance is any pattern of inheritance in which traits do not segregate in accordance with Mendel's laws.

1. Intermediate dominance (incomplete dominance)



2. Codominance



3. New character

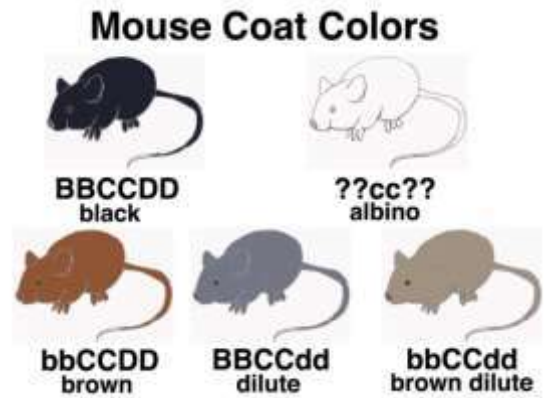




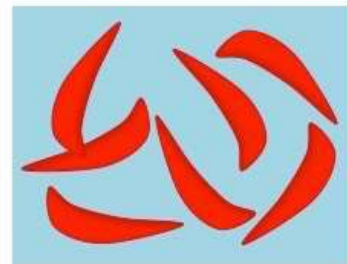
KEY POINTS

4. New mutations with a dominant effect

5. Epistasis



6. Pleiotropy



aa
Resistant to malaria
but has fatal sickle cell disease



Lecture 10 Questions Practice

Q1:- Define the followings:

- a. Non-Mendelian inheritance.
- b. Pleiotropy.

Q2:- Enumerate the followings:

- a. Enumerate the Non-Mendelian inheritance.

Q3:- MCQ

- 1. ----- in the heterozygous state there is no recessive allele, but both behave as dominant, such as in intermediate inheritance, but unlike the latter, both features are manifested without mixing.
 - a. Co-dominance.
 - b. New character.
 - c. New mutations with a dominant effect.
 - d. Epistasia.
 - e. Pleiotropy.



Cytogenetic

9th lecture

Dominant & Recessive Inheritance

OBJECTIVES



→ Dominant Inheritance

→ Recessive Inheritance

→ Types of Inheritance



Dominant Inheritance

Dominant allele is a type of allele whose trait always shows up in an individual phenotype when the allele present.

If the alleles of a gene are different, one allele will be expressed, that is the dominant gene. The effect of the other allele, called recessive, is masked.

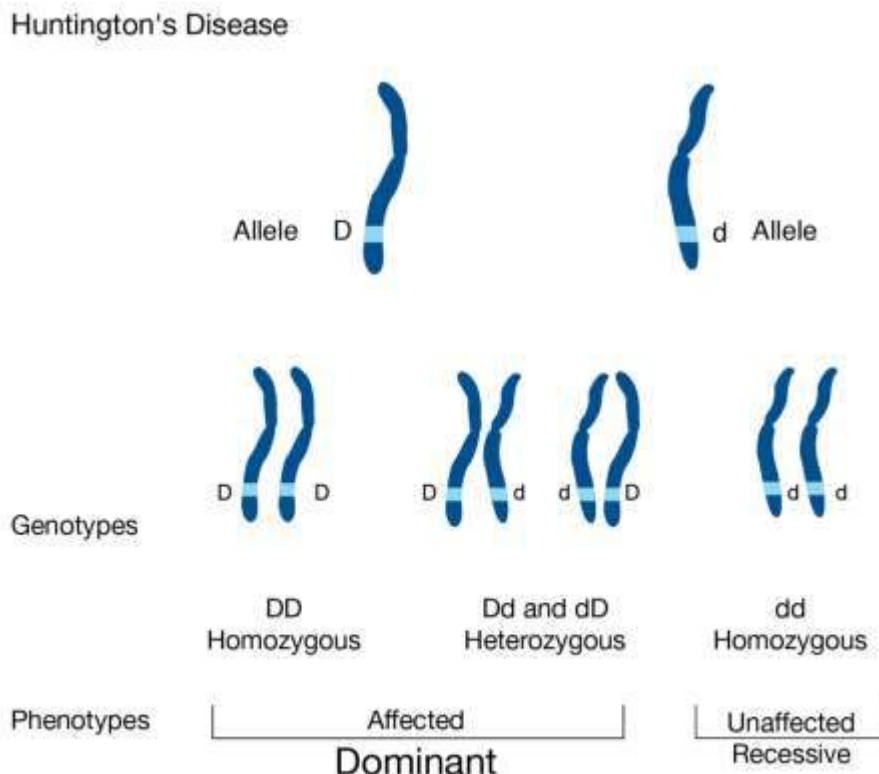
A dominant gene, or a dominant version of a gene, is a particular variant of a gene, which for a **variety of reasons, expresses itself more strongly all by itself** than any other version of the gene which the person is carrying, and, in this case, the recessive.

Biochemically, the **dominant alleles can induce a function in a cell**, which is either **beneficial** or **detrimental**, that the other version of the gene (**recessive alleles**) can't cover up or compensate for.

Dominant Inheritance

A **dominant mutation** can be **benign** (it can refer to eye color) or it can refer to a **disease** (Huntington's disease).

Huntington's disease is a **dominant mutation**. Where, if a person is carrying that version of the Huntington gene (**DD, Dd, dD**), will give that individual the disease regardless of what that person's other Huntington's disease gene allele is.





Recessive Inheritance

Recessive allele is a type of allele which will not be manifested in an individual phenotype unless both of the individual's copies of that gene have that particular genotype.

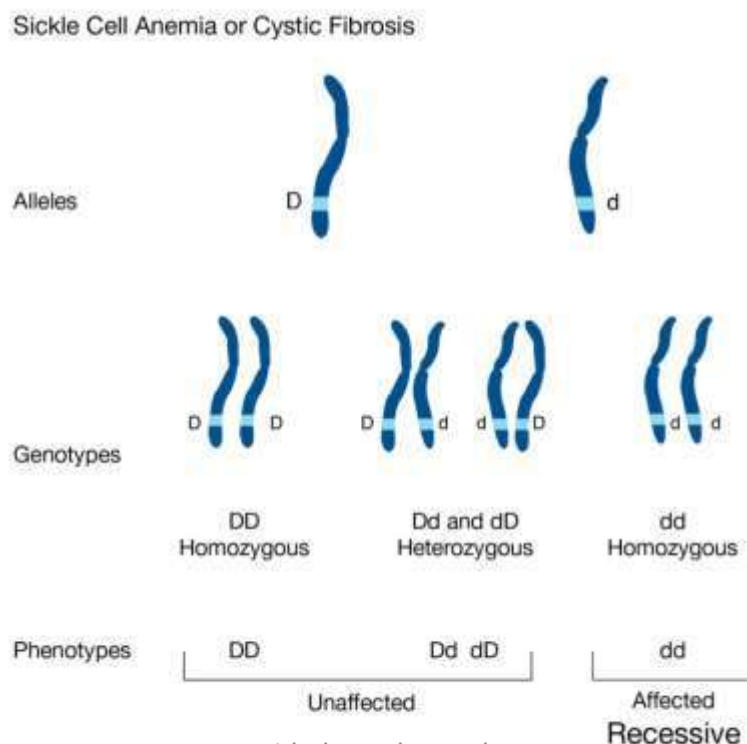
Individuals receive one version of a gene, called an allele, from each parent. If the alleles are different, the dominant allele will be expressed, while the effect of the other allele, called recessive, is **masked**.

In the case of a **recessive genetic disorder**, an individual **must inherit two copies of the mutated allele in order for the disease to be present**.

Recessive Inheritance

A **recessive mutation** can be **benign** (it can refer to eye color) or it can refer to a **disease or loss of function** (Sickle Cell Anemia, Cystic Fibrosis).

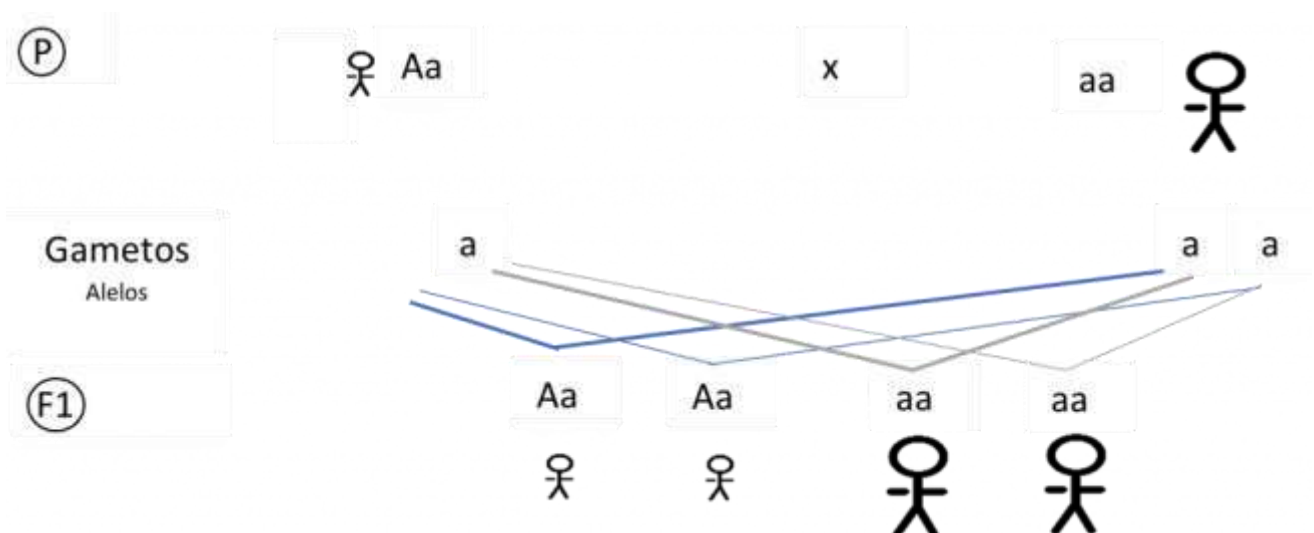
Cystic fibrosis is a disease exists only when there's a malfunction of **both alleles (dd)** that correspond to cystic fibrosis. If there is only one mutation (**occurs in one allele Dd or dD**), then that recessive mutation can be **compensated for** by the **normal allele**.



Types of Inheritance

1. **Autosomal dominant inheritance (AD):** this type of inheritance affects autosomal chromosomes, and the phenotype will be determined by the dominant allele.

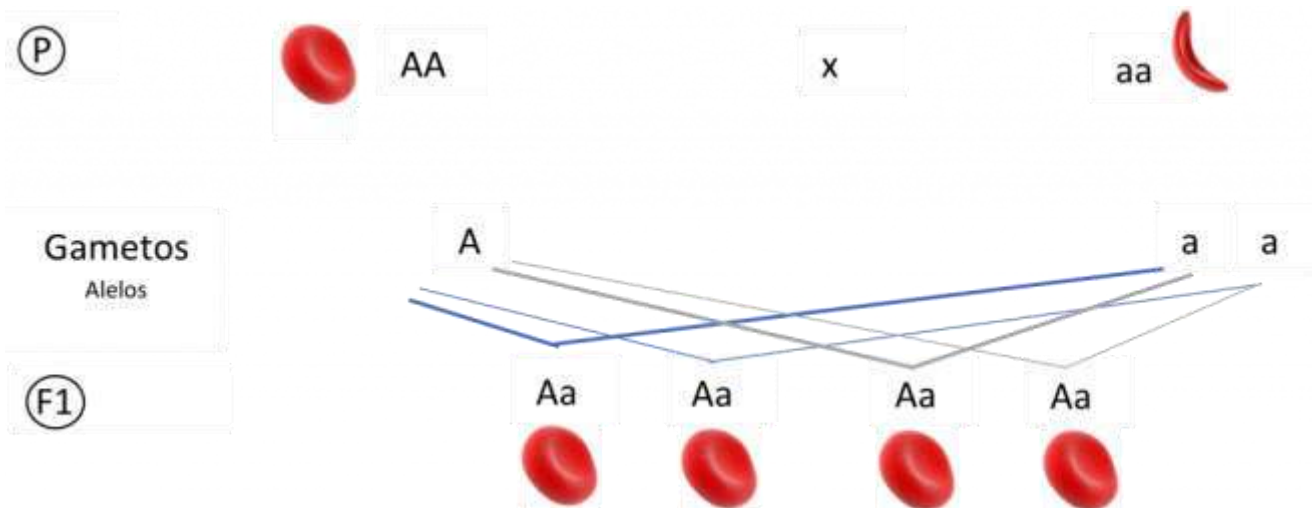
A dominant allele is one that predominates over other whether we have one copy (heterozygous) or two dominant (homozygous). An example of AD inheritance is **Achondroplasia**, the most common form of dwarfism as shown in the illustration below.



Types of Inheritance

2. **Autosomal recessive inheritance (AR):** this type of inheritance affects autosomal chromosomes. In this case, we will need two copies of the allele associated with the disease for the individual to present a disease phenotype.

An example of a disease that follow this pattern is sickle cell anemia - alteration of red blood cells as shown in the illustration below.

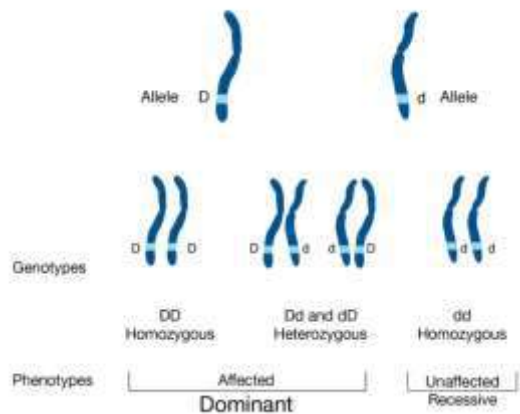




KEY POINTS

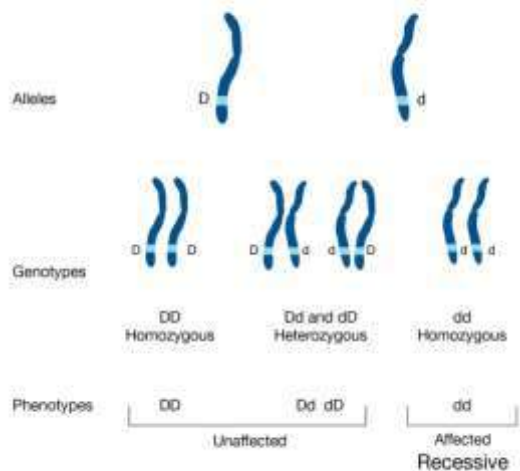
Dominant allele is a type of allele whose trait always shows up in an individual phenotype when the allele is present.

Huntington's Disease



Recessive allele is a type of allele which will not be manifested in an individual phenotype unless both of the individual's copies of that gene have that particular genotype.

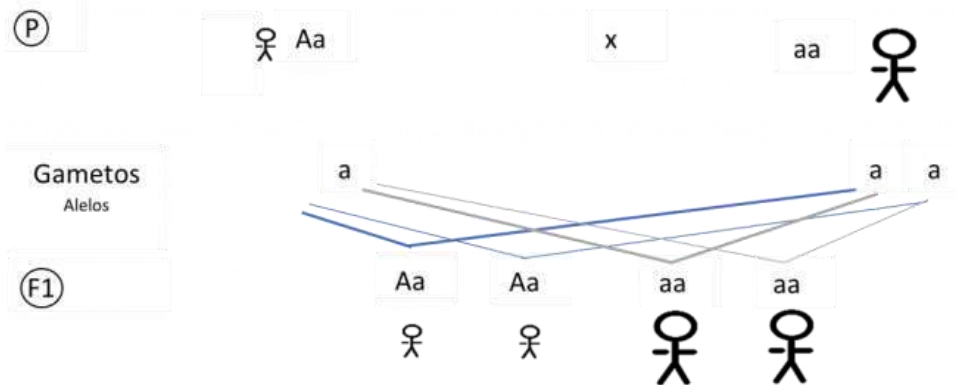
Sickle Cell Anemia or Cystic Fibrosis



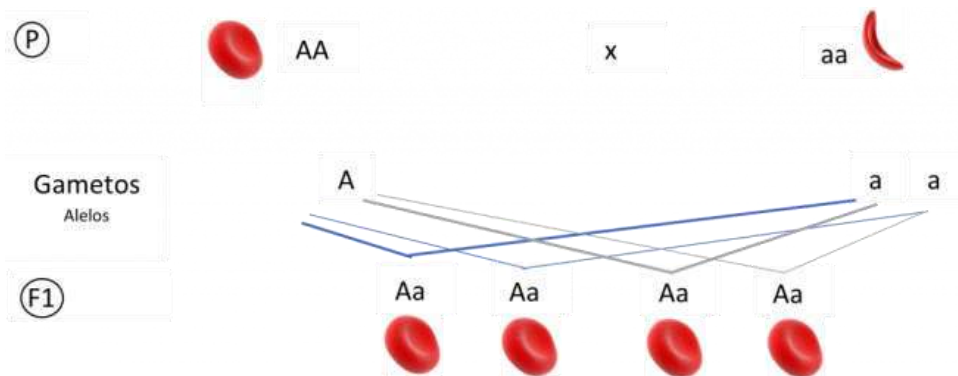


KEY POINTS

1. **Autosomal dominant inheritance (AD):** this type of inheritance affects autosomal chromosomes, and the phenotype will be determined by the dominant allele.



2. **Autosomal recessive inheritance (AR):** this type of inheritance affects autosomal chromosomes. In this case, we will need two copies of the allele associated with the disease for the individual to present a disease phenotype.





Lecture 9 Questions Practice

Q1:- Define the followings:

- a. Recessive alleles.
- b. Autosomal dominant inheritance.

Q2:- MCQ

1. Biochemically, the dominant alleles can induce a function in a cell, which is either?
 - a. Beneficial.
 - b. Beneficial or detrimental.
 - c. Detrimental.
 - d. Nor beneficial neither detrimental.

2. Huntington's disease is a dominant mutation. Where, if a person is carrying that version of the Huntington gene -----, will give that individual the disease regardless of what that person's other Huntington's disease gene allele is.
 - a. DD.
 - b. Dd.
 - c. dD.
 - d. All the answers.



Cytogenetic

8th lecture

Pattern of Inheritance Mendel's Laws

OBJECTIVES



- Law of dominance and uniformity
- Law of segregation
- Law of independent assortment



Mendel's Law of Dominance and Uniformity

Law of dominance and uniformity

Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.

Alleles Can Be Dominant or Recessive

Most familiar animals and some plants have paired chromosomes and are described as diploid. They have two versions of each chromosome, one contributed by the female parent in her ovum and one by the male parent in his sperm. These are joined at fertilization. The ovum and sperm cells (the gametes) have only one copy of each chromosome and are described as haploid.

Mendel's law of dominance states that in a heterozygote, one trait will conceal the presence of another trait for the same characteristic. Rather than both alleles contributing to a phenotype, the dominant allele will be expressed exclusively.



Mendel's Law of Dominance and Uniformity

The recessive allele will remain “latent,” but will be transmitted to offspring by the same manner in which the dominant allele is transmitted. The recessive trait will only be expressed by offspring that have two copies of this allele. These offspring will breed true when self-crossed.

If a genetic trait is recessive, a person needs to inherit two copies of the gene for the trait to be expressed. Thus, both parents have to be carriers of a recessive trait in order for a child to express that trait.

Since Mendel's experiments with pea plants, other researchers have found that the law of dominance does not always hold true. Instead, several different patterns of inheritance have been found to exist.



Mendel's Law of Segregation

Law of segregation

During gamete formation, the alleles for each gene segregate from each other so that each gamete carries only one allele for each gene.

The law of segregation states that each individual that is a diploid has a pair of alleles (copy) for a particular trait. Each parent passes an allele at random to their offspring resulting in a diploid organism. The allele that contains the dominant trait determines the phenotype of the offspring. In essence, the law states that copies of genes separate or segregate so that each gamete receives only one allele.



Mendel's Law of Segregation

The physical basis of Mendel's law of segregation is the first division of meiosis in which the homologous chromosomes with their different versions of each gene are segregated into daughter nuclei. The behavior of homologous chromosomes during meiosis can account for the segregation of the alleles at each genetic locus to different gametes. As chromosomes separate into different gametes during meiosis, the two different alleles for a particular gene also segregate so that each gamete acquires one of the two alleles.

In Mendel's experiments, the segregation and the independent assortment during meiosis in the F1 generation give rise to the F2 phenotypic ratios observed by Mendel. The role of the meiotic segregation of chromosomes in sexual reproduction was not understood by the scientific community during Mendel's lifetime.



Mendel's Law of Independent Assortment

Law of independent assortment

Genes of different traits can segregate independently during the formation of gametes.

Mendel's law of independent assortment states that genes do not influence each other with regard to the sorting of alleles into gametes. Since, every possible combination of alleles for every gene is equally likely to occur.

The independent assortment of genes can be illustrated by the dihybrid cross. A cross between two true-breeding parents that express different traits for two characteristics. Consider the characteristics of seed color and seed texture for two pea plants: one that has green, wrinkled seeds (yyrr) and another that has yellow, round seeds (YYRR).



Mendel's Law of Independent Assortment

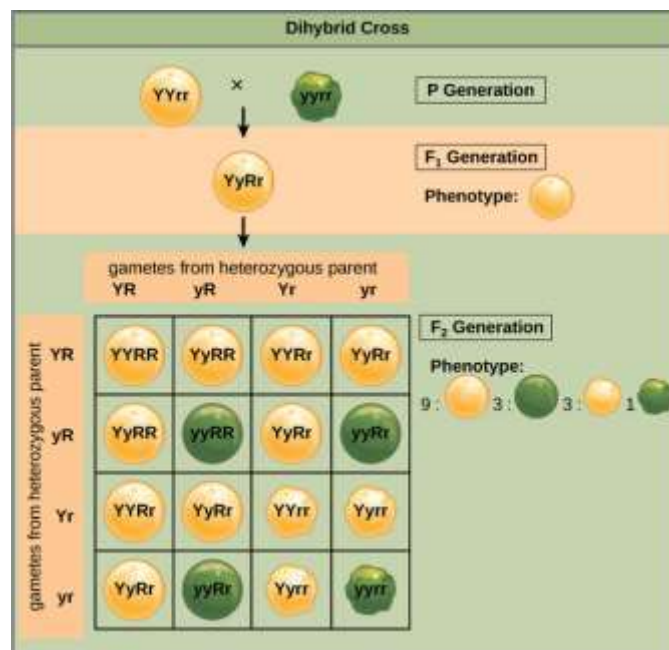
Because each parent is homozygous, the law of segregation indicates that the gametes for the green/wrinkled plant all are yr, while the gametes for the yellow/round plant are all YR. Therefore, the F_1 generation of offspring all are YyRr.

For the F_2 generation, the law of segregation requires that each gamete receive either an R allele or an r allele along with either a Y allele or a y allele. The law of independent assortment states that a gamete into which an r allele sorted would be equally likely to contain either a Y allele or a y allele.

