

GENETICS FOR CONCEPT

JTEFA DEGEFA



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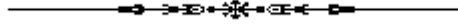
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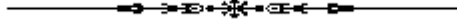
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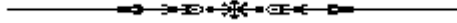
First of all I would like to thank GOD who above all nature. Those who supported me in powering of my idea and editing of this book are secondly acknowledged.

DEDICATION



I dedicate this book for my beloved wife Ebenezer Gutu and my son Burka Itefa because of their jogging to me while I was writing and editing this material all the time I sit with them.

PREFACE



The aim of this book is to show brief concept of genetics based on selected ideas and related facts. Additional information is presented in the introduction, with a chronological list of important discoveries and advances in the history of genetics, in an appendix with supplementary data in tables, and in references. This book is written for two kinds of readers: for students of biology and genetics, as an introductory overview, and for their teachers, as a teaching aid. Other interested individuals will also be able to gain information about current developments and achievements in this rapidly growing field.

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CHAPTER ONE

INTRODUCTION GENETICS



Genetics is an important branch of biology which came from the word “gene” studying of heredity, genes and variation. Although molecular nature of the gene was not understood late 1950s because of its hereditary unit in which some scientists envisioned a gene as being a particle-like entity that could not be further subdivided into additional parts, at the time of Mendel, geneticists had considered a gene to be the smallest unit of heredity, which provided an organism with its inherited traits. So, genetics is centered on the study of genes which is classically defined as a unit of heredity, but such a vague definition does not do justice to the exciting characteristics of genes as intricate molecular units that manifest themselves as critical contributors to cell structure and function. At the molecular level, a gene is a segment of DNA that has the information to produce a functional product.

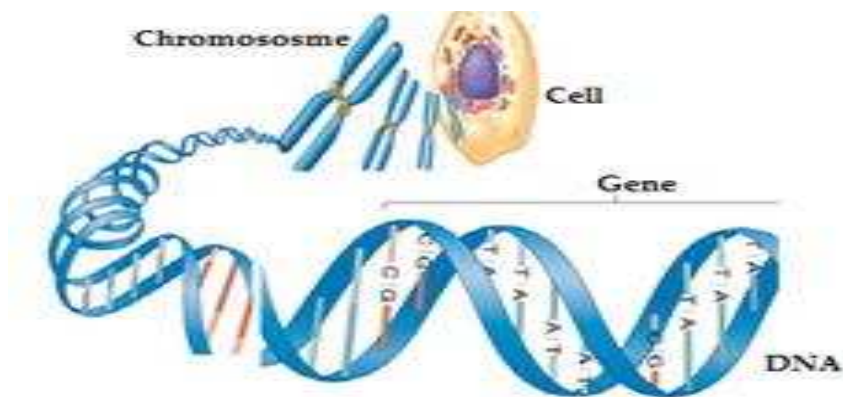


Figure 1: Arrangement of genes on chromosomes found in a cell

Genes are always central studies of molecular, cellular, organismal, family, population, or evolutionary level. Heredity relates to that science by which living beings resembles to their relatives and ancestors. Variation means the science by which living being differs from their relatives and ancestors. Thus genetics is the Science to study how

various characters are transferred from parents and develop into off springs. Now a day the sphere of genetics is extremely wide. It studies how genes are developed, what is their chemical structure and how these effect the development and behavior of living beings (Fig 1). Genetics has been divided into six branches: Cytogenetics), Physiological genetics, Biochemical genetics, Population genetics, Eugenics and Applied genetics including cancer genetics, apoptosis & stem cell.

1.1. Why Studying Genetics Is Important?

Genetics is comparatively a recent science and has been widely used to develop improved types of cereals, vegetables, fruits, ornamental plants, medicinal and aromatic plants, spices etc. and various animals.

1.1.1. Improvement of agricultural plants:

Improvement in disease resistance: One of the main agricultural problems to the whole world is occurrence of diseases which cause economic loss to crops. The best solution to this problem is development of disease resistant varieties using the principles of genetics.

Improvement of insect resistance: Crops also suffers serious economic loss due to various types of insects such as aphids, sucking insects, mites, nematodes etc. This problem can also be solved by breeding for resistance following the principles of genetics.

Synthesizing of plants with multiple qualities: With the help of genetics nowadays plant breeder are synthesizing plants with multiple qualities such as high yield, superior quality, resistance to diseases and insects and more adoptability to the existing agro-climate. Breeders do it by multiple crossing.

1.1.2. Use of genetics for improvement in animals

Improvement for disease resistance: Due to occurrence of some diseases in animals the farmer suffers economic loss. Several medicines are invented to control these diseases. A better method of control is to develop disease resistance breeds. For example, typhoid resistant breeds of poultry.