Therefore, there are four equally likely gametes that can be formed when the YyRr heterozygote is self-crossed as follows: YR, Yr, yR, and yr. Arranging these gametes along the top and left of a 4×4 Punnett square gives us 16 equally likely genotypic combinations. From these genotypes, we infer a phenotypic ratio of 9 round/yellow:3 round/green:3 wrinkled/yellow:1 wrinkled/green. These are the offspring ratios we would expect, assuming we performed the crosses with a large enough sample size.

Mendel's Law of Independent Assortment

Therefore, the proportion of round and yellow F_2 offspring is expected to be $(3/4) \times (3/4) = 9/16$, and the proportion of wrinkled and green offspring is expected to be $(1/4) \times (1/4) = 1/16$. These proportions are identical to those obtained using a Punnett square. Round/green and wrinkled/yellow offspring can also be calculated using the product rule as each of these genotypes includes one dominant and one recessive phenotype. Therefore, the proportion of each is calculated as $(3/4) \times (1/4) = 3/16$.





KEY POINTS

Law of dominance and uniformity

Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.

Law of segregation

During gamete formation, the alleles for each gene segregate from each other so that each gamete carries only one allele for each gene.

Law of independent assortment

Genes of different traits can segregate independently during the formation of gametes.



Lecture 8 Questions Practice

Q1:- Define the followings:

1. Mendel's first law.
2. Mendel's second law.
3. Mendel's third law.

Q2:- Explain briefly the followings:

- a. Mendel's first law.
- b. Mendel's second law.
- c. Mendel's third law.



Cytogenetic

7th lecture

Pattern of Inheritance Mendel's Laws

OBJECTIVES



- Introduction
- Mendel's Laws
- Mendel's Laws of Inheritance



Introduction

Mendelian inheritance or **Mendelian genetics** or **Mendelism**, is a set of primary tenets relating to the transmission of hereditary characteristics from parent organisms to their offspring.

The tenets were initially derived from the work of **Gregor Mendel** published in 1865 and 1866, which was re-discovered in 1900, which were initially very controversial, but they soon became the **core of classical genetics**.

The laws of inheritance were derived by **Gregor Mendel**, a 19th century monk conducting hybridization experiments in garden peas (*Pisum sativum*). Between 1856 and 1863, he cultivated and tested about 28,000 pea plants. From these experiments, he deduced **two generalizations** that later became known as **Mendel's Laws of Heredity** or **Mendelian inheritance**.



Introduction

Mendelian inheritance is a type of biological inheritance that follows the principles originally proposed by **Gregor Mendel** in 1865 and 1866, re-discovered in 1900 by Hugo de Vries and Carl Correns, and popularized by William Bateson.

When Mendel's theories were integrated with the Boveri–Sutton chromosome theory of inheritance by Thomas Hunt Morgan in 1915, they became the **core of classical genetics**.



Mendel's Laws

Mendel discovered that by crossing **true-breeding** white flower (**purebred of certain phenotypic traits**) and true-breeding purple flower plants, the result was a hybrid offspring. Rather than being a mix of the two colors, the offspring was purple flowered.

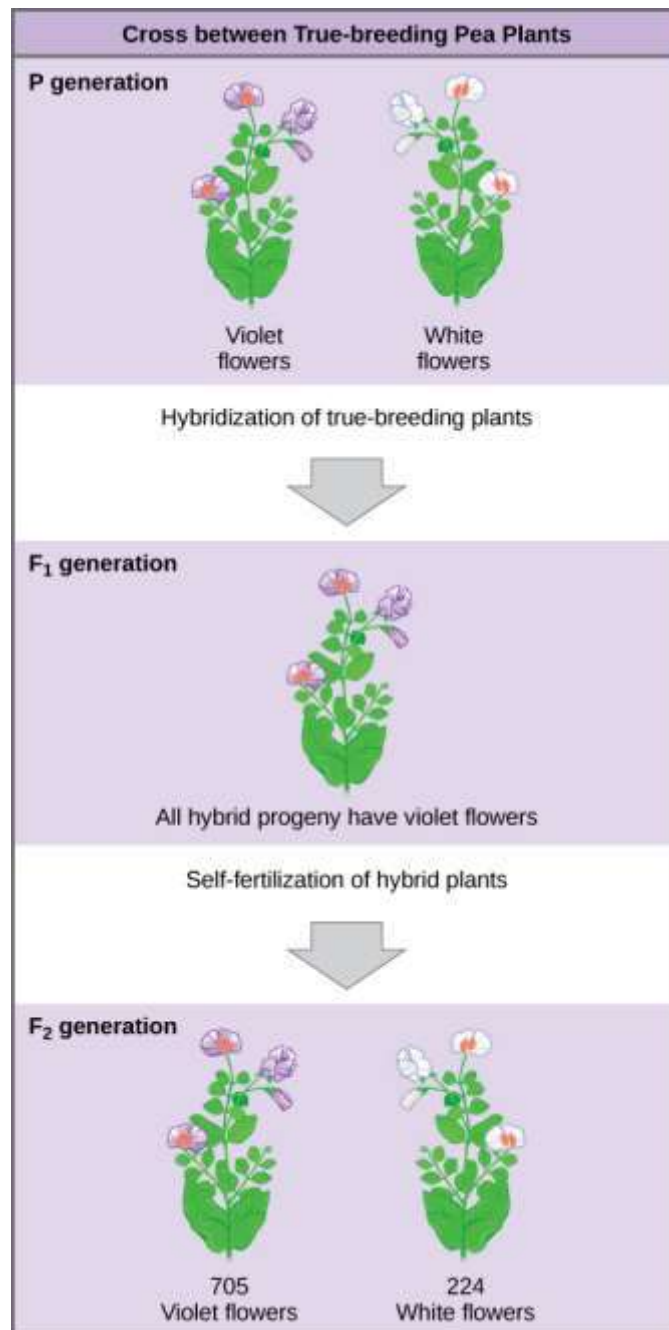
He then conceived the idea of **heredity units**, which he called "**factors**" one of which is a **recessive characteristic** and the other **dominant**. Mendel said that factors (later called genes) are normally occur in pairs in ordinary body cells, yet segregate during the formation of sex cells. Each member of the pair becomes part of the separate sex cell.



Mendel's Laws

The dominant gene, such as the purple flower in Mendel's plants, will hide the recessive gene, the white flower. After Mendel self-fertilized the F1 generation and obtained an F2 generation with a 3:1 ratio, he correctly theorized that genes can be paired in three different ways for each trait: AA, aa, and Aa. The **capital A** represents the dominant factor while the **lowercase a** represents the recessive.

Mendel's Laws





Mendel's Laws

Mendel stated that each individual has **two alleles for each trait**, one from each parent. Therefore, he formed the **First Rule: The Law of Segregation**, which states individuals possess two alleles and a parent passes only one allele to his/her offspring. One allele is given by the female parent and the other is given by the male parent.

The two factors may or may not contain the same information. If the two alleles are identical, the individual is called **homozygous** for the trait. If the two alleles are different, the individual is called **heterozygous**.

The presence of an allele does not promise that the trait will be expressed in the individual that possesses it. In heterozygous individuals, the only allele that is expressed is the dominant. The recessive allele is present, but its expression is hidden.



Mendel's Laws

Mendel also analyzed the pattern of inheritance of seven pairs of contrasting traits in the domestic pea plant. He did this by cross-breeding dihybrids. That means, plants that were heterozygous for the alleles controlling two different traits.

Mendel then crossed these dihybrids. If it is inevitable that round seeds must always be yellow and wrinkled seeds must be green, then he would have expected that this would produce a typical monohybrid cross: 75 percent round-yellow; 25 percent wrinkled-green.

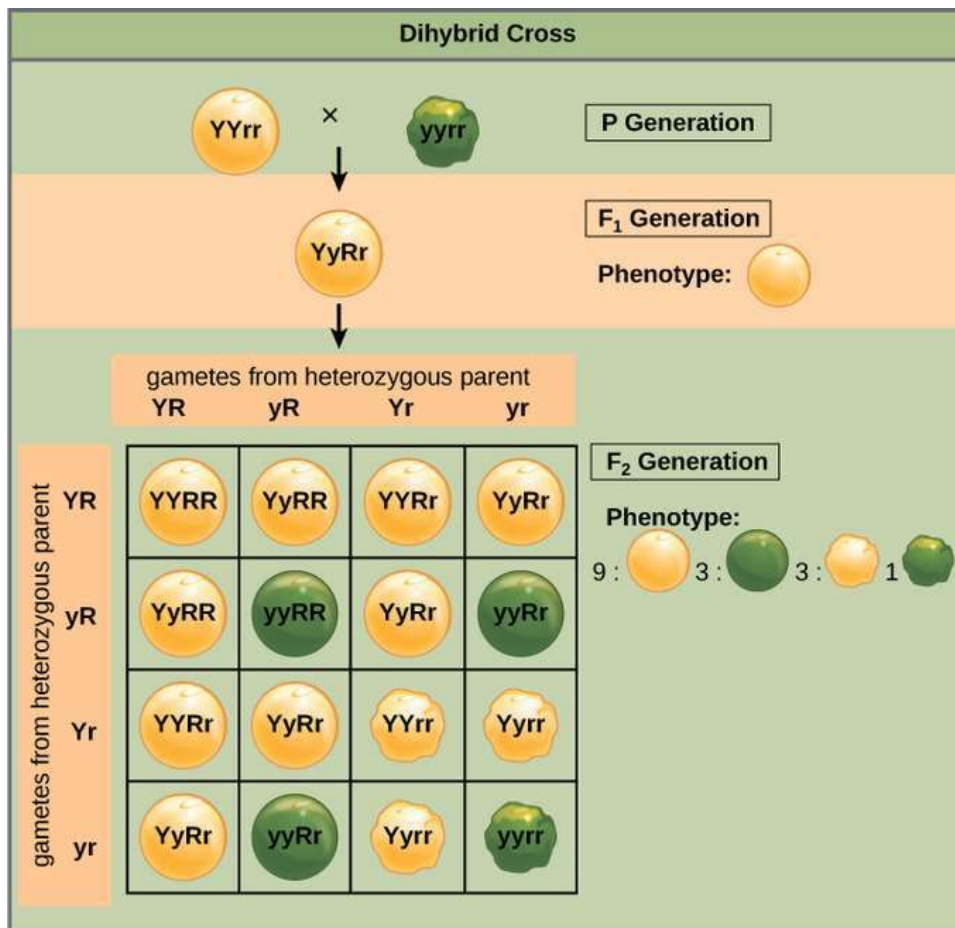


Mendel's Laws

But, in fact, his mating generated seeds that showed all possible combinations of the color and texture traits. He found 9/16 of the offspring were round-yellow, 3/16 were round-green, 3/16 were wrinkled-yellow, and 1/16 were wrinkled-green.

Finding in every case that each of his seven traits was inherited independently of the others, he formed his **Second Rule: The Law of Independent Assortment**, which states the inheritance of one pair of factors (genes) is independent of the inheritance of the other pair.

Mendel's Laws





Mendel's Laws of Inheritance

1. Law of dominance and uniformity

Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.

2. Law of segregation

During gamete formation, the alleles for each gene segregate from each other so that each gamete carries only one allele for each gene.

3. Law of independent assortment

Genes of different traits can segregate independently during the formation of gametes.



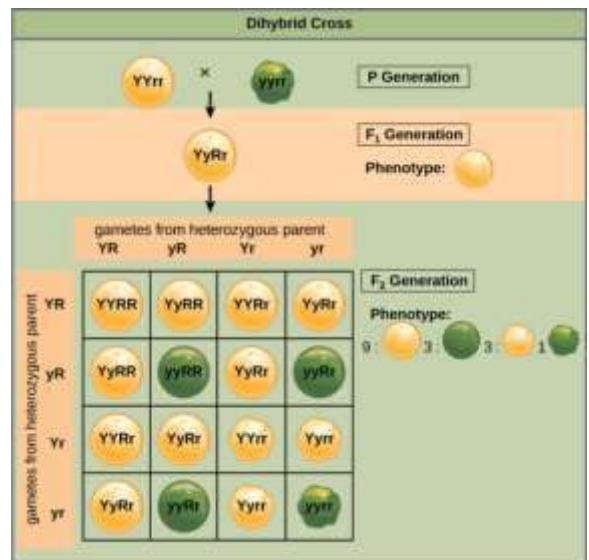
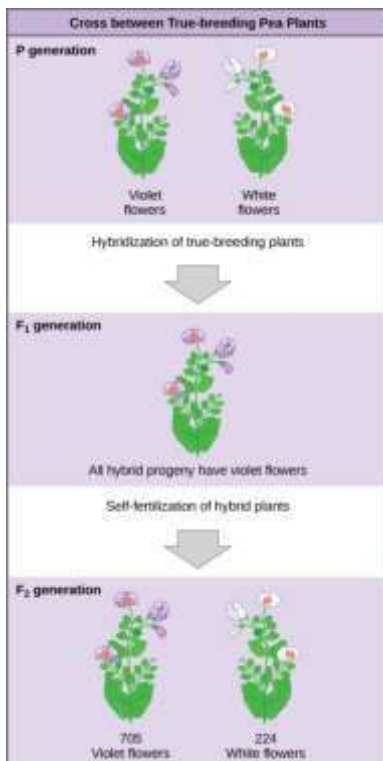
KEY POINTS

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Mendelian inheritance is a type of biological inheritance that follows the principles originally proposed by Gregor Mendel in 1865 and 1866, re-discovered in 1900 by Hugo de Vries and Carl Correns, and popularized by William Bateson.

First Rule: The Law of Segregation

Second Rule: The Law of Independent Assortment





KEY POINTS

1. **Law of dominance and uniformity**
2. **Law of segregation**
3. **Law of independent assortment**



Lecture 7 Questions Practice

Q1:- Define the followings:

- a. Mendelian inheritance.

Q2:- Enumerate the followings:

- a. Enumerate Mendel laws.

Q3:- MCQ

1. Mendel stated that each individual has?
 - a. One allele for each trait.
 - b. Two alleles for each trait, one from each parent.
 - c. Three alleles for each trait.
 - d. Four alleles for each trait, two from each parent.

2. In heterozygous individuals, the only allele that is expressed is the dominant. The recessive allele is present, but its expression is?
 - a. Hidden.
 - b. Masked.
 - c. Doesn't show up.
 - d. All the answers.



Cytogenetic

6th lecture

Genetic Diseases due to Chromosomal Abnormalities

OBJECTIVES



- Genetic Diseases due to Chromosomal Abnormalities
- Trisomies (Trisomy 21: Down Syndrome, Trisomy 18: Edward Syndrome, Trisomy 13: Patau Syndrome, Klinefelter Syndrome (XXY Syndrome), Jacob's Syndrome (XYY Syndrome), Turner Syndrome (X0 Syndrome), Triple X Syndrome.
- Structural Abnormalities Syndromes



Genetic Diseases due to Chromosomal Abnormalities

Genetic disorder is a health problem caused by one or more abnormalities in the **genome**. It can be caused by a mutation in a single gene (monogenic mutation) or multiple genes (polygenic mutation) or by a **chromosomal abnormality**.

Chromosomal abnormalities are common causes of birth defects that can affect the brain and other parts of the body. The normal fertilized ova cell contains 23 chromosomes from the mother and 23 from the father. Thus, there are normally 23 pairs of chromosomes in the fertilized ovum. These include two sex chromosomes: XX for females and XY for males.



Genetic Diseases due to Chromosomal Abnormalities

When the genetic disorder is inherited from one or both parents, it is also classified as a **hereditary disease**. Some disorders are caused by a mutation on the X chromosome and have X-linked inheritance. Very few disorders are inherited on the Y chromosome or mitochondrial DNA.

Genetic disorder → is a disease caused by a change or mutation in an individual's DNA sequence.

Genetic disease → genetic disorder.

Hereditary disease → has the potential of being carried from generation to generation.



Trisomies

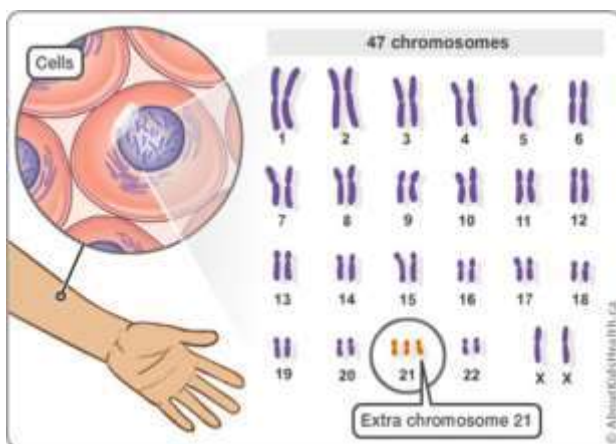
The term trisomy means that there are **three chromosomes**, rather than the usual pair of chromosomes.

For instance, if an infant has **Down syndrome**, he in most cases, have **three copies of chromosome 21**, and the condition is thus called “trisomy 21”. Other common Trisomies are **trisomy 18** and **trisomy 13**, which means that there are **three copies of chromosome 18** or **13**, respectively, in each cell of the body, rather than the usual pair.

Trisomy 21: Down Syndrome

Trisomy 21 is when there is an **extra copy of chromosome 21**. This causes a condition called **Down syndrome**.

The risk of having a baby with Down syndrome increases with the mother's age. Because of this, women over age 35 are offered special tests during pregnancy such as **amniocentesis** to check the baby's chromosomes.





Trisomy 21: Down Syndrome

The features of Down syndrome include **intellectual disability, slow growth, abnormalities of the face or skull** such as upward slanting eyes and a flattened face, and **heart conditions**.

The major problem is overall **developmental and intellectual disability**. Toddlers born with Down syndrome can learn basic skills like sitting, walking, and talking, but at a delayed pace compared with other children.

Down syndrome is associated with chronic health problems. Therefore, they should also **receive regular heart checkup, vision and hearing tests, thyroid evaluations, and immunizations for common diseases**.



Trisomy 18: Edward Syndrome

Trisomy 18, also called **Edwards syndrome** after the physician who first described the disorder, is a rare chromosome abnormality that affects approximately one in every 6,000-8,000 live births. These children have severe developmental delay, as well as severe birth defects and health problems involving nearly every organ system in the body.

Fifty per cent of babies born with trisomy 18 survive beyond their first six to nine days. About 12% of babies born with trisomy 18 survive the first year of life. About 10% of children born with trisomy 18 survive until 10 years of age.

Babies with trisomy 18 have low birth weight, have a weak cry, and startle to sound. They have problems feeding and fail to thrive. They have a small head size, with a prominent back of the head (occiput). Their ears are usually low set and the opening of their eyes; their nose and their mouth are small. Their sternum (breastbone) is typically short.

Trisomy 18: Edward Syndrome

Almost all babies with trisomy 18 have heart defects. They have clenched fists from before birth and extending the fingers fully is difficult. Their elbows and knee joints are in a bent position rather than relaxed. They typically have club feet and their feet have been described as a "rocker bottom" due to their shape. Babies with trisomy 18 may also have spina bifida, cleft lip and palate, eye problems, and hearing loss.





Trisomy 13: Patau Syndrome

Trisomy 13, also called **Patau syndrome** after the physician who first described the disorder, affects one in every 8,000-12,000 live births. Babies with trisomy 13 have many abnormalities, involving nearly every organ system in the body, as well as developmental delay.

Fifty per cent of babies born with trisomy 13 survive beyond their first 7.5-12.5 days. About 20% of babies born with trisomy 13 survive the first year of life. About 13% of children born with trisomy 13 survive until 10 years of age.

Babies with trisomy 13 often have a normal birth weight, a small head and a sloping forehead. Noses are usually large “bulbous”, ears are low-set and unusual in shape, eye defects occur frequently, and cleft lip and palate as well as heart defects are very common. Many babies with trisomy 13 are born with small areas of missing skin on the scalp (cutis aplasia), which resemble ulcers.

Trisomy 13: Patau Syndrome

The brains in babies with trisomy 13 usually have major structural problems and often, the brain does not divide properly into two hemispheres, resulting in a condition called holoprosencephaly. Many babies with trisomy 13 have extra fingers and toes (polydactyly). Some present with a sac attached to the abdomen in the area of the umbilical cord (omphalocele), which contains some of the abdominal organs, as well as spina bifida. Girls may have an abnormally shaped uterus, called a bicornuate uterus. In boys, the testes sometimes fail to descend into the scrotum.





Klinefelter Syndrome (XXY Syndrome)

Babies with Klinefelter syndrome have **one or two extra sex chromosome(s)**. These babies are **always boys** and, instead of having an XY chromosome pair, they have XXY or XXXY.

Usually boys with Klinefelter syndrome are not diagnosed until puberty. The features of this condition include infertility, shrinkage of the testicles, and development of breasts. Intellectual disability is not usually associated with Klinefelter syndrome, although it does sometimes occur.

Treatment of Klinefelter syndrome does not begin until the child is older. Around 11 or 12 years of age, the child's testosterone levels will be measured. If the levels are low, they will be given testosterone injections on a regular basis. Testosterone injections help to increase body hair on the face, underarms, and genitals, increase muscle development and sex drive, and shrink enlarged breasts.



Jacob's Syndrome (XYY Syndrome)

The XYY syndrome, also known as **47 XYY syndrome**, **XYY Karyotype**, or **Jacob's syndrome**, is a genetic disorder that occurs in about one in every 1,000 newborn **boys**. It often results from a random event while sperm cells are forming. Boys with XYY syndrome have three sex chromosomes instead of two.

Despite this extra chromosome, most boys can expect to lead a healthy and normal life. It is common for XYY syndrome to go undetected because symptoms are usually non-existent or very mild.



Turner Syndrome (X0 Syndrome)

Infants with Turner syndrome, **always girls**, lack one of their **X chromosomes**. Therefore, only have **45 chromosomes (XO)**. The features of this condition include the absence of **functioning ovaries**, short stature, a webbed neck, skeletal deformities, and a broad chest with widely spaced nipples.

Because most girls with Turner syndrome lose their ovarian function in early childhood, they do not enter puberty at the normal age. Generally, if a girl with Turner syndrome has not had her first menstrual period by the age of 15 years, she will be given estrogen to induce breast development and other features of puberty. **Girls with Turner syndrome are infertile**. These girls need to remain on estrogen to maintain their sexual development and protect their bones from osteoporosis.



Triple X Syndrome (XXX Syndrome)

Infants with triple X syndrome, **always girls**, have three XXX chromosomes instead of the usual two. Some girls with this condition have **no symptoms**. Others may have learning disabilities, problems with speech or language, or intellectual disability.

Other features may include tall stature, a small head, problems with motor skills, and infertility. There is no cure for triple X syndrome.



Structural Abnormalities Syndromes

Some chromosomal abnormalities occur when a segment of a chromosome is deleted or duplicated. These types of abnormalities can cause birth defects in one or more organ systems.

Some structural abnormalities are as follows:-

Cri-du-chat syndrome: Infants with this condition have a cry that sounds like a cat. They also may have intellectual disability and congenital heart defects. There is no cure for this syndrome.

Angelman syndrome: Infants with this syndrome have intellectual disability, cannot speak, and have problems with their motor development. There is no standard course of treatment for Angelman syndrome.



Structural Abnormalities Syndromes

Prader-Willi syndrome: This condition causes obesity, intellectual disability, lower than normal amounts of testosterone in boys, testes that do not descend properly into the scrotum, and muscles that are too relaxed in tone. There is no cure for this syndrome, but the physical symptoms can be managed. Obesity can be controlled with a strict diet and daily exercise.

Fragile X syndrome: This is the second most common chromosomal cause of severe intellectual disability, after Down syndrome. Other characteristic features include an elongated face, prominent jaw, large ears, and in boys, enlargement of the testicles. There may also be behavioural and cognitive problems. There is no cure for Fragile X syndrome.



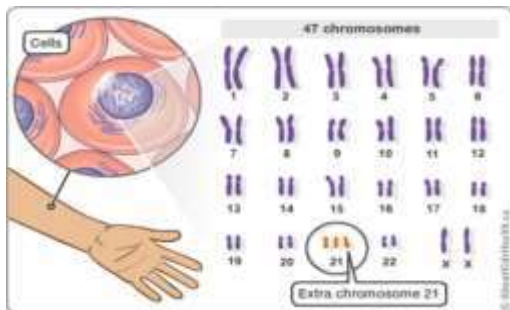
KEY POINTS

Genetic disorder= Genetic disease → is a disease caused by a change or mutation in an individual's DNA sequence.

Hereditary disease → has the potential of being carried from generation to generation.

Trisomy means that there are **three chromosomes**, rather than the usual pair of chromosomes.

Trisomy 21 is when there is an **extra copy of chromosome 21**. This causes a condition called **Down syndrome**.



Trisomy 18, also called **Edwards syndrome**.





KEY POINTS

Trisomy 13, also called **Patau syndrome**.



Klinefelter syndrome have **one or two extra sex chromosome(s)**. These babies are **always boys** and, instead of having an XY chromosome pair, they have XXY or XXXY.

Jacob's Syndrome (XYY Syndrome).

Turner Syndrome (X0 Syndrome).

Triple X Syndrome (XXX Syndrome).

Structural Abnormalities Syndromes:-

Cri-du-chat syndrome, Angelman syndrome, Prader-Willi syndrome, Fragile X syndrome.



Lecture 6 Questions Practice

Q1:- Define the followings:

- a. Genetic disorder.
- b. Hereditary disease.

Q2:- Enumerate the followings:

- a. Enumerate the trisomy syndromes.
- b. Enumerate the syndromes that results from chromosomal structural abnormalities.

Q3:- MCQ

- 1. Holoprosencephaly, polydactyly and omphalocele are conditions appears in?
 - a. Edward syndrome.
 - b. Down syndrome.
 - c. Klinefelter syndrome.
 - d. Patau syndrome.
- 2. Spina bifida is a condition appears in?
 - a. Edward syndrome.
 - b. Down syndrome.
 - c. Klinefelter syndrome.
 - d. Patau syndrome and Edward syndrome.
 - e. None of the answers.



Cytogenetic

5th lecture

The Chromosomal Abnormalities

OBJECTIVES



- Chromosomal Abnormalities
- How Do Chromosomal Abnormalities Happens?
- Aneuploidy, Monoploidy and Polyploidy



Chromosomal Abnormalities

There are many types of chromosome abnormalities. However, they can be organized into two basic groups: **numerical abnormalities** and **structural abnormalities**.

Numerical Abnormalities:-

1. **Monosomy**, when an individual is **missing one of the chromosomes** from a pair, such as Turner syndrome, a female is born with only one sex chromosome X0.
2. **Trisomy**, when an individual has **more than two chromosomes** instead of a pair, such as Down syndrome individual has three copies of chromosome 21 rather than two.



Chromosomal Abnormalities

Structural Abnormalities:-

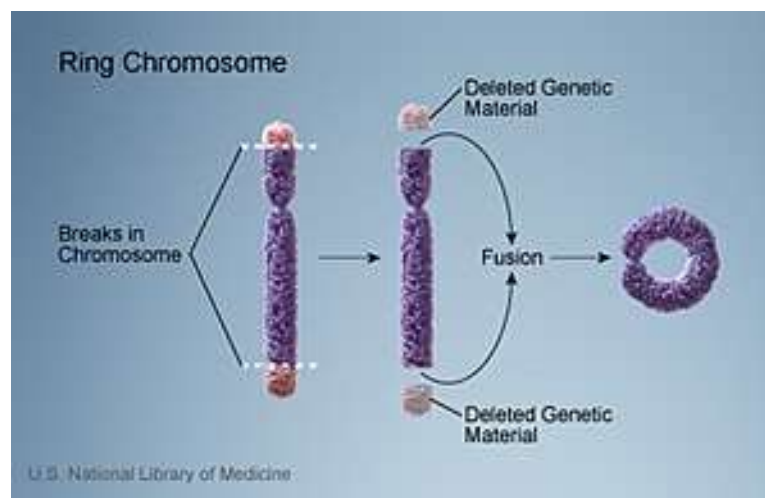
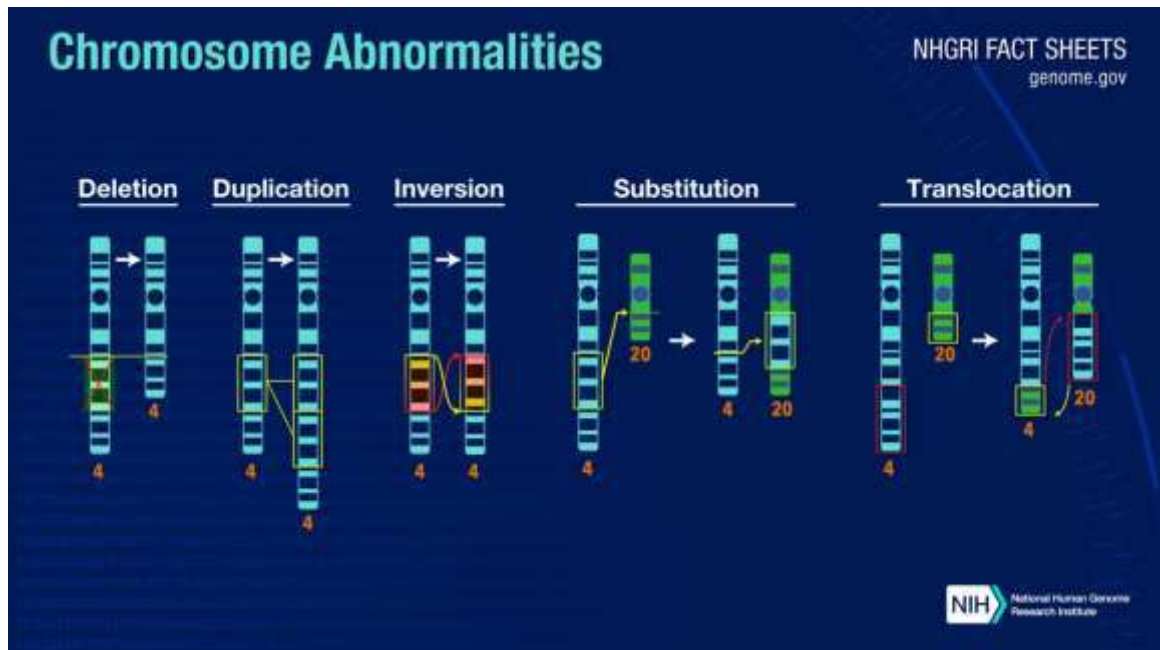
A chromosome's structure can be altered in several ways.

1. **Deletions:** A portion of the chromosome is missing or deleted.
2. **Duplications:** A portion of the chromosome is duplicated, resulting in extra genetic material.
3. **Translocations:** A portion of one chromosome is transferred to another chromosome.

There are **two main types of translocation**, **reciprocal translocation** (segments from two different chromosomes have been exchanged), and **Robertsonian translocation** (entire chromosome has attached to another at the centromere).

4. **Inversions:** A portion of the chromosome has broken off, turned upside down, and reattached. As a result, the genetic material is inverted.
5. **Substitution:** Replacement of one or more chromosome by others (totally or partially homologous).
6. **Rings:** A portion of a chromosome has broken off and formed a circle or ring. This can happen with or without loss of genetic material.

Chromosomal Abnormalities





Chromosomal Abnormalities

Most chromosome abnormalities occur **accidentally** in the **ovum** or **sperm**. In these cases, the abnormality is present in **every cell of the body**. **Some chromosomal abnormalities**, happen after **conception**, then some cells have the abnormality and some do not.

Chromosome abnormalities can be inherited from a parent such as a translocation. This is why, when a child is found to have an abnormality, chromosome studies are often performed on the parents.



How Do Chromosomal Abnormalities Happens?

Chromosome abnormalities usually occur when there is an **error in cell division**. There are two kinds of cell division, mitosis and meiosis. In both processes, the **correct number of chromosomes** is supposed to end up in the resulting cells. However, errors in cell division can result in cells with **too few** or **too many** copies of a chromosome. Errors can also occur when the chromosomes are being duplicated.

Other factors that can increase the risk of chromosome abnormalities are:-

- 1. Maternal Age:** Women are born with all the ova they will ever have. Some researchers believe that errors can happen in ova's genetic material as they age. Older women are at higher risk of giving birth to babies with chromosome abnormalities than younger women. Because men produce new sperm throughout their lives, paternal age does not increase risk of chromosome abnormalities.
- 2. Environment:** Although there is no conclusive evidence that specific environmental factors cause chromosome abnormalities, it is still possible that the environment may play a role in the occurrence of genetic errors.



Aneuploidy, Polyploidy and Monoploidy

Aneuploidy having or missing extra chromosomes. Trisomy is the most common aneuploidy. In trisomy, there is an extra chromosome, the condition of having an abnormal number of chromosomes in a haploid set.

Polyploidy is the heritable condition of possessing more than two complete sets of chromosomes. Polyploids are common among plants, as well as among certain groups of fish and amphibians.



Aneuploidy, Polyploidy and Monoploidy

Monoploidy having one set of the chromosomes or having a single set of chromosomes. In most animals, a monoploidy instead of a diploidy is lethal. This condition may be tolerated more in plant species and therefore they may survive despite the condition.

Monoploidy, in most animal species mean death. Nevertheless, there are few animal species where monoploidy is **a normal part of the life cycle** such as in male wasps, ants, and bees. The offspring that arise from monoploidy are those that have developed from unfertilized eggs.



KEY POINTS

The chromosome abnormalities → **numerical abnormalities** and **structural abnormalities**.

Numerical Abnormalities:-

1. **Monosomy** → missing one of the chromosomes from a pair.
2. **Trisomy** → has more than two chromosomes instead of a pair.

Structural Abnormalities:-

Deletions, Duplications, Translocations (reciprocal translocation, Robertsonian translocation, Inversions, Substitution and Rings.

Most chromosome abnormalities occur **accidentally** in the **ovum** or **sperm**.

How Do Chromosomal Abnormalities Happens?

Chromosome abnormalities usually occur when there is an **error in cell division**.

FACTORS ARE:- Maternal Age & Environment.

Aneuploidy, Polyploidy and Monoploidy



Lecture 5 Questions Practice

Q1:- Define the followings:

- a. Aneuploidy.
- b. Monoploidy.

Q2:- Enumerate the followings:

- a. Enumerate the numerical chromosomal abnormalities.
- b. Enumerate the structural chromosomal abnormalities.

Q3:- MCQ

- 1. Errors in cell division can result in cells with?
 - a. Too few chromosomes.
 - b. Too many chromosome.
 - c. Incorrect number of chromosomes.
 - d. All the answers.
 - e. None of the answers.

- 2. Errors in cell division can also occur when the chromosomes are being?
 - a. Duplicated.
 - b. Synthesized.
 - c. Copied.
 - d. All the answers.
 - e. None of the answers.



Cytogenetic

4th lecture

The Chromosomes History, Structure, Number & Karyotyping

OBJECTIVES



- Genetics Related Terminology
- Chromosomes Number
- Karyotyping



Genetics Related Terminology

Ploidy the number of sets of chromosomes in a cell.

Haploid (n) or monoploid is a cell or organism that has just a single copy of each chromosome.

Diploid (2n) is a cell or organism that has paired or two sets of chromosomes, one from each parent.

Somatic cells are all the cells in the body of organisms except the sex cells or the gametes.

Gametes are an organism's reproductive cells. They are also referred to as sex cells. Female gametes are called ova cells, and male gametes are called sperm.



Genetics Related Terminology

Zygote is a cell that results from the union of a female gamete (ovum) with a male gamete (sperm).

Gonads are the primary reproductive organs, the testes in the male and the ovaries in the female.

Fertilization is the process of combining the male gamete, sperm, with the female gamete, ovum. The product of fertilization is a cell called a zygote.



Chromosome Number

There are normally **two copies** of each chromosome present in **every somatic cell**.

The number of unique chromosomes (n) in such a cell is known as its **haploid number**, and the total number of chromosomes ($2n$) is its **diploid number**.

A chromosome consists primarily of **DNA** and **proteins** with a **small amount of RNA**. Chromosomes are duplicated and transmitted, via cell division (mitosis or meiosis), to the next cell generation.

The **different chromosome types** have been distinguished by **size** and **shape**. A chromosome must include **structures** that **enable it to replicate** and **remain intact**.



Chromosome Number

The essential parts of a chromosome are:-

Telomeres are chromosome tips. In humans, each telomere repeats the sequence **TTAGGG**. Telomeres function is to **protect** and **stabilize** the chromosome ends.

Replication sites (origin) are the sites where DNA synthesis begins, they are not easily observed by microscopy. In preparation for cell division, each chromosome replicates, making a copy of itself. These two initially identical copies, called **sister chromatids**, are held together at the **centromere**.

Centromere is the largest constriction of a chromosome. It is where **spindle fibers** attach when the cell divides. On the basis of the location of the centromere, chromosomes are classified into four types: **metacentric**, **submetacentric**, **acrocentric**, and **telocentric**.



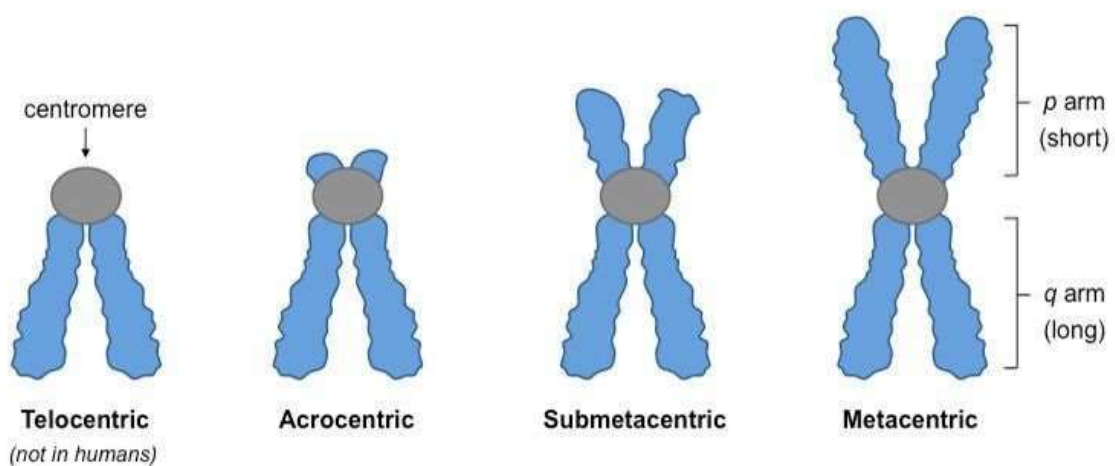
Chromosome Number

Types of human chromosomes There are four types of chromosomes based upon the position of the centromere in human's chromosome.

1. **Metacentric:** In this type of chromosome the centromere occurs in the center and all the four chromatids are of equal length.
2. **Submetacentric:** In this type of chromosome the centromere is a little away from the center and therefore chromatids of one side are slightly longer than the other side

Chromosome Number

3. **Acrocentric:** In this type of chromosome the centromere is located closer to one end of chromatid.
4. **Telocentric:** In this type of chromosome the centromere is placed at one end of the chromatid and has only one arm. Such telocentric chromosomes are not seen in human cells.





Karyotyping

Like all other eukaryotes, humans contain a fixed number of chromosomes within each of the nuclei in all their cells. There are essentially two types of chromosomes as characterized by **karyotyping** at the metaphase of cell division.

These include:-

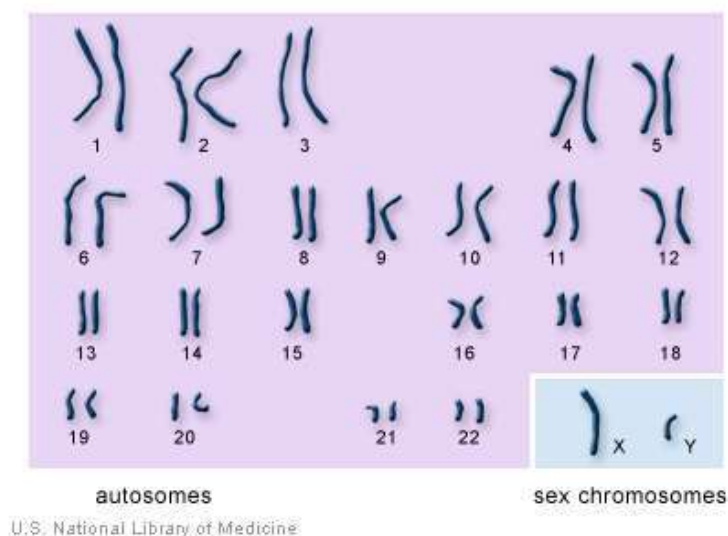
Autosomes, there are 22 pairs of autosomes in humans. These code for most of the genetic traits in the body. The 22 autosomes are numbered by **size**.

Gonosomes or **sex chromosomes**, human has two types of sex chromosomes including X and Y. While males have an X and a Y chromosome, females possess two X chromosomes.

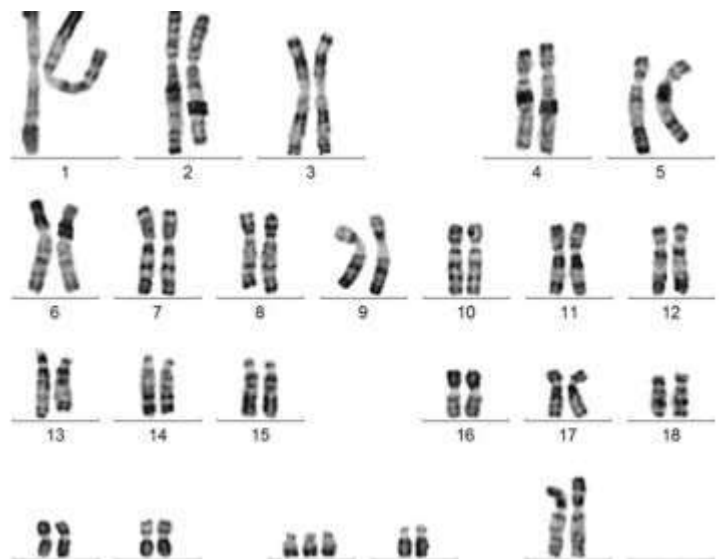
Karyotyping

This picture of the human chromosomes lined up in pairs is called a **karyotype**. Each human cell thus contains **46 chromosomes in 23 pairs**. The ovum produced by the female ovaries and the sperm produced by the male testicles, however, contain only 23 chromosomes. This ensures that when the ova and the sperm get fertilized to form a baby, it contains **23 pairs** and restores the total **chromosomal count to 46**.

Apart from chromosomes present in the nuclei, humans also possess mitochondrial genome, present in the mitochondria of cells.



Karyotyping





Karyotyping

Each of the chromosomes contains highly condensed and coiled DNA consisting of millions of gene sequences. While some of the sequences are essential for life and code for essential proteins, some are "**silent**," meaning they do not code for any proteins.

The complete human genome database is being compiled based on the Sanger Institute's human genome information in the **Vertebrate Genome Annotation (VEGA)** database.



Karyotyping

The term **karyotype** refers to the chromosomal pattern inside the nucleus of an animal cell (eukaryote), as well as to describes the set of chromosomes in a species or in an individual organism. The study of karyotypes in eukaryotic cells is a branch of science termed **cytogenetics**, from "**cyto**" meaning **cell** and "**genetics**" meaning the **cell's chromosomal make up**.

A karyotype will be shared by organisms from the same species, but the following intra-species variations are seen:-

1. The karyotype of males and females may differ. For instance, in humans the male karyotype contains an X and Y chromosome while in human females there are two X chromosomes.



Karyotyping

2. There are karyotypic differences between body (somatic) cells and gametes.
The sperm and egg cells each contain half the amount of chromosomes a somatic cell contains, and only make a complete cell with the full number of 46 chromosomes when they combine during fertilization.
3. Karyotypes may also differ within a population due to genetic polymorphism.
4. The karyotype of a species may vary by geographical location and racial differences are also seen.
5. Genetic abnormalities may also give rise to abnormal and different karyotypes.



Karyotyping

Karyotyping refers to the **process used** to **examine** a **cells karyotype** while it is locked in **metaphase** during cell division. This is done using the drug **Colchicine*** or demecolcine (colcemid). At this stage of cell division, the chromosomes are condensed into dense thread-like structures that are easily distinguishable on staining and imaging. The autosomes are then arranged in order of their length followed by the sex chromosomes to create a **karyogram***.

The human karyotype and number of chromosomes was first discovered early in the 20th century. By the mid 1950's, the human karyotype composed of its 46 chromosomes was finalized.

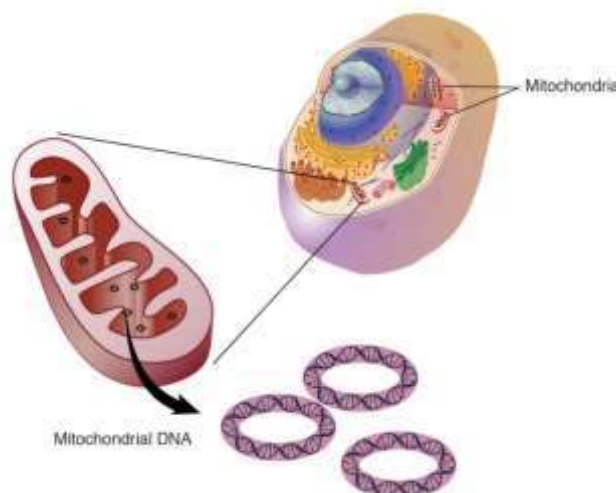
****Colchicine is a type of plant alkaloid that inhibits mitosis by preventing the formation of the spindle fibers to arrest cell at metaphase.***

****Karyogram is a photograph of the chromosomes of an organism arranged in a homologous pairs in a numbered sequence.***

Mitochondrial Chromosome

The pattern of inheritance is different for the small circular chromosome found in mitochondria. Only egg cells, and not sperm cells, keep their mitochondria during fertilization.