Improvement in utility of domesticated animals: Such improvement in animals can be possible by research on quantitative inheritance & by help of proper hybridization and selection.

1.1.3. Genetics for treatment of diseases:

Treatment of cancer is done by gene therapy, surgery, radiation therapy, chemotherapy, hormone therapy, immunotherapy or biological therapy, adjuvant therapy (combining two or more treatments), prophylactic or preventive treatment.

1.1.4. Genetics for betterment of human race

In this science geneticist investigate those factors which effect hereditary characters in human and which can make such characters more useful to mankind. To improve human being two methods may be used: First method is eugenics which means improving the environment and surroundings. The Second method is eugenic where improvements in hereditary constitution are studied. Eugenics is the study of those factors by which development of mental and physical characters takes place in human beings. In another words it is the branch of genetics in which the laws of inheritance are used to improve human beings. Aims and ideals of eugenics are improvement for mental and physical health, intelligence, moral character and to attain specialization in knowledge is very useful to the person and society.

1.2. Relation between Genetics and Other Fields

Genetics closely associated with other sciences such as morphology, taxonomy, embryology, cytology, biochemistry, ecology, evolution, bacteriology, statistics etc.

Genetics and Morphology: Morphologies studies various morphological features of living beings. Growth and development of tissues are effected by mutations - a branch of genetics

Genetics and Taxonomy: Classification of various living beings, their species, genus, family and order depends on their genetics. Development of a living being is governed by it's genetically constitution.

Genetics and Embryology: Theoretical and practical embryology is governed by its

genetics. Genetically constitution of a living being conditions its development.

Genetics and Cytology: Cytology of a living being is concerned with its genetics. Studies on Cytology and genetics are collectively grouped as cytogenetics. Cytology is the pillar of genetics.

Genetics and Biochemistry: To understand the nature and function of genetic material a geneticist has to take help of biochemistry. For example due to reduction of an amino acid tyrosine by an enzyme, homo genes tic acid is formed in human body which causes a disease Alkatopnuria in which urine on keeping in air turns black. This disease is controlled by a simple genetic factor.

Genetics and Ecology: Ecology means study of living being in natural environment. Now a day's significant progress has been made in ecology by the help of genetics. Adaptation of various polyploidy in different environment reveals close relationship between ecology and genetics. This fact reveals that ecology is dependent on heredity of the organism.

Genetics and Statistics: Biometry helps significantly in genetically research. Statistics has greatly helped in development of genetics.

Genetics and Botany & Zoology: Botany and Zoology are different sciences for studies of plants and animals. However, genetics correlates both these sciences. Both express similarly in inheritance.

1.3. Some Genetics Terms

Gene: A genetic factor (region of DNA) that helps determines a characteristics or traits.

Allele: One of two or more alternate forms of a gene

Locus: Specific place on a chromosome occupied by an allele

Genotype: Set of alleles possessed by an individual organism

Heterozygote: An individual organism possessing two different alleles at a locus

Homozygote: An individual organism possessing two of the same alleles at a locus

Phenotype or trait: The appearance or manifestation of a character

Autosome: Except sex chromosomes other chromosomes are called autosomes.

Autopolyploid: It is that polyploidy in which all chromosomes are similar in sets.

Allopolyploid: It is that polyploidy in which chromosomes are different in sets.

Aneuploidy: Improper multiplication of chromosomes number is called aneuploidy. It is always minus or plus of a few chromosomes.

Asynapsis: During meiosis absence of pairing between homologues chromosome.

Back cross: Crossing of hybrid with any parent is called back cross.

Bivalent: In first meiotic cell division, pairing of chromosomes is called bivalent.

Breeding: It is the science to change the genetic structure of plant or animal.

Chiasma: While pairing of chromosome attachment with in two chromatids is called chiasma.

Chromatid: In beginning of meiosis each chromosomes is divided into two threads like structures. These threads are called chromatid.

Chromosome: Thread like structures present in nucleus are called chromosomes. At various stages of meiosis shape of chromosomes changes. For each kind of organism number chromosomes is same.

Crossing over: It is the exchange of segment between chromatids of a chromosome. It happens because of break and joins in chromatids during meiosis.

Deficiency: Removal or absence of segments or gene from chromosome is called deficiency.

Dihybrid: Hybridization between male and female having two pair of contrasting characters is called dihybrid.

Diploid: It is that organism which has two sets of chromosome.

Diplotene: In meiosis after pachytene the stage of diplotene comes. In diplotene each bivalent form 4 chromatids. These four chromatids appear in pairs, but are attached at chiasma.

Disjunction: Separation of chromosomes at anaphase.