Thus, **mitochondrial DNA is always inherited from the female parent**. In humans, a **few conditions**, including some forms of **hearing impairment**, **visual impairment**, **cancer**, **Alzheimer's disease**, **muscular dystrophy** and **diabetes**, have been **associated** with **DNA** found in the **mitochondria**.





KEY POINTS

Genetics Related Terminology

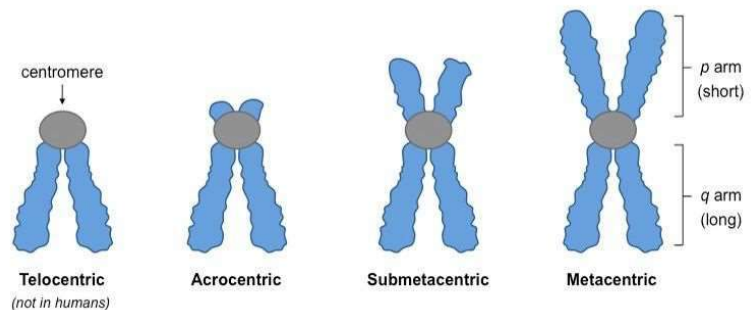
Chromosomes number → diploid or haploid

The **different chromosome types** have been distinguished by **size** and **shape**.

Telomeres → TTAGGG

Replication sites (origin) → replication bubble

Centromere →



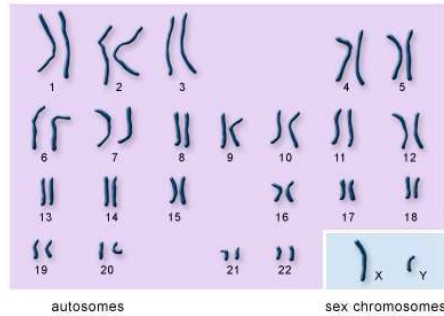
Autosomes, there are 22 pairs of autosomes in humans. These code for most of the genetic traits in the body. The 22 autosomes are numbered by **size**.

Gonosomes or **sex chromosomes**, human has two types of sex chromosomes including X and Y. While males have an X and a Y chromosome, females possess two X chromosomes.



KEY POINTS

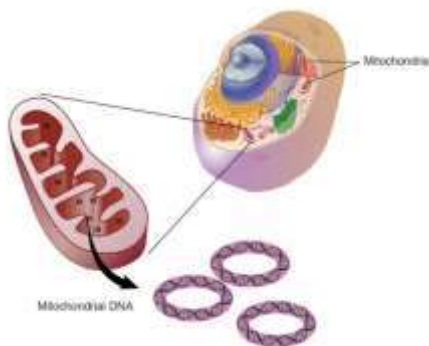
Karyotyping →



A karyotype will have intra-species variations:-

1. The karyotype of males and females may differ.
2. There are karyotypic differences between body (somatic) cells and gametes.
3. Karyotypes may also differ within a population due to genetic polymorphism.
4. The karyotype of a species may vary by geographical location and racial differences.
5. Genetic abnormalities may also give rise to abnormal and different karyotypes.

Karyotyping → Colchicine is a type of plant alkaloid that inhibits mitosis by preventing the formation of the spindle fibers to arrest cell at metaphase.



hearing impairment, visual impairment, cancer, Alzheimer's disease, muscular dystrophy and diabetes



Lecture 4 Questions Practice

Q1:- Define the followings:

- a. Karyotype.
- b. Karyotyping.

Q2:- Enumerate the followings:

- a. Enumerate types of chromosomes based on centromere position.
- b. Enumerate the intra-species variations in the karyotype of an organism.

Q3:- MCQ

- 1. The study of karyotypes in eukaryotic cells is a branch of science termed?
 - a. Pharmacogenetics.
 - b. Cytogenetics.
 - c. Medical genetics.
 - d. Inheritance.

- 2. There are essentially two types of chromosomes as characterized by karyotyping at the metaphase of cell division, these include?
 - a. Autosomes and sex chromosomes.
 - b. Autosomes and gonosomes.
 - c. Sex chromosomes and autosomes.
 - d. Gonosomes and autosomes.
 - e. All the answers.



Cytogenetic

3rd lecture

The Chromosomes History, Structure, Number & Karyotyping

OBJECTIVES



→ Chromosomes History

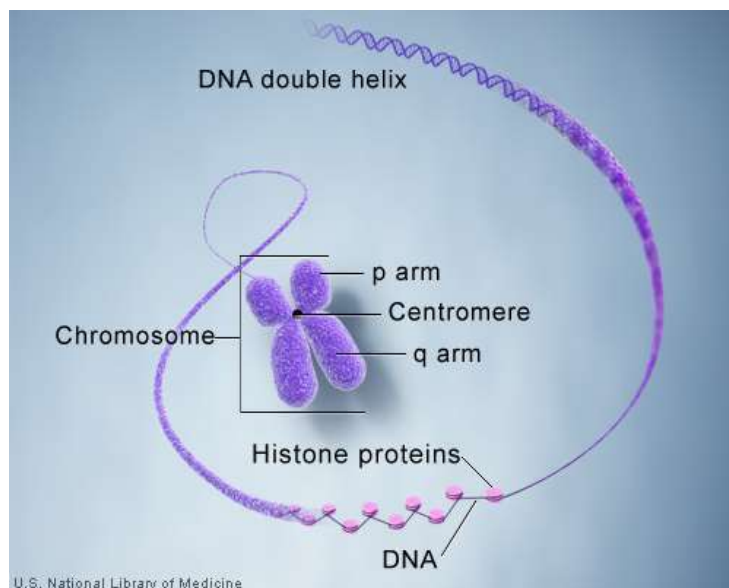
→ Chromosomes Structure

Chromosome History

Chromosome a threadlike structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes.

A chromosome is a single chain of DNA that is coiled and super coiled to form dense threadlike pieces. The term chromosome is derived from the **Greek** words “**Chroma**” or color and “**Soma**” or body and is so named because chromosomes have the ability to be stained with dyes.

Chromosomes also contain DNA-bound proteins or **histones** that consolidate and **stabilize** the **DNA** and **regulate** its **functions**.





Chromosome History

DNA is the **genetic instruction book** for enabling the **production** of **proteins** and **cell processes** that are **essential** to **life** and **inherited** from generation to generation. Every piece of DNA is composed of **gene sequences containing instructions** for each **cell's development, reproduction** and **death**. Each of the DNA chains within chromosomes may contain anywhere between **10,000** to **6,000,000,000** nucleotides.

DNA and histone proteins are packaged into structures called chromosomes. A chromosome may be circular or linear in shape, with nucleated or **Eukaryotic** cells having **linear chromosomes**, and **Prokaryotic** cells usually containing **circular chromosomes**.



Chromosome History

Chronological order of events in genetics and chromosomal research:-

1. **1860s, Mendel** proposed **laws of inheritance** that are independent of gametes.
2. **1875**, the process of **cell division** in somatic cells or mitosis was discovered.
3. **1890**, the process of reduction cell division in formation of gametes or **meiosis** was discovered.
4. **1900**, Mendel is rediscovered by botanists Correns, de Vries, and von Seysenegg independently.



Chromosome History

5. **1900**, Thomas Hunt Morgan from Columbia University confirms the presence of Mendel's inherited factors on chromosomes from *Drosophila melanogaster* (fruit flies). He also found sex chromosomes and sex linked diseases and traits.

6. **1902**, the laws of inheritance and behaviour of chromosomes are found to be parallel as noted by Walter Sutton, Theodor Boveri and others. They noted that chromosomes are paired in somatic cells, that reduction division or meiosis occurs within gametes, and finally that fertilization restores the paired status of chromosomes.



Chromosome in Eukaryotes

Cells with nuclei are known as **Eukaryotic cells**, the cells that make up **animals, plants, fungi** and **yeast**. The nucleus is the organelle that contains the majority of the cell's genetic material, where it is organized into dense linear complexes called **chromosomes**. The number of these chromosomes varies from species to species. Each chromosome has a central, bulb-like thickening called the **centromere** which separates the chromosome into **two arms**, a **long arm (q)** and a **short arm (p)**.

Eukaryotic cells also store genetic information in another organelle, the mitochondria. **Mitochondria** have their own independent genome, the **mitochondrial DNA (37 genes)**. Mitochondrial DNA may be small and circular in shape or linear like nuclear DNA.



Chromosome in Eukaryotes

The **DNA** within **nucleus** is organized into a **coil** with **histone proteins** at its center.

Histones are the structural proteins that compact the DNA and this combination of DNA and histones forms the ultimate, dense chromosomal package inside the nucleus called chromatin.

Chromatin is only found in eukaryotic cells, with prokaryotic cells having a different arrangement of their genetic material called a **genophore**, a chromosome that doesn't contain chromatin.

The structure of chromatin varies according to the stage of the cell cycle. For instance, when the cell is not dividing or is in interphase, the chromatin may be present in two forms, as **euchromatin**, the active part of the genome that is usually undergoing transcription, or **heterochromatin**, which contains mainly inactive DNA, but provides structural support to the chromosomes.



Chromosome in Prokaryotes

Prokaryotes are the group of organisms including bacteria and archaea that do not have a nucleus and instead have a circular, double-stranded molecule of DNA called a **nucleoid**, that is not contained in a nuclear envelope.

The **nucleoid** occupies a central position in the bacterial cell as the nucleus does in eukaryotic cells. However, unlike the nucleus, the nucleoid constantly undergoes structural changes.



Chromosome in Prokaryotes

The chromosomes within the prokaryotes are also found in the form of small molecules of DNA called **plasmids**. Plasmids are generally super coiled like eukaryotic DNA and this needs to be uncoiled to allow for transcription and translation of proteins.

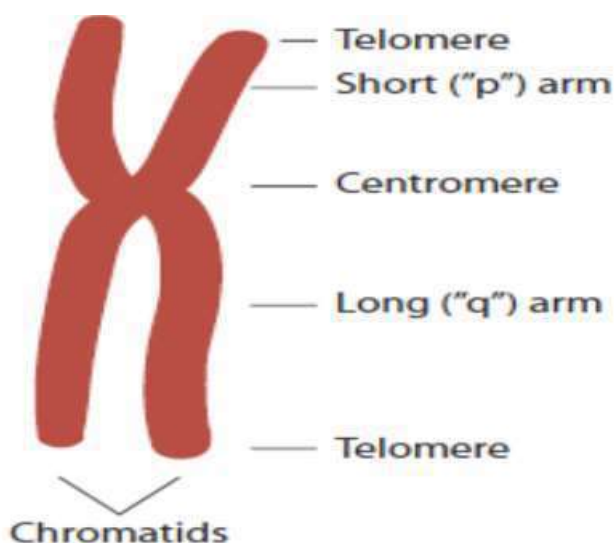
Earlier it was believed that prokaryotes only ever contained a **single chromosome**. Recently, **number of chromosomes in prokaryotes** has been determined, such as that of *Vibrio* species of bacteria that causes diseases such as cholera in fact contains **two large, circular-mapping chromosomes**.

Chromosome Structure

German biologist **Walther Flemming** in the early 1882 revealed that during cell division the **nuclear material organize themselves into visible thread like structures** which were named as **chromosomes** that stains deep with basic dyes.

The term **chromosome** was named by **Heinrich Wilhelm Waldeyer** in 1888.

Chromosomes **vary** both in **number** and **structure** among organisms and the number of chromosomes is **characteristic** of every species.





Chromosome Structure

The human genome is 6.4×10^9 base pairs of DNA and the extended length of DNA that makes up the human genome is about 3m long. The human genome is distributed among **24 chromosomes (22 autosomes and 2 sex chromosomes)**.

The sex chromosomes are denoted by **X** and **Y** and they contain genes which **determine the sex of an individual**; **XX** for female and **XY** for male. The rest are known as autosomes.

The haploid human genome contains about 23,000 protein-coding genes, which are far fewer than had been expected before sequencing. In fact, only about 1.5% of the genome codes for proteins, while the rest consists of non-coding genes, regulatory sequences, introns, and noncoding DNA.



Chromosome Structure

Chromosomes are stained with A-T (**G bands**) and G-C (**R bands**) base pair specific dyes. When they are stained, the **mitotic chromosomes** have a **banded structure** that **identifies** the **shape** of each **chromosome** of a **karyotype**.

G-banding is obtained with **Giemsa stain** yielding a series of **lightly and darkly stained bands**. The dark regions tend to be **heterochromatic** that is A-T rich. The light regions tend to be **euchromatic** and G-C rich.

R-banding is the **reverse** of G-banding where the dark regions are **euchromatic** and the bright regions are **heterochromatic**.

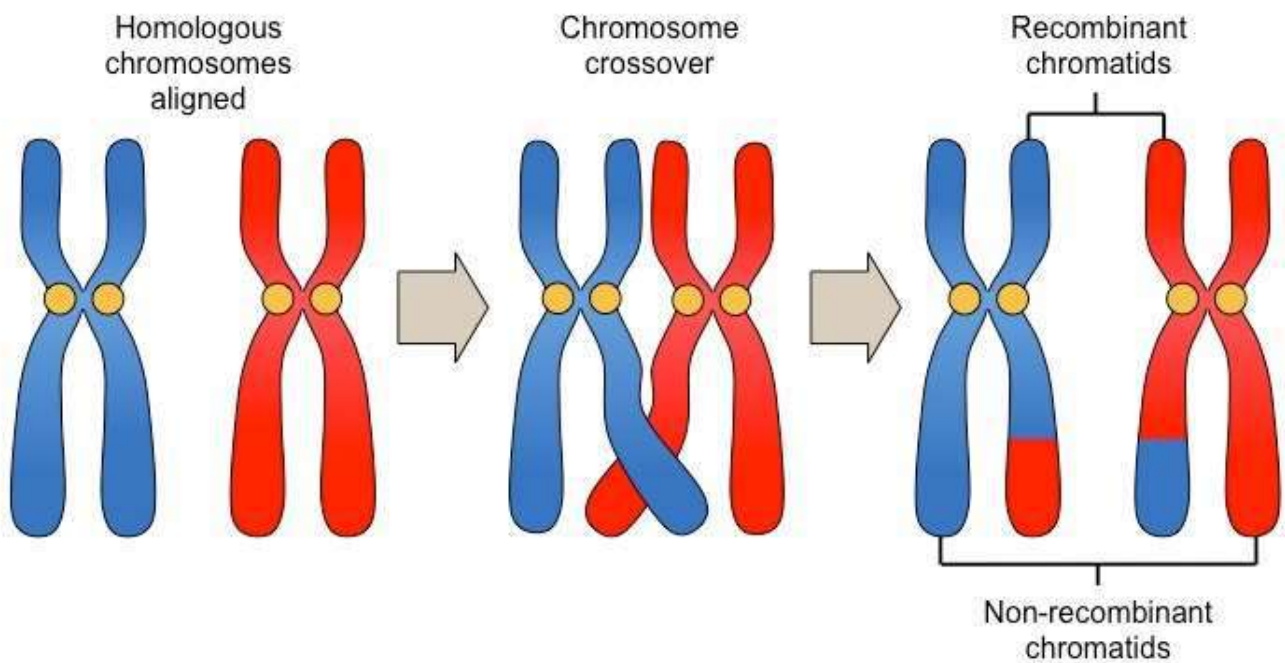


Chromosome Structure

Chromosomes remain important not simply because they carry the genes, but because **their behavior determines the mechanism of inheritance**. The distribution of genes to daughter cells at mitosis and meiosis is a direct consequence of **chromosome behavior**. **Genetic linkage** is a direct result of numerous genes being contained in the same chromosome.

The **crossing-over** and **re-assortment** of **genes** at **meiotic prophase** is also a **chromosomal phenomenon**, which has consequences **providing genetic variation** among individuals. **Genetic variation** is also provided by the fusion of ova and sperm nuclei at fertilization, to produce a **diploid zygote** containing two sets of chromosomes, each derived from a different individual.

Chromosome Structure





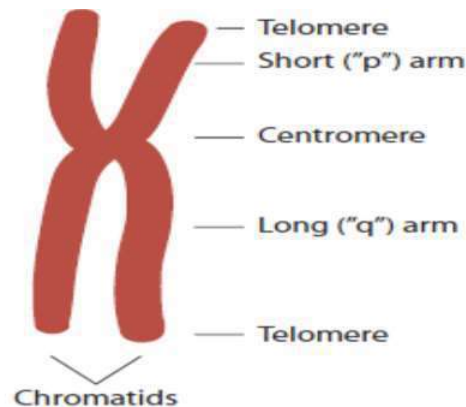
KEY POINTS

Chromosome a threadlike structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes.

- **1900**, Mendel's inherited factors on chromosomes also found sex chromosomes and sex linked diseases and traits.
- **1902** Walter Sutton, Theodor Boveri noted that chromosomes are paired in somatic cells, that reduction division or meiosis occurs within gametes.

Chromosome in Eukaryotes different from **Chromosomes in Prokaryotes**

Chromosome structure



The human genome **24 chromosomes** (**22 autosomes** and **2 sex chromosomes**).

Chromosomes are stained with A-T (**G bands**) and G-C (**R bands**) base pair specific dyes.

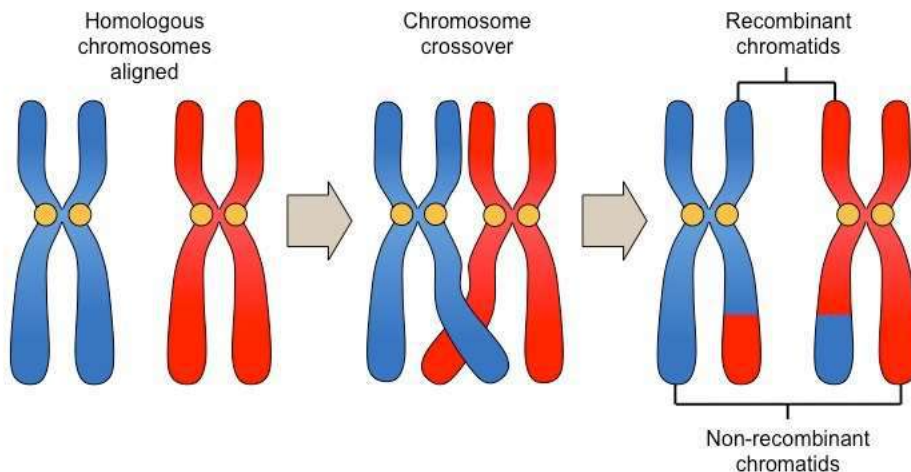


KEY POINTS

G-banding is obtained with **Giemsa stain** yielding a series of **lightly and darkly stained bands**. The dark regions tend to be **heterochromatic** that is A-T rich. The light regions tend to be **euchromatic** and G-C rich.

R-banding is the **reverse** of G-banding where the dark regions are **euchromatic** and the bright regions are **heterochromatic**.

Chromosomes crossover → providing genetic variation





Lecture 3 Questions Practice

Q1:- Define the followings:

- a. Centromere.
- b. Chromosome.

Q2:- Mark the following sentences TRUE OR FALSE:

- a. During cell division the nuclear material organize themselves into visible thread like structures which were named as chromosomes that stains deep with basic dyes.
- b. Chromatin is only found in eukaryotic cells, with prokaryotic cells having a different arrangement of their genetic material called a genophore, a chromosome that doesn't contain chromatin.

Q3:- MCQ

- 1. Eukaryotic cells having?
 - a. Circular chromosomes.
 - b. Linear chromosomes.
 - c. Zigzag chromosomes.
 - d. Chromosomes like structures.
- 2. Prokaryotic cells usually containing?
 - a. Circular chromosomes.
 - b. Linear chromosomes.
 - c. Zigzag chromosomes.
 - d. Chromosomes like structures.



Cytogenetic

2nd lecture

Mitosis & Meiosis

OBJECTIVES



→ Cell Cycle

→ Mitosis

→ Meiosis

OBJECTIVES



→ Pull your socks up



Cell Cycle- Cell Division Cycle

The **cell cycle**, or **cell-division cycle**, is the series of events that take place in a cell that cause it to divide into two daughter cells. These events include the duplication of its **DNA (DNA replication)** and some of its **organelles**, and subsequently dividing of its **cytoplasm** and other **components** into two **daughter cells**.

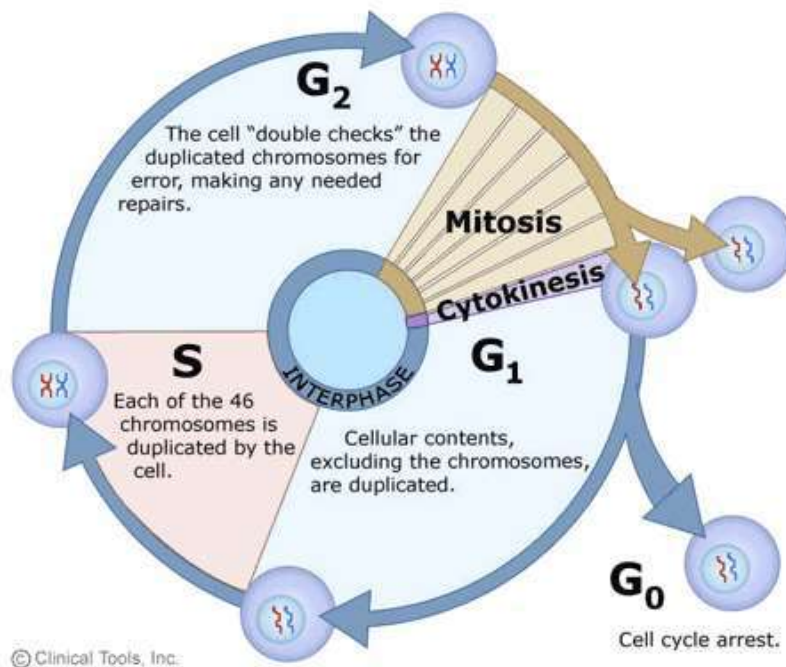
A cell spends **most** of its **lifetime** in what is called **interphase**, and during this time it **grows, replicates its chromosomes**, and **prepares for cell division**. The cell then leaves interphase, undergoes **mitosis**, and **completes its division**. The resulting cells, known as **daughter cells**, each enter their own interphase and begin a new round of the cell cycle.

Cell Cycle- Cell Division Cycle

In **Eukaryotic cells**, or cells with a nucleus, the stages of the cell cycle are divided into **two major phases: interphase** and the **mitotic (M) phase**.

During **interphase**, the cell **grows** and makes a **copy** of its **DNA**.

During the **mitotic (M) phase**, the cell **separates** its **DNA** into **two sets** and **divides** its **cytoplasm**, forming two new cells.





Cell Cycle- Cell Division Cycle

1. **G1 (Gap 1) phase.** The cell grows.
2. **S (Synthesis) phase.** The cell makes copies of its chromosomes. Each chromosome now consists of two sister chromatids.
3. **G2 (Gap 2) phase.** The cell checks the duplicated chromosomes and gets ready to divide.
4. **M (Mitotic) phase.** The cell separates the copied chromosomes to form two full sets (mitosis) and the cell divides into two new cells (cytokinesis).
5. The period between cell divisions is known as **interphase**. Cells that are not dividing leave the cell cycle and stay in **G0 (Gap 0)**.



Interphase

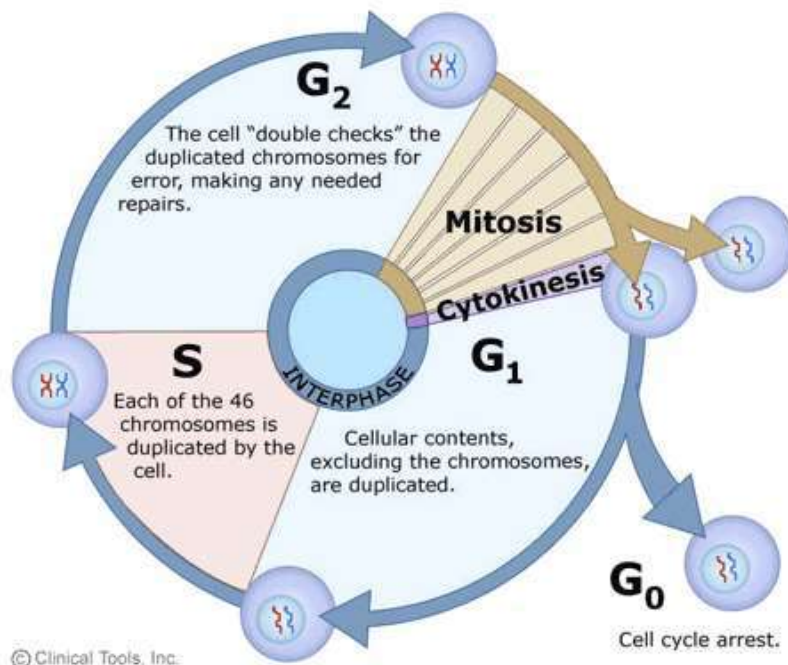
The cell cycle starts just as a cell forms, by division of its mother cell. What must this newborn cell do next if it wants to go on and divide itself? Preparation for division happens in **three steps:-**

1. **G1 phase**, first gap phase, the **cell grows physically larger**, copies organelles, and makes the molecular building blocks it will need in later steps.
2. **S phase**, synthesis phase, the **cell synthesizes a complete copy of the DNA** in its nucleus. It also duplicates a microtubule-organizing structure called the **centrosome**. The centrosomes help **separate DNA during M phase**.

Interphase

3. **G₂ phase**, second gap phase, the cell grows more, makes proteins and organelles, and begins to reorganize its contents in preparation for mitosis. G₂ phase ends when mitosis begins.

The G₁, S and G₂ phases together are known as **interphase** (inter, means between) reflecting that interphase **takes place between** one **mitotic (M) phase** and the next.





Mitotic (M) Phase

Mitosis is a type of cell division that results in two daughter cells each having the same number and kind of chromosomes as the parent nucleus, typical of ordinary tissue growth.

During the mitotic (M) phase, the cell divides its copied DNA and cytoplasm to make two new cells. M phase involves two distinct division-related processes, karyokinesis (**mitosis**) and **cytokinesis**.

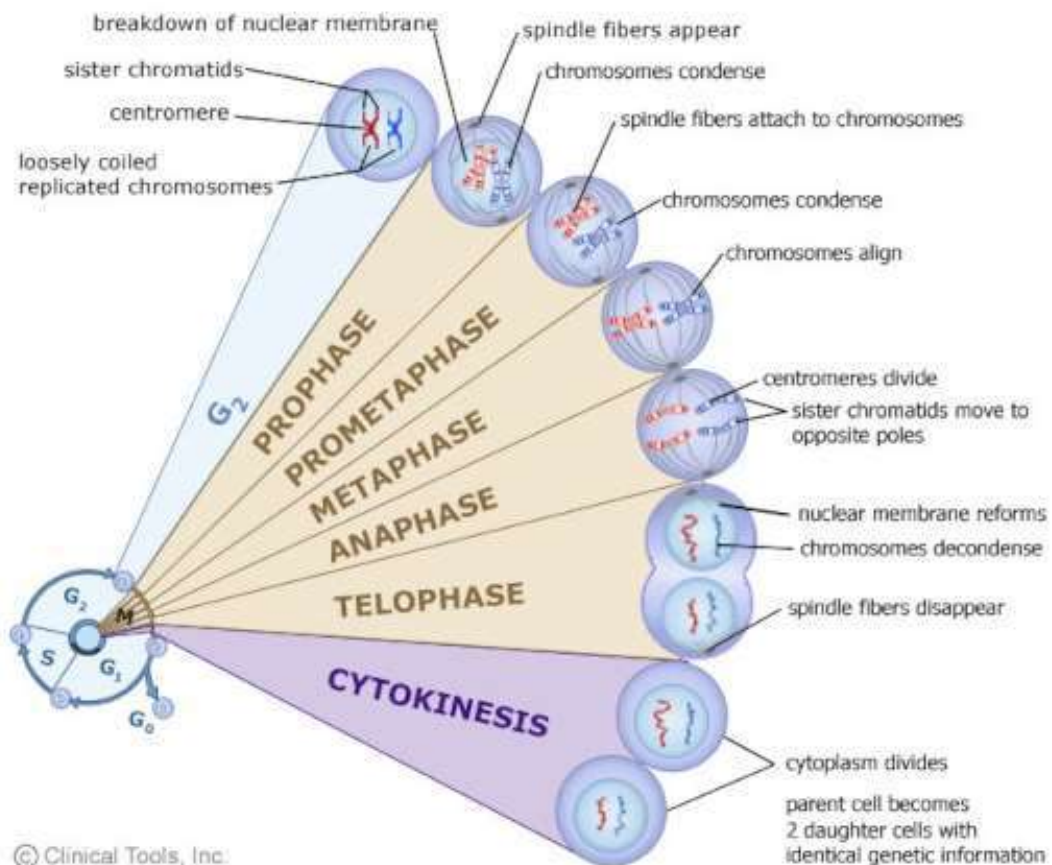
In **mitosis (karyokinesis)**, the nuclear DNA of the cell **condenses** into **visible chromosomes** and is pulled apart by the **mitotic spindle**, a specialized structure made out of microtubules.

Mitosis takes place in four stages: **prophase, prometaphase, metaphase, anaphase, and telophase.**

Mitotic (M) Phase

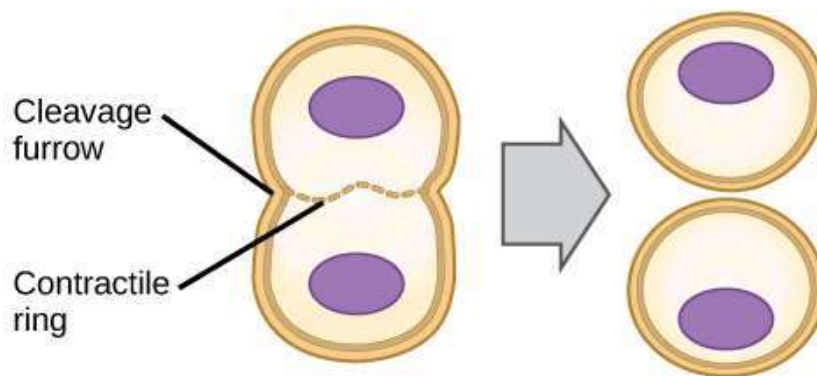
In **cytokinesis**, the cytoplasm of the cell is split in two, making two new cells. Cytokinesis usually begins just as mitosis is ending, with a little overlap. Importantly, cytokinesis takes place differently in animal and plant cells.

The process of mitosis involves a number of different stages.



Mitotic (M) Phase

In animals, cell division occurs when a band of cytoskeletal fibers called the **contractile ring** contracts inward and pinches the cell in two, a process called contractile cytokinesis. The indentation produced as the ring contracts inward is called the **cleavage furrow**. Animal cells can be pinched in two because they're relatively soft and squishy.





Cell Cycle Exit and G0

What happens to the two daughter cells produced in one round of the cell cycle?

This depends on what type of cells they are. Some types of cells divide rapidly, and in these cases, the daughter cells may immediately undergo another round of cell division. For instance, many cell types in an early embryo divide rapidly, and so do cells in a tumor.

Other types of cells divide slowly or not at all. These cells may exit the G1 phase and enter a resting state called G0. In G0, a cell is not actively preparing to divide, it's just doing its function. For instance, it might conduct signals as a neuron or store carbohydrates as a liver cell. G0 phase is a permanent state for some cells, while others may re-start division if they get the right signals.



Cell Cycle Time

How long does the cell cycle take?

Different cells take different lengths of time to complete the cell cycle. A typical human cell might take about 24 hours to divide, but fast-cycling mammalian cells, like the ones that line the intestine, can complete a cycle every 9-10 hours when they're grown in culture.

Different types of cells also split their time between cell cycle phases in different ways. In early frog embryos, cells spend almost no time in G1 and G2 and instead rapidly cycle between S and M phases, resulting in the division of one big cell, the zygote, into many smaller cells.



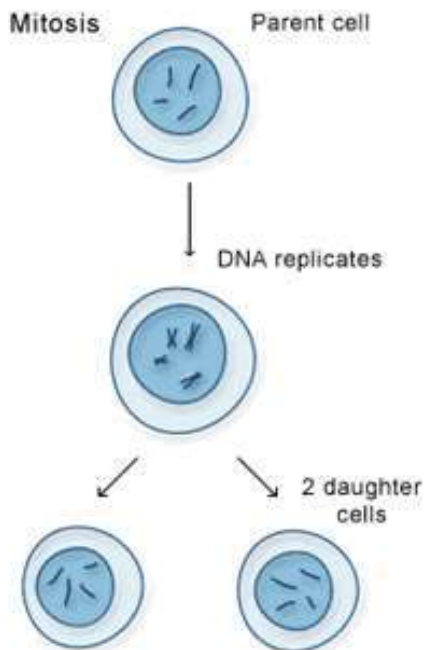
Meiosis

Meiosis is a type of cell division that results in four daughter cells each with half the number of chromosomes of the parent cell, as in the production of gametes and plant spores.

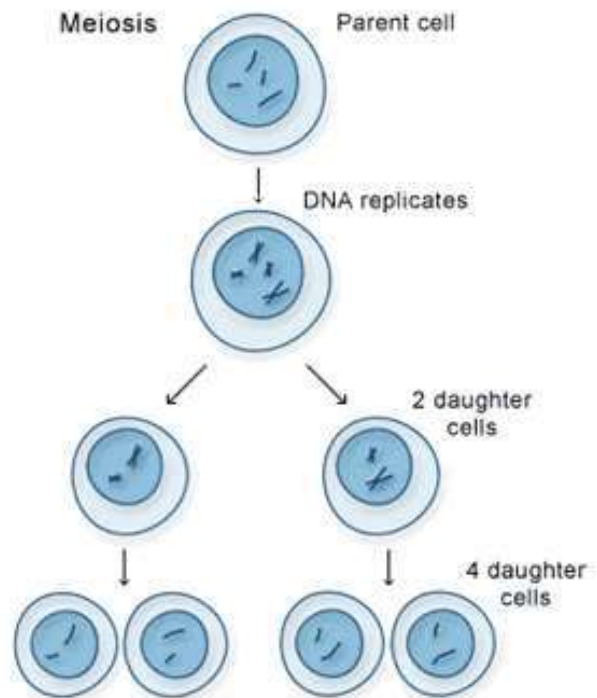
Meiosis is used to make **special cells** such as **sperm** cells and **ovum** cells which have **half the normal number of chromosomes (n)**. It **reduces** the number from **23 pairs of chromosomes** to **23 single chromosomes**.

The cell **copies** its **chromosomes**, but then **separates** the **23 pairs** to ensure that each **daughter cell** has only **one copy** of **each chromosome**. A **second division** that **divides** each **daughter cell** again to produce **four daughter cells**.

Meiosis



U.S. National Library of Medicine





Meiosis

Meiosis separates the pairs of matching (homologous) chromosomes, so that sperm cells and ovum cells have only one copy of each. That way, when an ovum cell fuses with a sperm cell (during fertilization), the fertilized ovum has a full set which means, two copies of every chromosome.

Meiosis involves two cell divisions, **Meiosis I** and **Meiosis II**.

Meiosis I separates the matching (homologous) pairs of chromosomes.

Meiosis II divides each chromosome into two copies (much like mitosis).

Meiosis

Two stages

Meiosis I

Segregation

Homologous pairs are separated
reducing chromosome number by half



Interphase germ cell in gonads



Prophase I *Synapsis for crossing over*



Metaphase I



Anaphase I *Independent assortment*



Telophase I

Meiosis II

Sister chromatids are separated
producing four haploid gametes



Prophase II



Metaphase II



Anaphase II



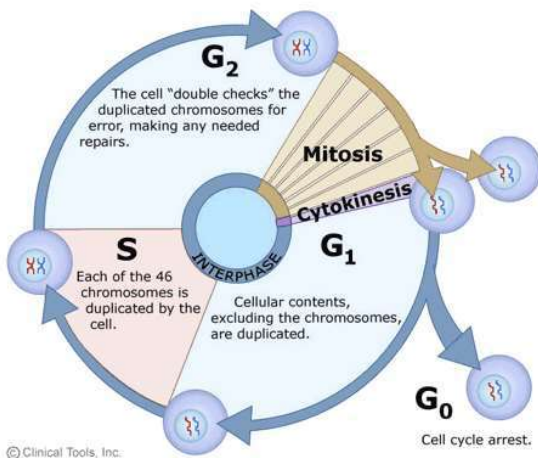
Telophase II





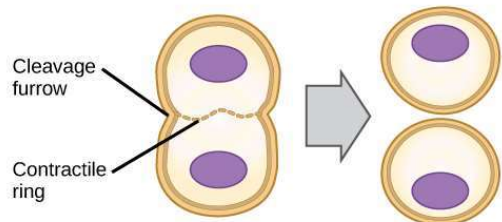
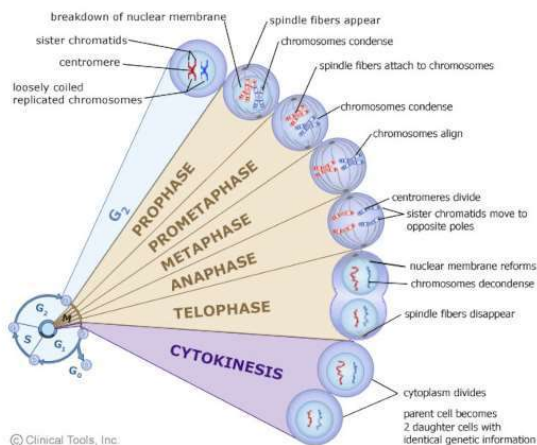
KEY POINTS

The **cell cycle**, or **cell-division cycle**, is the series of events that take place in a cell that cause it to divide into two daughter cells.



Mitosis is a type of cell division that results in two daughter cells each having the same number and kind of chromosomes as the parent nucleus, typical of ordinary tissue

The process of mitosis involves a number of different stages.





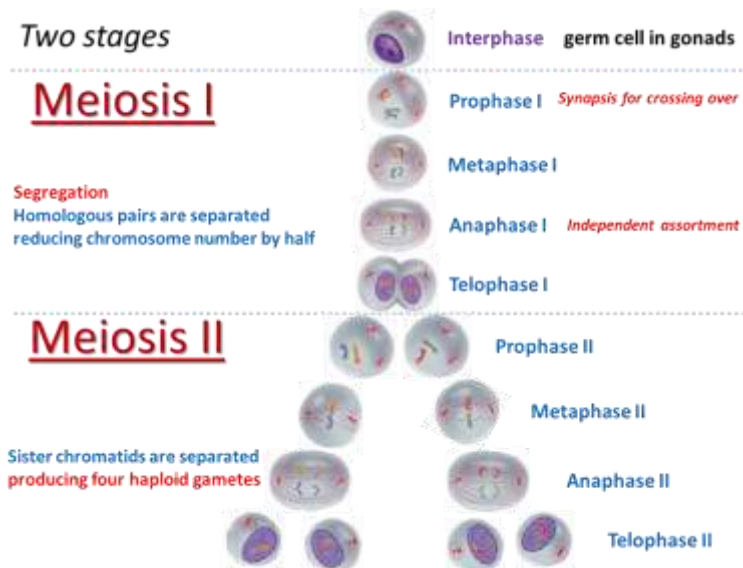
KEY POINTS

Meiosis is a type of cell division that results in four daughter cells each with half the number of chromosomes of the parent cell, as in the production of gametes and plant spores.

Meiosis involves two cell divisions, **Meiosis I** and **Meiosis II**.

Meiosis I separates the matching (homologous) pairs of chromosomes.

Meiosis II divides each chromosome into two copies (much like mitosis).





Lecture 2 Questions Practice

Q1:- Define the followings:

- a. Centrosome.
- b. Meiosis.

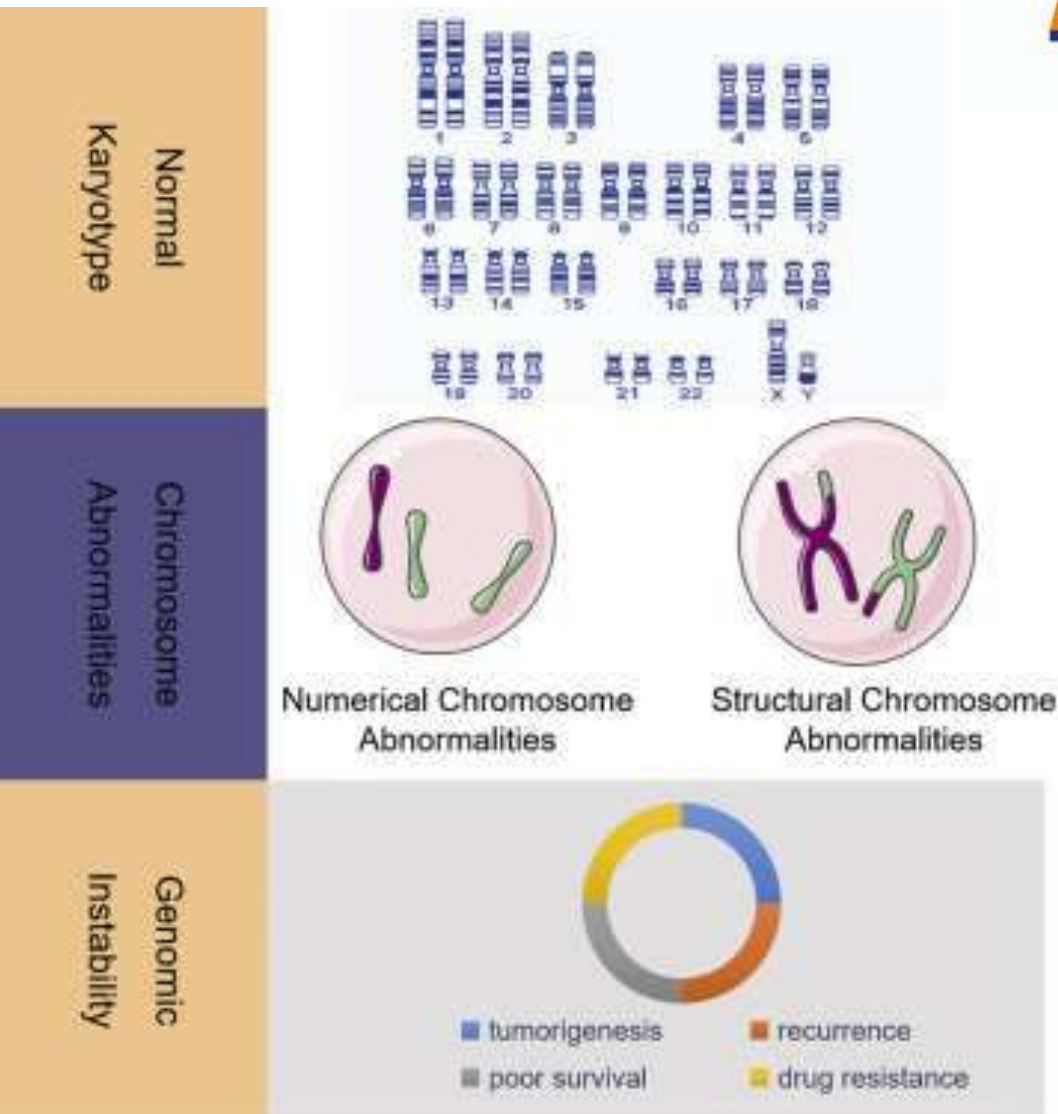
Q2:- Describe BRIEFLY the followings:

- a. G₂ (Gap₂) phase.
- b. M (Mitotic) phase.

Q3:- MCQ

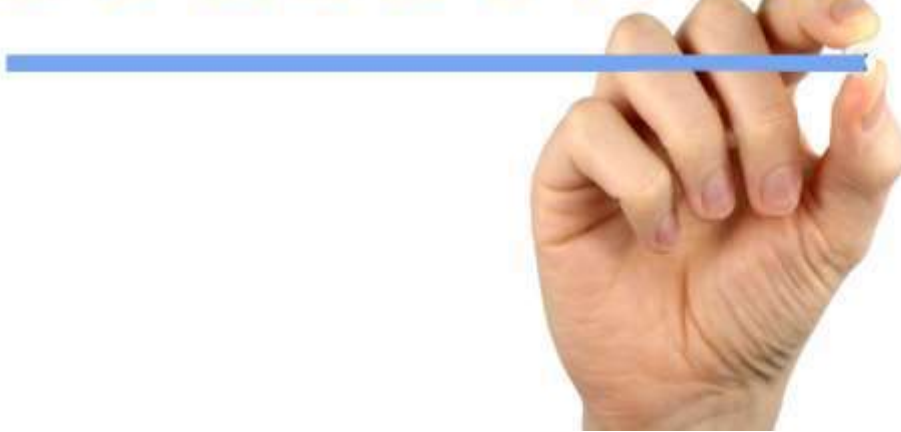
1. Mitosis takes place in ----- stages?
 - a. One stage.
 - b. Two stages.
 - c. Three stages.
 - d. Four stages.
 - e. Five stages.
2. Meiosis involves two cell divisions?
 - a. Meiosis II and Meiosis III.
 - b. Meiosis I and Meiosis II.
 - c. Meiosis III and Meiosis IV.

Cytogenetic



17th lecture Chromosomes and Cancer Oncogenes

OBJECTIVES



- Introduction
- Chromosomal Instability CIN & Chromosome Structure Instability CSI
- Mechanism of CIN & CSI
- Oncogenes
- Proto-Oncogenes
- Oncogene Activation
- Oncoproteins



Introduction

Normal cells have **46 chromosomes**, but cancer cells often have **fewer or extra** chromosomes. A missing or extra copy of chromosomes creates an **imbalance** called **aneuploidy**. This imbalance can **skew** the activity of hundreds or thousands of genes.

Approximately 90% of solid tumors exhibit aneuploidy, and aneuploid tumors are associated with **decreased overall survival in patients**.

Despite the prevalence of aneuploidy in cancer, scientists have a limited understanding of how aneuploidy affects cancer and how it affects patients' responses to treatment.

Scientist found that increasing the number of specific chromosomes in colon cancer cells had distinct effects on the cancer's invasive behavior. For instance, addition of an extra copy of the studied chromosomes had **no effect** or **stopped the growth and spread** of colon cancer. Nonetheless, an **extra copy of chromosome 5 helped cancers spread**.



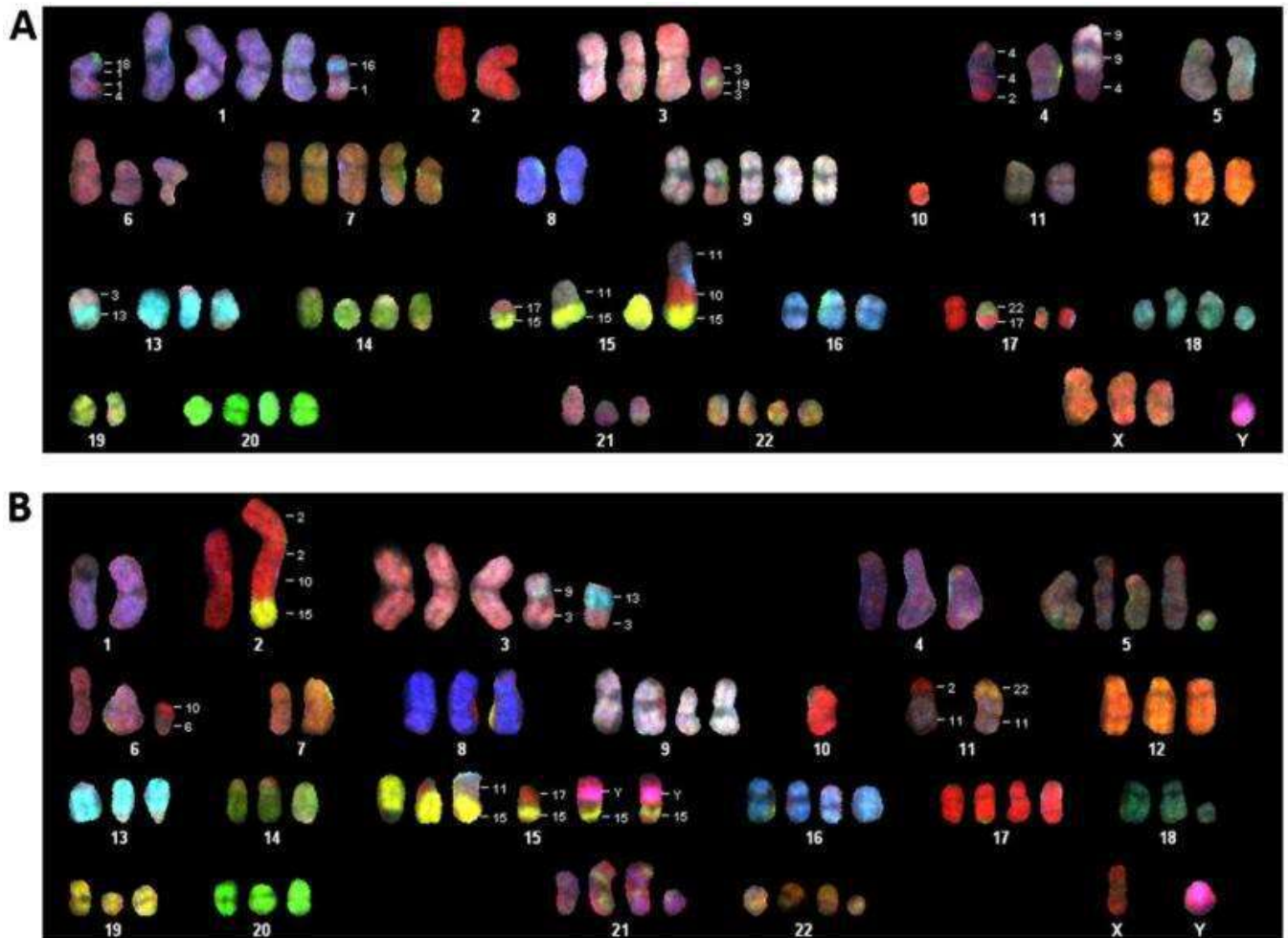
Chromosome Instability CIN & Chromosome Structure Instability CSI

Two prominent features of cancer cells are **abnormal numbers of chromosomes** (aneuploidy) and **large-scale structural rearrangements of chromosomes**. These chromosome aberrations are caused by **genomic instabilities** inherent to most cancers.

Aneuploidy arises through **chromosomal instability (CIN)** by the persistent **loss** and **gain** of **whole chromosomes**. Chromosomal rearrangements occur through **chromosome structure instability (CSI)** as a consequence of **improper repair of DNA damage**. Both, CIN and CSI are evident in the **karyotypes of cancer cells**.

Equally, CIN and CSI are associated with advanced stage tumors with increased **invasiveness** and **resistance** to **chemotherapy**, indicating that targeted inhibition of these instabilities might slow tumor growth.

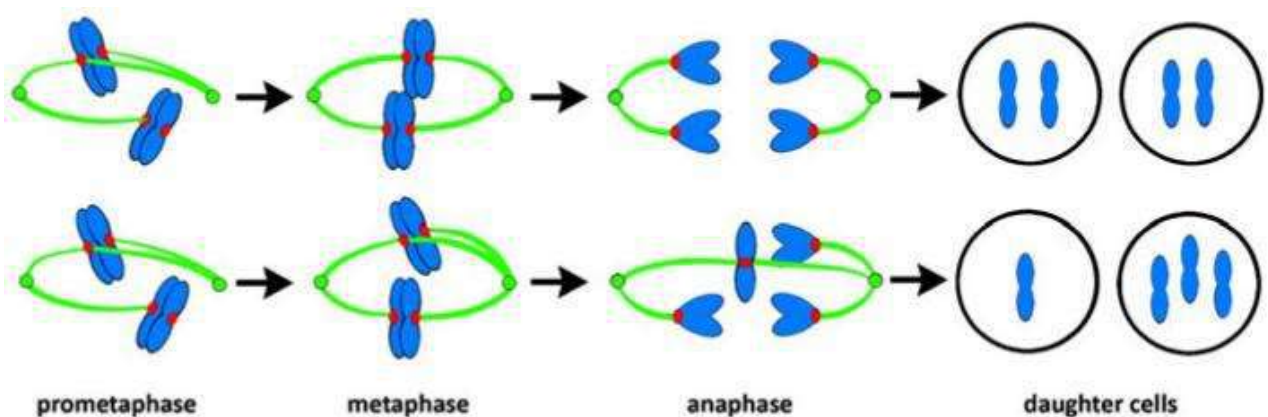
Spectral Karyotyping (SKY) Showing Both CIN & CSI



Mechanism of CIN

Whole chromosome instability occurs through **mis-segregation of chromosomes** during mitosis. Cancer cells with CIN mis-segregate a chromosome about once every one to five divisions, compared to rates of one chromosome per a hundred cell divisions in stable, diploid cell lines.

CIN may occur due to errors in the **mitotic spindle checkpoint** and sister chromatid cohesion. Evidence from human cancer cell lines suggests a specific **kinetochore-microtubule (kMT)** attachment error called **merotely** is the major source of chromosome segregation errors causing CIN.





Mechanism of CSI

In addition to alterations in whole chromosome numbers, cancer cells often contain chromosomes with large **structural rearrangements**, including deletions, duplications, inversions, isochromosomes, ring structures and marker chromosomes, and unbalanced translocation (inherited from a parent) and balanced translocations (not inherited).

Balanced translocations are frequently associated with **leukemias** and **lymphomas**.

Unbalanced translocations associated with ~1% of **developmental delay** and **intellectual disability**.

These translocations usually represent the **single oncogenic change** responsible for these cancers as they create **driver mutations that initiate and maintain the cancer cell phenotype**.



Mechanism of CSI

Chromosomal translocations arise through **inappropriate repair of DNA double strand breaks**. Developing tumors often go through a period of elevated rates of chromosome structure change termed the **breakage–fusion–bridge cycle**.

This occurs when the number of telomere repeats (*6-bp-repeat sequences which cap the ends of each chromosome—in humans, telomeres become shorter after each division*) drop below a critical threshold where they no longer prevent chromosomes from **fusing to each other**, leading to the formation of **dicentric chromosomes (possessing two centromeres)**.

Dicentrics form bridges between daughter cells during late mitosis and frequently break during abscission. DNA double strand break repair mechanisms then fuse the broken chromosomes generating chromosomal translocations that are, again, dicentric, and this cycle continues for several cell cycles.

Incorrect copying of chromosomes can lead to other problems as well. Genes that should be present may be deleted or deactivated. But if the **repair genes** themselves don't work properly, there may be little to prevent this loss of control.



Oncogenes

Oncogenes first were discovered in certain **retroviruses** (viruses composed of RNA instead of DNA and that contain **reverse transcriptase**) and were identified as **cancer-causing agents** in many animals.

In the mid-1970s, the American microbiologists John Michael Bishop and Harold Varmus tested the theory that healthy body cells contain dormant viral oncogenes which, when triggered, cause cancer. They showed that oncogenes are actually derived from normal genes (**proto-oncogenes**) present in the body cells of their host.

Oncogene is a gene that has the potential to cause cancer. An oncogene is a mutated gene that contributes to the development of a cancer. In their normal, unmutated state, onocgenes are called **proto-oncogenes**, and they play roles in the **regulation of cell division**.



Proto-Oncogenes

Within every cell in our body is a class of genes known as **proto-oncogenes**, which play important roles in **controlling cell division and cell death** during our growth and development.

However, if a **proto-oncogene becomes mutated**, or the cell makes extra copies of the proto-oncogene, it can become **hyper-activated** and lead to the appearance of **uncontrolled cell division**. This therefore contributes to the development of a **cancer cell** from a normal cell.

Once a **proto-oncogene** is **activated** by a **mutation**, it become an **oncogene**. So the activation of oncogenes that's one type of **genetic lesion** that contributes to the development of a **tumor**.



Oncogene Activation

There are a number of ways in which normal proto-oncogenes can become activated (changed) so that they become oncogenes.

The process can begin when carcinogens (cancer-causing agents) in the environment cause a mutation or amplification of a proto-oncogene.

Studies on animals have shown that chemical carcinogens can cause the mutations that convert *ras* proto-oncogenes to oncogenes. This finding is fitting, as KRAS mutations in lung cancer are more common in people who have smoked than never smokers.

It's well known that DNA damage may occur as an accident during the normal growth of cells. Therefore, even if we lived in a world free from carcinogens, cancer would occur.



Oncogene Activation

DNA damage can take one of several forms:-

Point mutations: Changes in a single base (nucleotide), as well as insertions or deletions in DNA can result in the substitution of a single amino acid in a protein that changes the function.

Gene amplifications: Extra copies of the gene result in more of the gene product (proteins that lead to cell growth) being produced or "expressed."

Translocations/rearrangements: Movement of a portion of DNA from one place to another can occur in a few ways. Sometimes a **proto-oncogene is relocated** to another site on a chromosome, and because of the location, there is a higher expression (larger amounts of the protein is produced). Other times, a **proto-oncogene may become fused with another gene** that change the proto-oncogene to an oncogene (more active).

Mutations may also occur in a **regulatory** or **promoter** region near the **proto-oncogene**.



Oncoproteins

Oncoproteins are the product (the proteins) that are coded for by oncogenes and are produced when the gene is transcribed and translated.

There are many types of oncoproteins depending on the specific oncogene present, but most work to:-

1. Stimulate cell growth and division.
2. Inhibit programmed cell death (apoptosis).
3. Inhibit cellular differentiation.
4. These proteins can also play a role in the **progression** and **aggressiveness** of a tumor that is already present.



KEY POINTS

4. xxxx



Lecture 17 Questions Practice

Q1:- Explain BRIEFLY the mechanism of the followings:

- a. CSI.
- b. CIN.

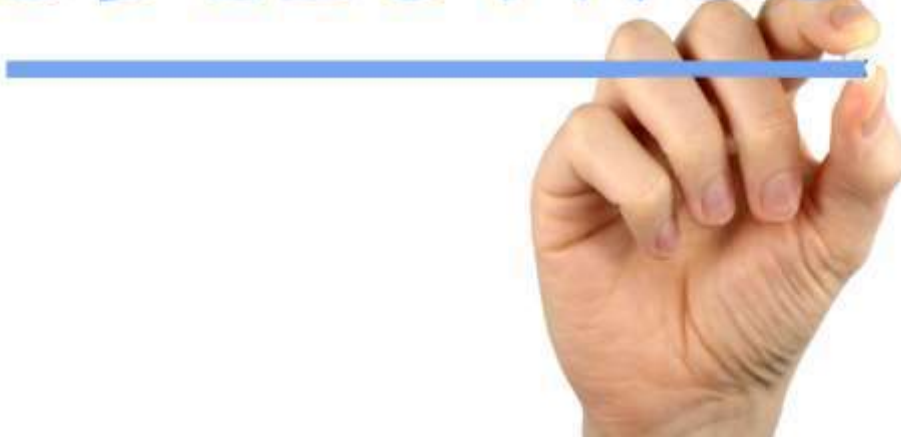


Cytogenetic

1st lecture

Cell Division

OBJECTIVES



- Human Genetics
- Introduction - The Cell Theory
- Cell Organelles

Human Genetics





Human Genetics

Human genetics is the study of inheritance as it occurs in human beings which involves a variety of overlapping fields including classical genetics, cytogenetics, molecular genetics, biochemical genetics, genomics, population genetics, developmental genetics, clinical genetics, and genetic counseling.

Study of human genetics can **answer questions** about **human nature**, can help **understand diseases** and the **development** of **effective treatment** and help us to understand the **genetics** of **human life**.



Human Genetics

Medical genetics is the branch of medicine that involves the diagnosis and management of hereditary disorders.

Medical genetics is the **application** of **genetics** to **medical care**. For instance, research on the **causes** and **inheritance** of **genetic disorders** would be considered within both **human genetics** and **medical genetics**, while the **diagnosis**, **management**, and **counseling** of individuals with genetic disorders would be considered part of **medical genetics**.



Human Genetics

Common Terms in Medical Genetics

Genetics is the study of genes and their effects.

Genomics is the study not just of single genes but of the functions and interactions of many genes in the genome.

Medical genetics is any application of genetic principles to medical practice. This includes studies of inheritance, mapping disease genes, diagnosis and treatment, and genetic counseling.

Pharmacogenetics is the study of how drugs affect the body with respect to specific genetic backgrounds. Knowledge of these effects can improve effectiveness of drugs and minimize side effects on an individual –patient basis.



Introduction- The Cell Theory

One very important similarity among all living things is that they are made of **cells**, the smallest units of life. In 1838, two biologists, **Schleiden** and **Schwann**, studied many cells and made some conclusions. From their observations they developed what is known as the **Cell Theory**. Since then, this theory has been central to our understanding of biology. This theory states that:

1. All life forms are made from one or more cells. Some organisms, like bacteria or paramecium, are only one cell big. These are called **unicellular organisms** (uni=one). Other organisms are **multicellular organisms** that means they are made up of more than one cell (multi=more than one). For example, the human body consists of billions of cells.



Introduction- The Cell Theory

2. **Cells** only **arise** from **pre-existing cells**. A cell can make copies of everything it has inside it, then divide itself in two, making **two new cells**. This process is called **mitosis**, or **cell division**. In this way, organisms can keep **growing** or replace **damaged** or **old** cells. For example, the formation of new cells is what allows your body to grow, or what replaces your damaged skin when you fall and skin your knee, making you good as new.

3. The cell is the **smallest form of life**. There is nothing smaller that is alive, and life requires what is inside a cell. For example, the molecules that make up the parts of the cell, such as **sugars**, **fats** and **proteins** are not alive. The separate regions of the cell are **not alive** on their own. Life can only be reduced down to the cellular level. Thus, cells are the smallest unit of life.

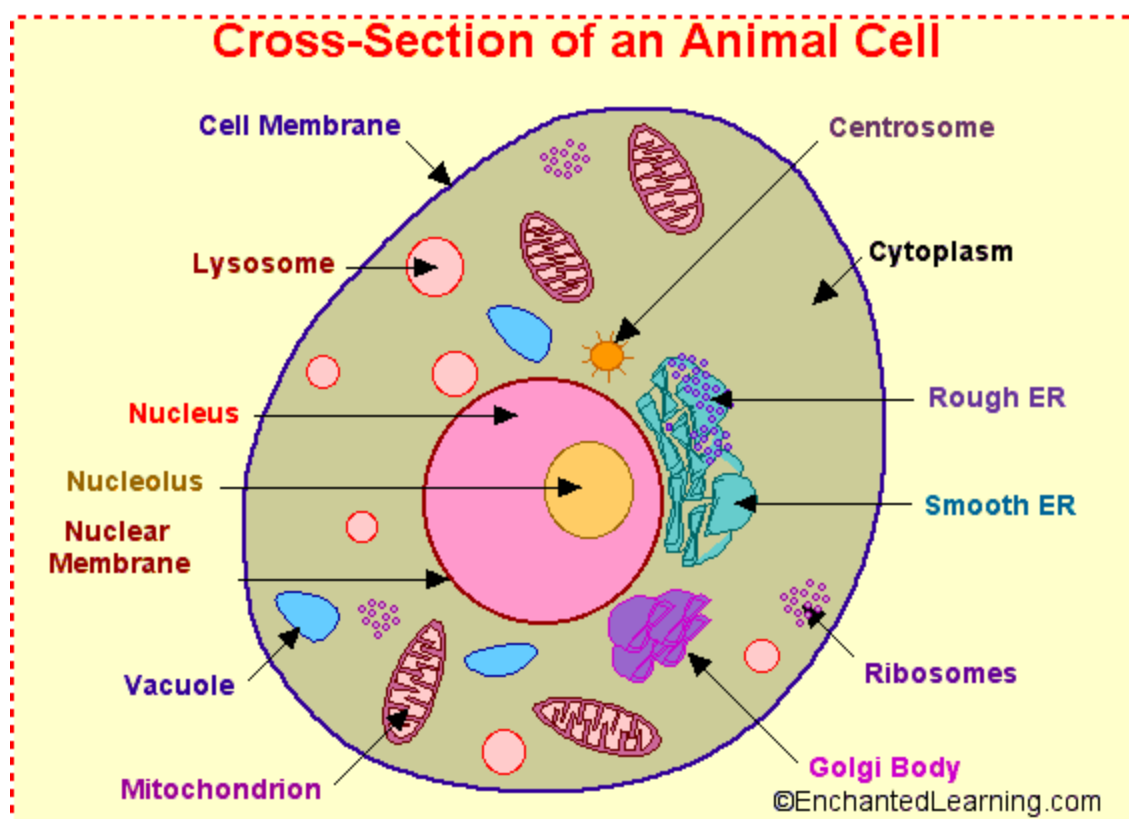


Cell Organelles

The cell is made up of smaller parts. These parts are call **organelles** (little organs). They **divide up** all the **work** that the cell has to do. In the human body, we have different organs to do different jobs that help us live. For instance, our lunges help us breathe while our brain helps us think. It's the same in a cell. The **different organelles** have **different jobs**, and **together** they help the **cell live**.

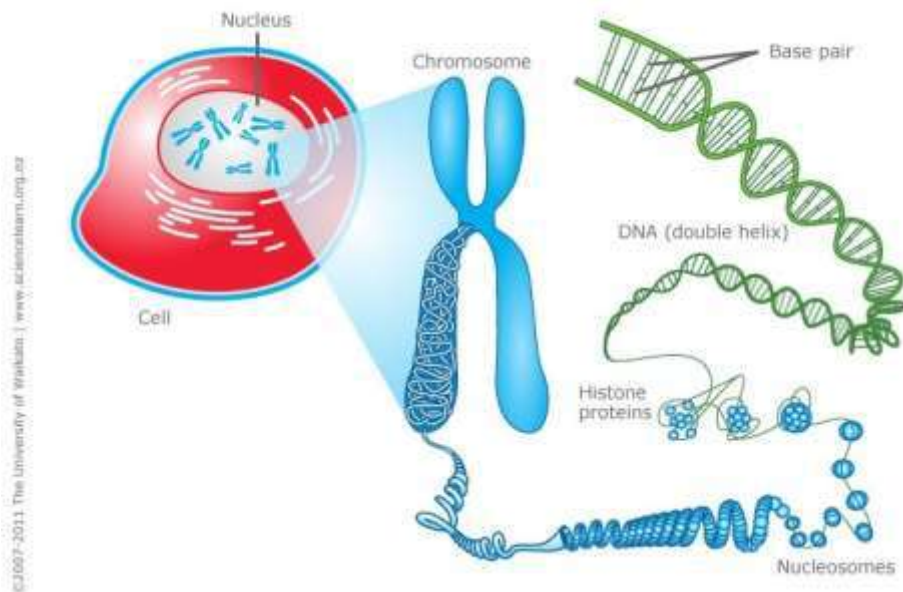
In a **unicellular organism**, one cell does all the jobs the being needs to survive, and the cell divides up these jobs among its organelles. In **multicellular organisms**, many cells come together to make a living being. Just like in unicellular organisms, the cells of a multicellular organism have organelles which **divide up the cell's work**.

Cell Organelles



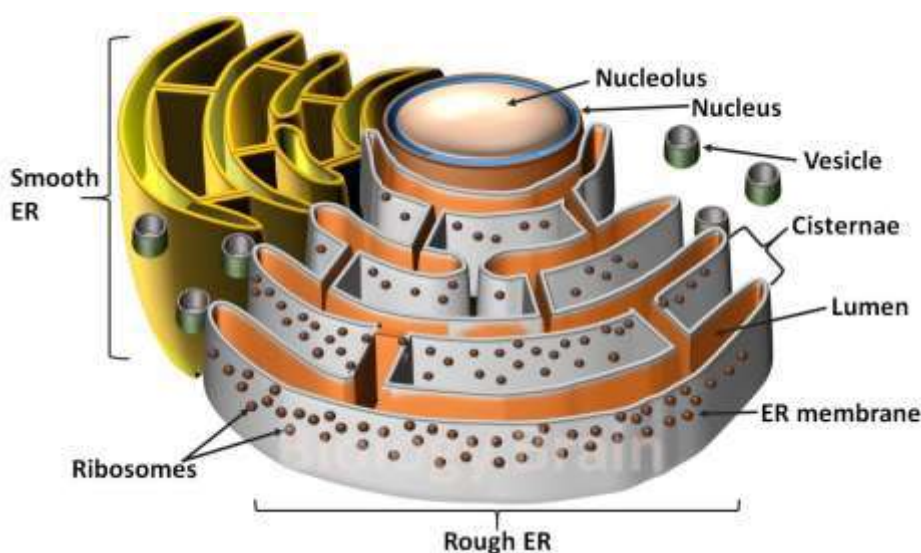
Nucleus

The nucleus is the **control center** of the cell. It **contains** all the genetic information, DNA in the form of chromatin, that informs the cell what to do. DNA contains all the instructions, and the **organelles** of the cell help to read it and build the final products **proteins**. When the cell reads its DNA instructions, it converts these instructions to another form called **messenger RNA (mRNA)**, which is like translating from one language to another in a process called **transcription**.



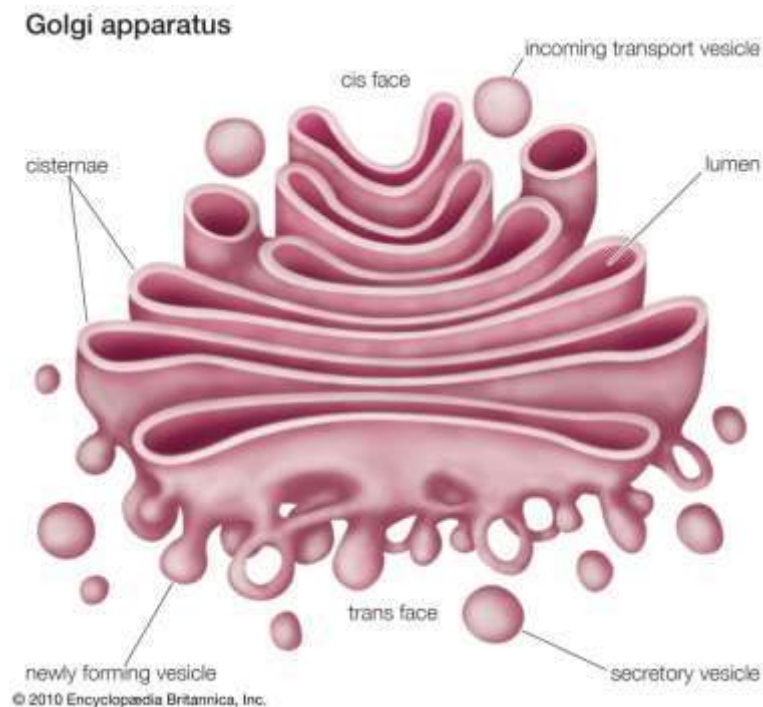
Endoplasmic Reticulum

The **ER** is like a little maze of tubes that are hollow inside which contains **ribosomes**, so called **rough ER**. After mRNA is made in the nucleus, it is sent to the ribosomes for reading the mRNA message and making the proper protein according to its instructions. This process is called **translation**. As a protein is made, or translated, the ribosomes sends it into the ER. A second type of ER, called the **smooth ER** is where fats are formed. It is called **smooth** ER because it has no **ribosomes** on it.



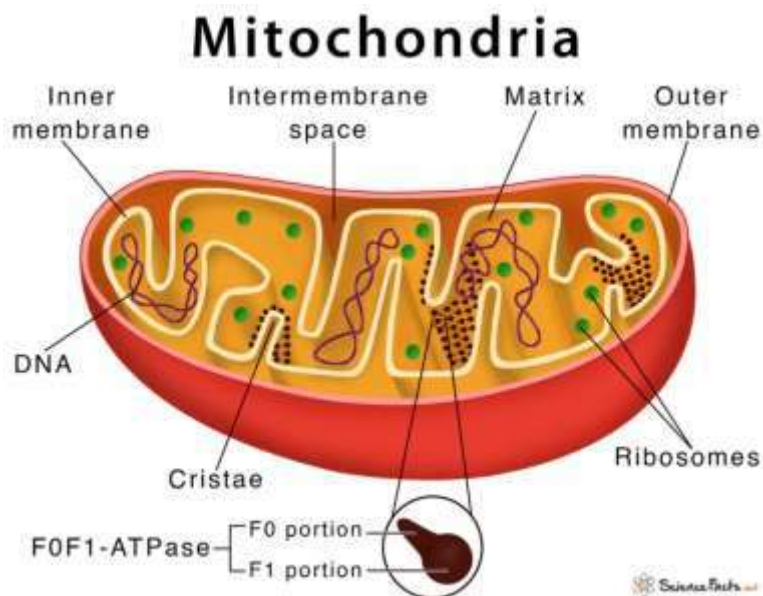
Golgi Apparatus

The proteins made by the ribosomes that are inside the ER are sent to the Golgi apparatus for **post translational modifications** and **distribution**. Here, the protein may be **packaged** or **changed**.



Mitochondria

Spherical to rod-shaped organelles with a double membrane. The inner membrane is folded many times, forming a series of projections called cristae. The mitochondrion **converts** the **energy** stored in **glucose** into **ATP** (adenosine triphosphate) for the cell.

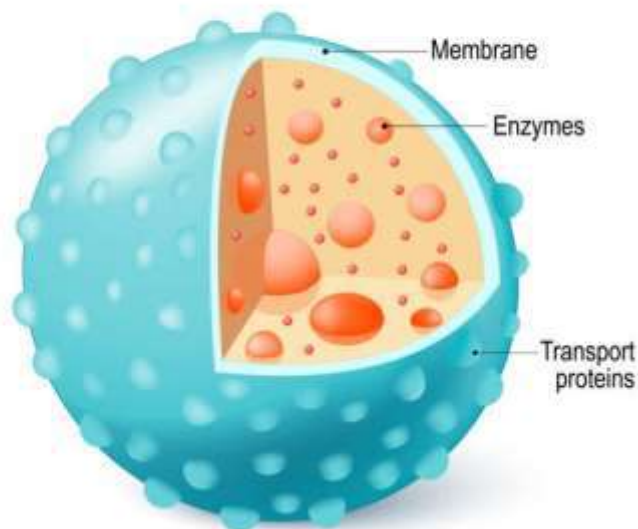


Lysosome

the **lysosome**, which is full of **enzymes** that can break down cellular debris.

Lysosomes are the **garbage dumps** of the cell, they break down waste and dispose of it properly.

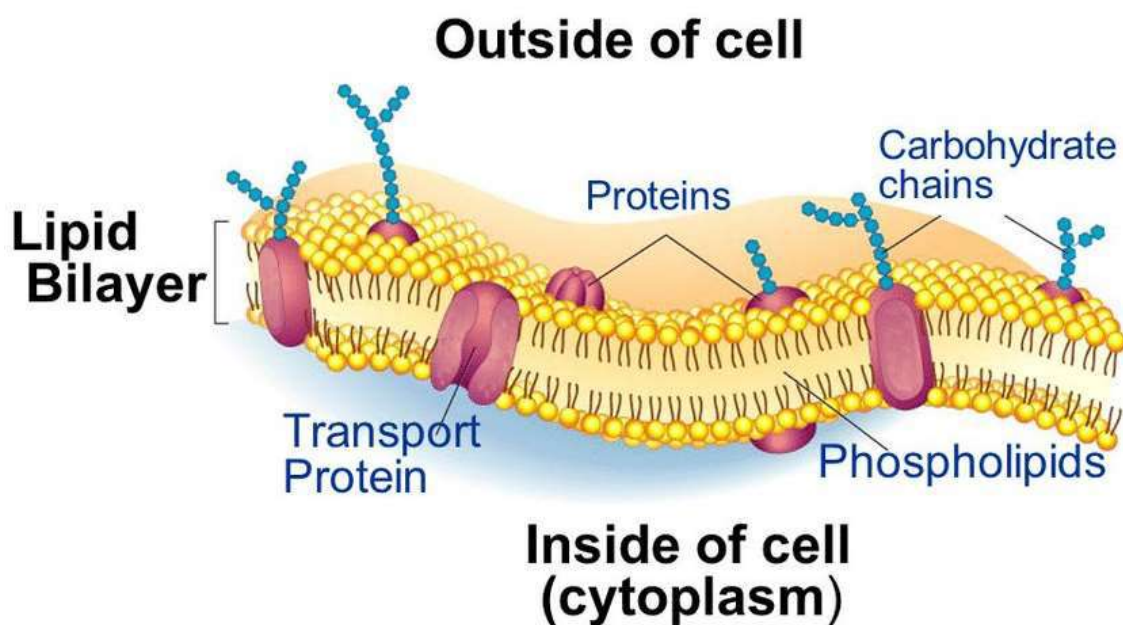
LYSOSOME



Plasma Membrane

Plasma membrane, that gives the cell its shape. This membrane helps control what **goes in and out** of the cell, and helps **protect** the cell from damaging effects of the environment.

Inside the plasma membrane is a gel-like fluid called the **cytosol** that surrounds the organelles.





Cell Division

The cell is the basic unit of life. They consist mostly of **carbohydrates, lipids, proteins, and nucleic acids.**

Cell division is **fundamental** to the **growth** of all living organisms. In Eukaryotes, somatic cell division involves the division of the nuclear (**mitosis**) contents and the cytoplasm(**cytokinesis**).

Germ cells (sperm, ovum) undergo a specialized form of cell division called **meiosis**. Meiosis results in the production of **haploid gametes** (n) and also provides the opportunity for **genetic recombination**.



Cell Division

A human body is built of about 100 trillion cells. About 10% of them are replaced daily. For normal growth, repair, and development to occur, the cell numbers in a human body must be in **balance**. Mitotic cell division, or mitosis, provides new cells by forming two cells from one. Mitosis occurs in somatic cells (all cells but the sperm and eggs).

Some cells must die as a **body forms**. An **embryo foot**, for example, starts out as a **webbed triangle of tissue**. Toes emerge as certain cells die. This type of cell death, which is a normal part of development, is termed **apoptosis**.

Another form of cell death, called **necrosis**, is a response to injury or trauma. It is not part of normal development.



KEY POINTS

Human genetics is the study of inheritance as it occurs in human beings which involves a variety of overlapping fields including classical genetics, cytogenetics, molecular genetics, biochemical genetics, genomics, population genetics, developmental genetics, clinical genetics, and genetic counseling.

Medical genetics is the branch of medicine that involves the diagnosis and management of hereditary disorders.

Common Terms in Medical Genetics

Genetics is the study of genes and their effects.

Genomics is the study not just of single genes but of the functions and interactions of many genes in the genome.

Medical genetics is any application of genetic principles to medical practice. This includes studies of inheritance, mapping disease genes, diagnosis and treatment, and genetic counseling.

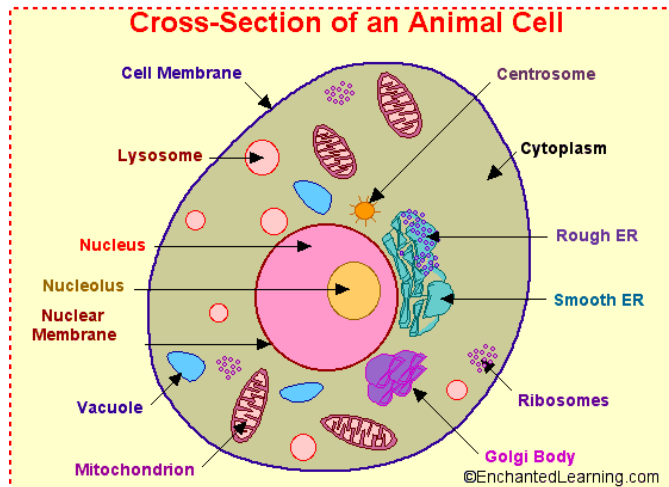
Pharmacogenetics is the study of how drugs affect the body with respect to specific genetic backgrounds. Knowledge of these effects can improve effectiveness of drugs and minimize side effects on an individual –patient basis.



KEY POINTS

The cell theory

1. All life forms are made from one or more cells.
2. **Cells** only arise from **pre-existing cells**.
3. The cell is the **smallest form of life**.



Cell division is **fundamental** to the **growth** of all living organisms. In Eukaryotes, somatic cell division involves the division of the nuclear (**mitosis**) contents and the cytoplasm(**cytokinesis**).

Germ cells (sperm, ovum) undergo a specialized form of cell division called **meiosis**. Meiosis results in the production of **haploid gametes** (n) and also provides the opportunity for **genetic recombination**.

Apoptosis & Necrosis



Lecture 1 Questions Practice

Q1:- Define the followings:

- a. Genetics.
- b. Genomics.

Q2:- Enumerate the followings:

- a. Numerate BRIEFLY cell theory aspects.

Q3:- MCQ

1. Some cells must die as a body forms. An embryo foot, for example, starts out as a webbed triangle of tissue. Toes emerge as certain cells die. This type of cell death, which is a normal part of development, is termed?
 - a. Necrosis.
 - b. Apoptosis.
 - c. Degeneration.
2. A type of cell death happens in response to injury or trauma is called?
 - a. Necrosis.
 - b. Apoptosis.
 - c. Degeneration.



Cytogenetic

16th lecture

The Genetic Basis of Cancer “Cancer and Genetics”

OBJECTIVES



- Introduction
- The Genetic Basis of Cancer
- Identifying Genetic Changes in Cancer
- Hereditary Cancer Syndrome



Introduction

Cancer is a genetic disease, caused by certain changes to genes that control the way cells function, **especially how they grow and divide**.

Genes carry the instructions to make proteins, which do much of the work in our cells. **Certain gene** changes can cause cells to **evade normal growth controls and become cancer**.

For instance, some **cancer-causing gene changes increase production of a protein** that makes **cells grow** nonstop. Others result in the production of a **nonfunctional protein** that normally repairs cellular damage.



The Genetic Basis of Cancer

Cancer is a **genetic disease** resulting from **inherited (congenital, germ line)** or **acquired (somatic)** mutations in some cells of the patient. Such changes may occur in particular oncogenes and are responsible for the tumor phenotype of the affected population of cells.

Oncogenes function by **continuous positive action** in the mitogenic “mitosis” pathway, and may become activated by **point mutations, chromosomal rearrangements or viral insertion events**.

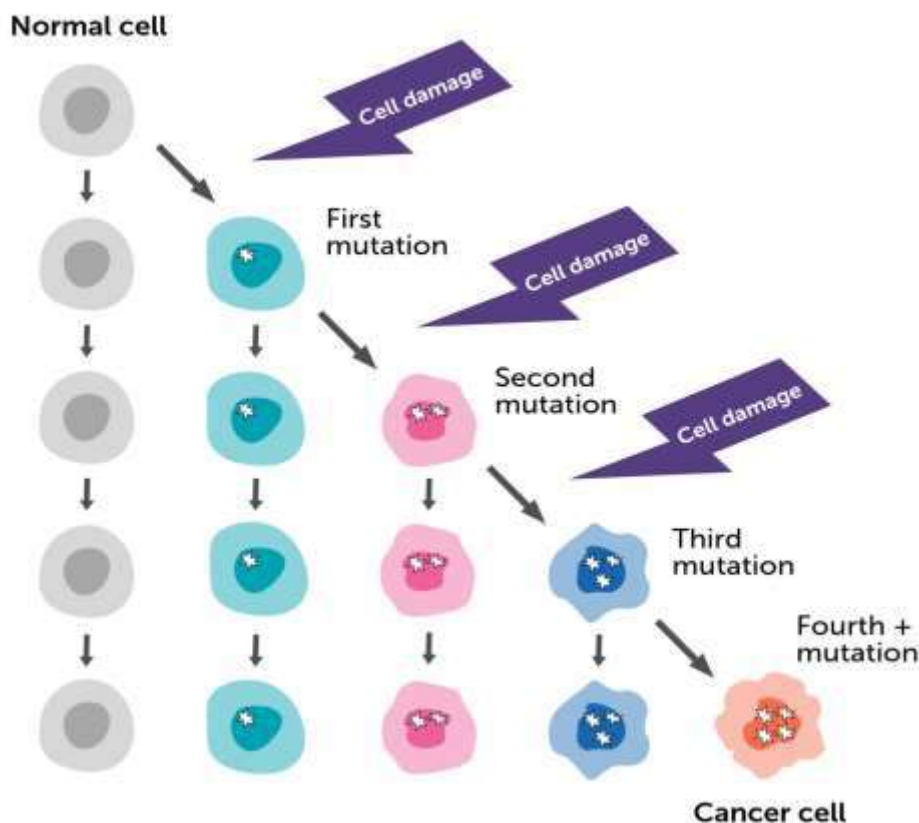
In contrast, unaltered **tumor-suppressor genes** are responsible for suppressing the **neoplastic phenotype**, and their inactivation by **deletion or mutation** permits **cancerous development** in the affected cells.

The Genetic Basis of Cancer

Oncogene → is a gene that has the potential to cause cancer.

Tumor suppressor genes (anti-oncogene) → is a gene that makes a protein called a tumor suppressor protein that helps control cell growth.

Neoplasm → is an abnormal growth of tissue that can be benign or malignant.



Adapted from "Understanding Gene Testing" - NIH 1995



The Genetic Basis of Cancer

Sometimes the changes are not in the **actual sequence of DNA**, for example, the **addition** or **removal** of **chemical marks**, called **epigenetic modifications** on DNA, which can influence whether the gene is **expressed** and **how much** protein is produced.

In general, cancer cells have **more genetic changes** than normal cells. Nevertheless, each **person's cancer** has a **unique combination of genetic alterations**.

Some of these changes may be the **result of cancer itself**, rather than the **cause**. As the cancer continues to grow, **additional changes** will occur. Even within the **same tumor**, cancer cells may have **different genetic changes**.



Identifying Genetic Changes in Cancer

Laboratory tests called **DNA sequencing tests** can “read” DNA, by **comparing** the sequence of DNA in cancer cells with that in normal cells. This information may help **physicians** to sort out which therapy might work best against a particular tumor.

Tumor DNA sequencing can also reveal the presence of inherited mutations. Indeed, in some cases, the genetic testing of tumors has shown that a patient’s cancer could be associated with a **hereditary cancer syndrome** that the family was not aware of.

As with testing for specific mutations in hereditary cancer syndromes, **clinical DNA sequencing** has implications that patients need to consider. For example, they may learn incidentally about the presence of inherited mutations that may cause other diseases, in them or in their family members.



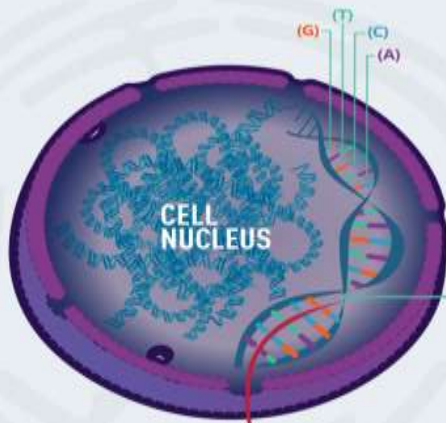
Hereditary Cancer Syndrome

hereditary cancer syndrome is a genetic predisposition to certain types of cancer, often with onset at an early age, caused by inherited pathogenic variants in one or more genes.

Most hereditary cancer syndromes exhibit **autosomal dominant inheritance**. The most common hereditary cancer syndromes related to women's cancer include hereditary breast, ovarian cancer syndrome and Lynch syndrome (HNPCC).

Hereditary cancer risk assessment is the key to identifying patients and families who may be at increased risk of developing certain types of cancer. Assessments should be performed by obstetrician–gynecologists.

An assessment includes information on **personal** and **family history**, including pathology, imaging reports, and evaluation of other medical risk factors for cancer.



DNA

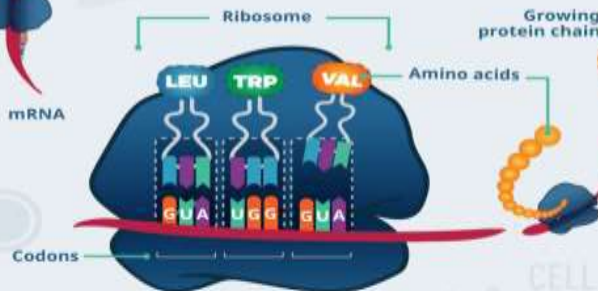
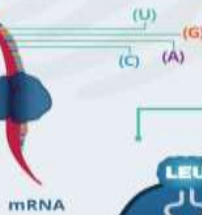
DNA is a molecule in the cell nucleus that contains instructions for making proteins. It is made of four different bases: adenine (A), thymine (T), guanine (G), and cytosine (C). A segment of DNA that contains the information for making a protein is called a gene. In the process of **transcription**, DNA that makes up a gene is copied into a complementary molecule called messenger RNA (mRNA).

GENETIC —CHANGES— AND CANCER

HOW GENETIC INFORMATION CREATES PROTEINS

RNA

mRNA is also made of four bases: adenine (A), uracil (U), guanine (G), and cytosine (C). mRNA moves from the nucleus to the cytoplasm where it interacts with ribosomes, the protein factories of the cell. There, through a process called **translation**, mRNA is translated into amino acids. A sequence of three mRNA bases is called a codon, and each codon is translated into a specific amino acid. There are 20 different kinds of amino acids in humans.



PROTEIN

As an mRNA molecule is translated, a chain of amino acids is formed. The chain eventually folds into a three-dimensional protein. The shape of a protein determines its function. Proteins have millions of functions in cells.

TYPES OF GENETIC MUTATIONS IN CANCER

DNA alterations can affect the structure, function, and amount of the corresponding proteins. All of these effects can change a cell's behavior from normal to cancerous. For example, a genetic alteration can intensify or eliminate the protein's function, which could make cells divide uncontrollably. Many different kinds of genetic mutations are found in cancer cells, including missense, nonsense, and frameshift mutations and chromosome rearrangements.

MISSENSE MUTATION

Original	CTA LEU (leucine)	TGG TRP (tryptophan)	GTA VAL (valine)	DNA Amino Acids
Mutation	CTA LEU (leucine)	TGT CYS (cysteine)	GTA VAL (valine)	DNA Amino Acids

A missense mutation is a change of a single DNA base that results in a change in the amino acid sequence. Sometimes a single amino acid change can greatly alter the protein's function.

NONSENSE MUTATION

Original	CTA LEU (leucine)	TGG TRP (tryptophan)	GTA VAL (valine)	DNA Amino Acids
Mutation	CTA LEU (leucine)	TGA (stop)	GTA VAL (valine)	DNA Amino Acids

A nonsense mutation is a change of a single DNA base that creates a "stop" codon, which terminates translation. The result is a shortened protein that may not function or that may have an abnormal function.

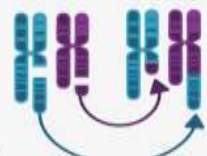
FRAMESHIFT MUTATION

Original	CTA LEU (leucine)	TGG TRP (tryptophan)	GTA VAL (valine)	DNA Amino Acids
Mutation	CTA LEU (leucine)	ATG MET (methionine)	GGT GLY (glycine)	DNA Amino Acids

A frameshift mutation results from the addition or removal of DNA bases that shifts the DNA sequence and the corresponding amino acid sequence. The result is a protein whose sequence and function are very different from those of the original protein.

CHROMOSOME REARRANGEMENTS

DNA is wound tightly into structures called chromosomes. Chromosome rearrangements can occur when a piece of a chromosome breaks and is lost entirely (deletion), moves to a different chromosomal location (translocation), flips directions (inversion), or is repeated (duplication). These rearrangements can alter several genes at once. For example, they can generate fusion genes, in which parts of two separate genes are joined together. Proteins made from fusion genes sometimes cause cancer.





KEY POINTS

Mutations



Lecture 16 Questions Practice

Q1:- Define the followings:

- a. Cancer.
- b. Oncogenes.
- c. Hereditary cancer syndrome.

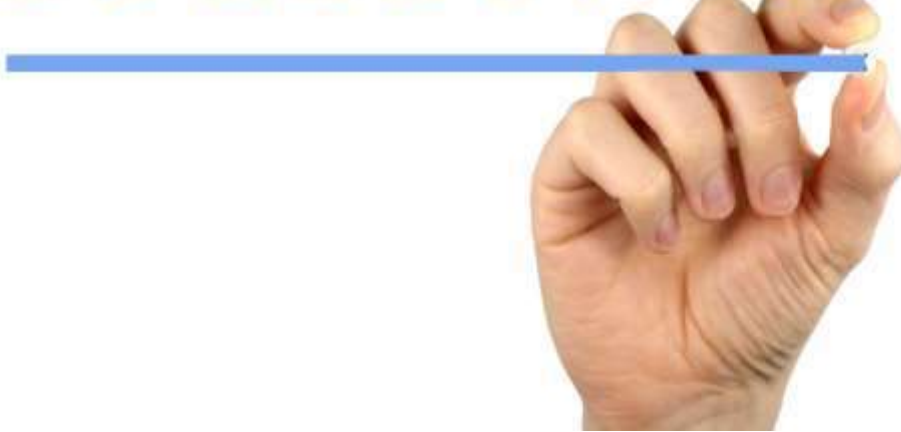


Cytogenetic

15th lecture

Mutagens are Carcinogenic in the Environment

OBJECTIVES



- Mutagens
- Mutagens and carcinogenic effect
- Environmental factors as carcinogenic
- The role of environmental factors as carcinogenic
- Cancer prevention



Mutagens

Mutagens → any material that causes mutation of the genome.

Carcinogens → any material that causes cancer.

Cancer → is a disease in which some of the body's cells grow uncontrollably and spread to near by tissues or other parts of the body.

Causes of cancer is either **internal factors** (inherited mutations, hormones, immune conditions) or **external factors** (chemical agents, physical agents, biological agents).

Environmental mutagens are chemical and physical agents in the environment that **induce genetic mutations or increase mutation rates** during the human life span.

Most mutagens act as human **carcinogens** or exert **genotoxic** effects on the next generation via germ cells.



Mutagens

Damage to DNA appears to be the **major cause** of most cancer and genetic birth defects and may contribute to aging and heart disease as well.

The agents that cause this damage must be identified. Many of these agents are:-

1. **Natural chemicals** present in the human diet as complex mixtures.
2. Tens of thousands of **man-made chemicals** that have been introduced into the environment in the last few decades.
3. **Physical agents**, both natural or man made.
4. **Biological agents** such as viruses or fungal toxins.



Mutagens and Carcinogenic Effects

Lifestyle behaviors and environmental factors account for around **70-90% of cancer cases**.

Researchers say up to **90%** of cancer cases are caused by **lifestyle** (smoking, alcohol consumption) and **environmental factors** (damages DNA).

Pollution is another environmental factor that contributes to increased cancer rate.

Studies of identical twins suggested that **genes are not** the source of most chronic illnesses. For instance, the concordance between identical twins for breast cancer was found to be only **20%** . Instead of our genes, our **lifestyle** and **environment** account for **90–95%** of our most chronic illnesses including **cancer**.



Environmental Factors as Carcinogenic

Most environmental factors associated with cancer **cause somatic mutations** that **stimulate abnormal cell division** or otherwise affect the process of **cancer progression**.

A number of environmental factors **contribute to cancer**, but those that have the greatest effects include:-

1. Tobacco use.
2. Diet.
3. Obesity.
4. Alcohol.
5. UV radiation.
6. Chemicals, such as benzene (used as an industrial solvent).

****Environmental factors may interact with genetic susceptibility to develop cancer.***



The Role of Environmental Factors as Carcinogenic

Even though cancer is a **genetic disease** most cancers are **not inherited**, and many are influenced by **environmental factors**. The role of environmental factors in cancer is suggested by differences in the incidence of specific cancer throughout the world.

The results of studies show that migrant populations typically take on the **cancer incidence** of their **host country**. For example, the overall rates of cancer are considerably lower in Japan than in Hawaii.

However, within a single generation after migration to Hawaii, **Japanese people develop cancer at rates similar to those of native Hawaiians**.

The increased cancer among the migrants is due to the fact that **they are exposed to the same environmental factors as are the natives**.



Cancer Prevention

1. Fruits and Vegetables.
2. Teas and Spices.
3. Wholegrain Foods.
4. Vitamins.
5. Exercise/Physical Activity.
6. Caloric Restrictions.



KEY POINTS

Mutations



Lecture 15 Questions Practice

Q1:- Define the followings:

- a. Mutagens.
- b. Carcinogens.
- c. Cancer.

Q2:- Enumerate the followings:-

- a. The environmental factors that contribute to cancer.
- b. Cancer prevention agents.



Cytogenetic

14th lecture

Mutations

Types of Mutations

Genetic Basis of Mutation

OBJECTIVES



- Mutations
- Causes of Mutations
- Types of Mutations
- Genetic Basis of Mutation



Mutations

Mutation is a change in a DNA sequence, either due to mistakes when the DNA is copied or as the result of environmental factors (chemical, physical, biological factors).

Mutations can result from:-

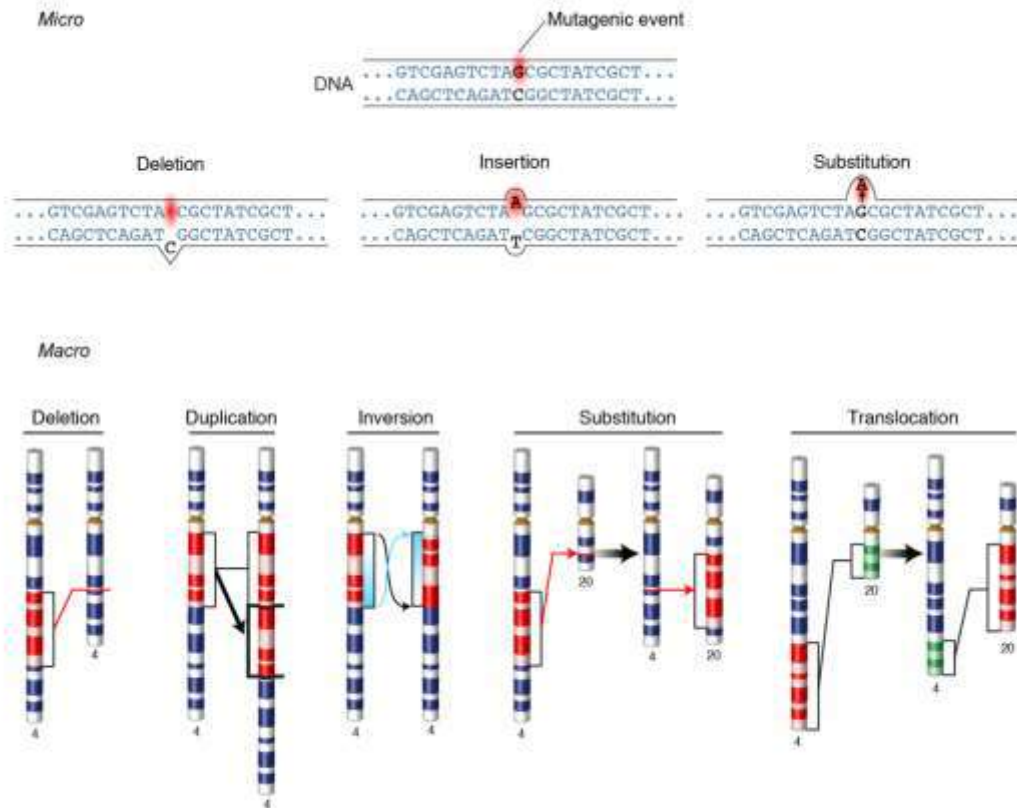
1. DNA copying mistakes made during cell division.
2. Exposure to ionizing radiation.
3. Exposure to chemical mutagens.
4. Infection by viruses.

Germ line mutations occur in the ova and sperm and can be passed on to offspring.

Somatic mutations occur in body cells and are not passed on to offspring.

Mutations

Structural



Numerical

- Aneuploidy
- Polyploidy

Monosomy
Trisomy
Tetrasomy
Triploidy
Tetraploidy



Causes of Mutations

1. Spontaneous mutations, that occur spontaneously, such as depurination, which may result in the incorporation of an incorrect base during the next round of replication.
2. Mutations due to DNA replication errors.
3. Errors introduced during DNA repair.
4. Mutagens (environmental factors) that induce mutations.



Types of Mutations

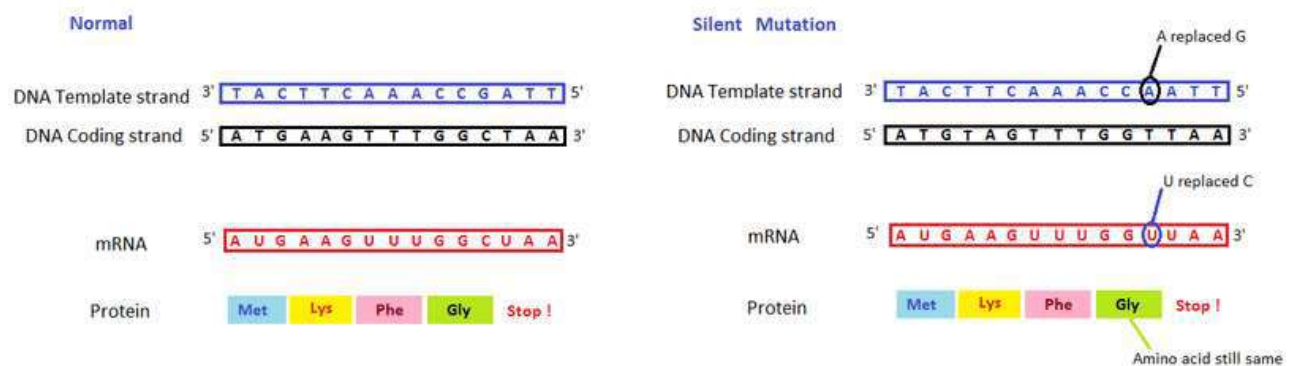
Point mutation is when a single base pair is altered.

Point mutations can have one of three effects:-

1. The base substitution can be a **silent mutation** where the altered codon corresponds to the same amino acid.
2. The base substitution can be a **missense mutation** where the altered codon corresponds to a different amino acid.
3. The base substitution can be a **nonsense mutation** where the altered codon corresponds to a stop signal.

Silent Mutation

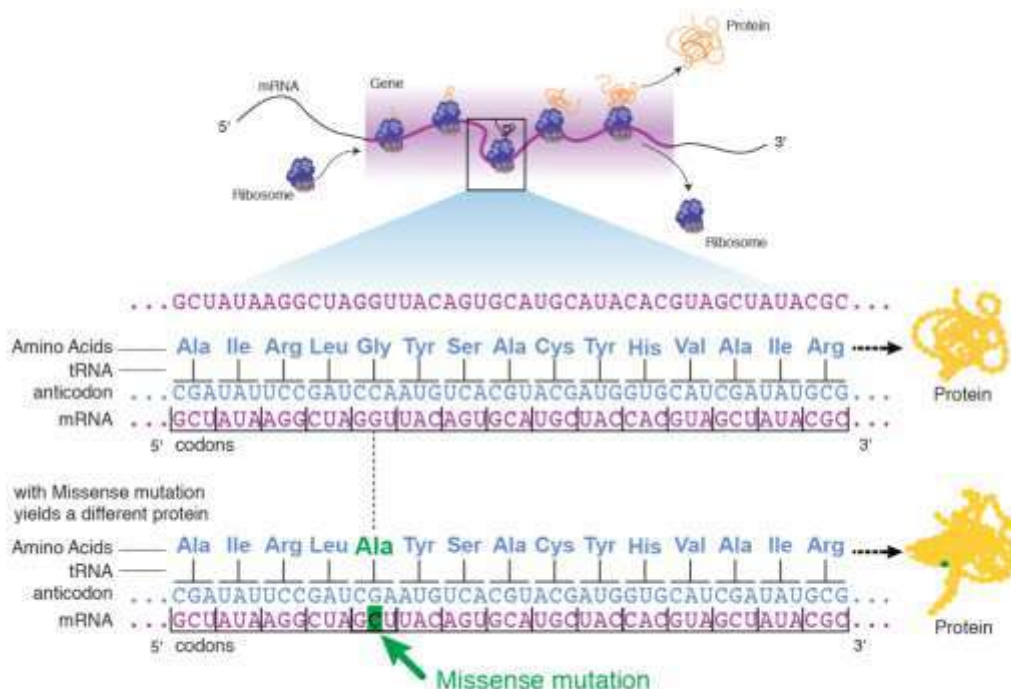
Silent mutation is when the change of a single base pair causes no subsequent changes in the amino acid or the function of the resulting protein.



Missense Mutation

Missense mutation is when the change of a single base pair causes the substitution of a **different amino acid in the resulting protein**.

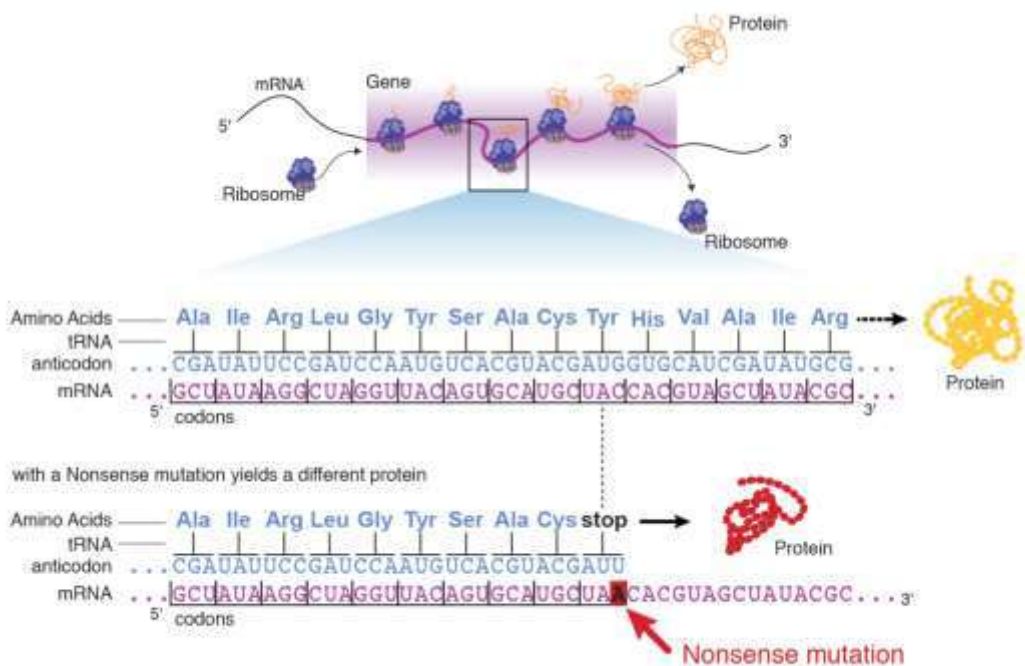
This amino acid substitution may have **no effect**, or it may render the **protein nonfunctional**.



Nonsense Mutation

Nonsense mutation is the substitution of a single base pair that leads to the **appearance** of a **stop codon** where previously there was a **codon** specifying an amino acid.

The presence of this premature stop codon results in the production of a **shortened and nonfunctional protein**.





Other Types of Mutation Classification

- 1. Mutation affects the structure, this includes:-**
 - a. Small scale mutation** such as **insertion, deletion or substitution** that affect a **single gene** or several nucleotides.
 - b. Large scale mutation** such as **insertion, deletion, inversion, translocation or duplication** that affect a whole **chromosome**.
- 2. Mutation affects the protein sequence, this includes:-**
 - a. Frame-shift mutation** is caused by insertion or deletion of a number of nucleotides that is not evenly divisible by three from a DNA sequence.
 - b. Point substitution mutation** results in a change in a single nucleotide and can be either synonymous or non-synonymous.



Other Types of Mutation Classification

3. Mutation affects the function, this includes:-

- a. **Loss-of-function mutations**, also called inactivating mutations, result in the gene product having **less or no function** (being partially or wholly inactivated).

- b. **Gain-of-function mutations**, also called activating mutations, change the gene product such that its effect **gets stronger** (enhanced activation) or even is superseded by a different and abnormal function.



Other Types of Mutation Classification

4. **Mutation affects the health**, this includes:-

- a. **Harmful or deleterious mutation** decreases the fitness of the organism. Many, but not all mutations in essential genes are harmful.
- b. **Beneficial or advantageous mutation** increases the fitness of the organism. Such as mutations that lead to antibiotic resistance in bacteria (which are beneficial for bacteria but usually not for humans).
- c. **Neutral mutation** has no harmful nor beneficial effect on the organism.



Genetic Basis of Mutation

The genetic basis of mutation is any change appears on the **gene level**. Hence, **point mutation** is the **simplest** form of **genetic change** that occur on the **gene level**.

Point mutation is when a single base pair is altered; inserted or deleted from a DNA or RNA sequence of an organism's genome.

Point mutations have three types:-

1. **Silent mutation.**
2. **Missense mutation.**
3. **Nonsense mutation.**



Genetic Basis of Mutation

-Consequences of Point Mutations

-Point mutations that occur in **non-coding sequences** are most often without consequences.

However, if the mutated base pair is in the **promoter sequence** of a gene, then the expression of that gene may change. Also, if the mutation occurs in the **splicing site** of an intron, then this may interfere with correct splicing of the transcribed pre-mRNA.



Genetic Basis of Mutation

-Point mutations that occur in **coding sequences** (most abundant class of mutation) are responsible for coding for the protein, the amino acid may be altered.

This slight change in the sequence of amino acids can cause a changes in:-

- a. **The protein function.**
- b. **Activation of the protein meaning how it binds with a given enzyme.**
- c. **Where the protein will be located within the cell.**
- d. **The amount of free energy stored within the protein.**



KEY POINTS

Mutations



Lecture 14 Questions Practice

Q1:- Define the followings:

- a. Germ line mutation.
- b. Nonsense mutation.

Q2:- Enumerate the followings:-

- a. Mutation that affects the function.
- b. Mutation that affects the health.

Q3:- Explain briefly the consequences of point mutation.

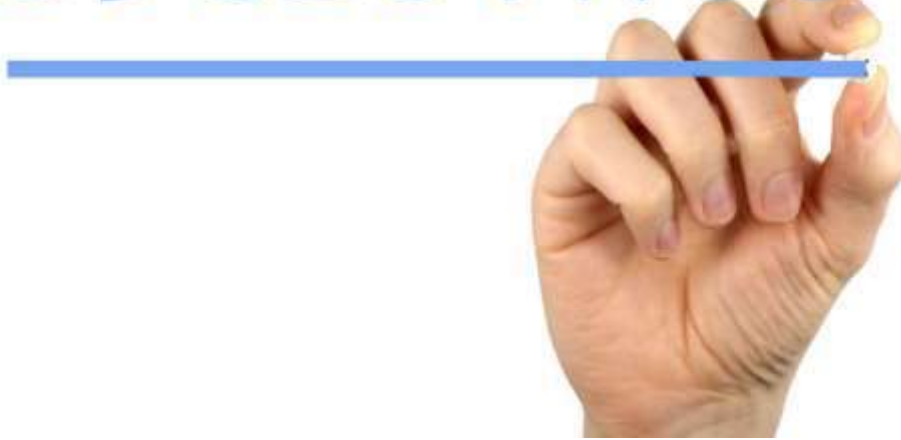


Cytogenetic

13th lecture

Sex Influenced Traits - Sex Limited Genes

OBJECTIVES



→ Reminder 😊

→ Sex-Linked Traits \ Sex-Influenced Traits
\ Sex-Limited Traits.



Reminder 😊

- Genes act in pairs, one from each parent.
- Gene pairs separate during meiosis and the formation of the sex cells along with the chromosomes.
- When the sperm fertilizes the egg, the father's genes (and chromosomes) join the mother's, both contribute to the genetic makeup of the offspring.
- One form of a gene may be dominant over another form which is recessive and the dominant form would be expressed.



Sex-Linked Traits \ Sex-Influenced Traits \ Sex-Limited Traits

Sex-linked traits are determined by genes located on the **sex chromosomes**.

Sex-influenced traits and **Sex-limited traits** are determined by genes located on **autosomes** and express only in one sex (sex that having the appropriate hormonal determiner\ activator).

Throughout the pedigree the trait appears in only **one sex**, but it need **NOT** occur in all member of that sex.

The genes for the trait can be carried and transmitted by the **opposite sex** although it is **NOT** displayed in that sex because of **anatomical** or **physiological differences**.



Sex-Linked Traits \ Sex-Influenced Traits \ Sex-Limited Traits

Sex-limited character, an observable feature appearing only in members of one sex of a given population of organisms, although organisms of both sexes may have the genetic constitution that determines the trait.

For example, the genes that control **milk yield** and quality in dairy cattle, are present in both bulls and cows, but their effects are expressed only in the **female cattle**.

For example, **premature baldness** and type of **beard growth** are human sex-limited characters, that found in both males and females, but only appear or expressed in the **males**.



Sex-Linked Traits Sex-Limited Traits

\

Sex-Influenced Traits

Sex-influenced traits and **Sex-limited traits** are determined by genes located on **autosomes** and express only in one sex (sex that having the appropriate hormonal determiner\ activator).

The genes for the trait can be carried and transmitted by the **opposite sex** although it is **NOT** displayed in that sex because of **anatomical** or **physiological differences**.

For example, the genes that control **milk yield** and quality in dairy cattle, are present in both bulls and cows, but their effects are expressed only in the **female cattle**.

For example, **premature baldness** and type of **beard growth** are human sex-limited characters, that found in both males and females, but only appear or expressed in the **males**.



Lecture 13 Questions Practice

Q1:- Define the followings:

- a. **Sex-influenced traits** and **Sex-limited traits**.

Q3:- MCQ

1. Sex-limited character is an observable feature appearing only in members of one sex of a given population of organisms, although organisms of -----
---- may have the genetic constitution that determines the trait.
 - a. Either sexes.
 - b. BOTH SEXES.
 - c. One sex.
 - d. None of the above.