Dominance: Out of two contrasting characters, the character expressed in first filial (F₁) generation is known as dominant the phenomenon.

Duplication: Double occurrence of a segment in a chromosome.

Epistasis: Dominance of gene over expression of non-allelic gene and whose effect is masked is called hypostatic.

Expressivity: Capacity to express genetic character.

Eugenics: Study of genetic for human improvement.

Gamete: Cells formed after meiosis.

Gene Frequency: It is the proportion of expression of alternative allele of an organism.

Gene Interaction: Gene interaction is the change in expression of a gene by non-allelic gene.

Genome: Haploid set of chromosome in organisms.

Haploid: Gametic chromosome number or half (n) chromosome number.

Heritability: The quantum of variability which is due to heredity.

Heterosis: If character of first filial (F₁) generation is superior to parents then it is

known as heterosis.

Heterozygous: Presence of unlike alleles on corresponding loci of homologous chromosome.

Homozygous: Presence of like alleles on corresponding loci of homologous chromosomes.

Hybrid: Hybrid is the organism borne by crossing parents of different genotype:

Inbreeding: Fertilization between members of close relatives.

Inversion: Rearrangement in segments of chromosome resulting alteration in sequence of genes.

Kinetochores: It is that place on chromosome where spindle fibers are attached.

Linkage: Certain genes located very close on chromosome are passed on together in next generation and phenomenon is linkage.

Linkage value: It is the recombination fraction which indicates the ratio of occurrence of parental type and cross over type in the progeny.

Locus: Locus is the position of genes on chromosome.

Meiosis: It is that type of cell division where number of chromosomes is reduced to half gametes is formed.

Metaphase: It is the stage of mitosis or meiosis where chromosomes arrive in center of spindle.

Mitosis: It is type of cell division which do not change number or characters of chromosomes.

Monohybrid: It is the hybrid produced by hybridization between parents having one contrasting character.

Multiple Allele: More than two alternative forms of a gene.

Mutation: Sudden and heritable change in structure of gene or chromosome.

Nullisomy: Absence of a pair of chromosome in a cell.

Pachytene: It is the double thread stage of chromosome in meiosis.

Pedigree: Record of past generations of an organism.

Polysomic: when in a diploid organism there are more than two homologous chromosomes.

Phenotype: Visible form of an organism.

Polyploidy: An organism is a polyploid which has more than two basic set of chromosomes.

Reciprocal cross: Reciprocal hybridization between male and female parents.

Recombination: New combination of genes due to hybridization of parents caused by crossing over and segregation.

REVIEWING THE KEY CONCEPTS

- Genetics study heredity, genes and variation
- Genes are always central studies of molecular, cellular, organismal, family and population
- Genetics is the recent science studied for the improvement of agricultural plants, animals and the betterment of human races
- Genetics closely associated with other sciences such as morphology, taxonomy, embryology, cytology, biochemistry, ecology, evolution, bacteriology, statistics etc.,

COMPREHENSION QUESTIONS

1. What is the importance association between genetics and other sciences do you think?
2. Define gene and heredity
3. What the cause of variation between and within organisms do you think?
4. Do you think genetics is important in treatment of human disease?

CHAPTER TWO

MENDEL'S HYBRIDIZATION

EXPERIMENTS AND RESULTS



Humans first applied genetics to the domestication of plants and animals between approximately 10,000 and 12,000 years ago. This domestication led to the development of agriculture and fixed human settlements. Before the rise of Mendel there were many views about genetics and theories were postulated by different scholars. People have understood the hereditary nature of traits and have practiced genetics for thousands of years. Here before looking Mendel's hybridization experiment it is important to see pre-Mendelian views relating to heredity.

2.1. Pre-Mendelian views relating to heredity

The concept of heredity was explained under many theories before the year 1900 which was a watershed in the history of genetics when Gregor Mendel's pivotal 1866 publication on experiments with pea plants, which revealed the principles of heredity, was "rediscovered."

2.1.1. Theory of pangenesis

Greek philosophers developed the concept of pangenesis. This theory says specific particles (later called gemmules) carry information from various parts of the body to the reproductive organs. Then they are passed to the embryo at the moment of beginning. Although incorrect, the concept of pangenesis was highly influential and persisted until the late 1800s.

2.1.2. Theory of the inheritance of acquired characteristics

Pangenesis led the ancient Greeks to propose the inheritance of acquired characteristics. It says traits acquired in a person's lifetime become incorporated into that person's hereditary information and are passed on to offspring. For example, people who developed musical ability through diligent study would produce children who are innately endowed with musical ability. The notion of the inheritance of acquired characteristics also is no longer accepted, but it remained popular through the twentieth century.

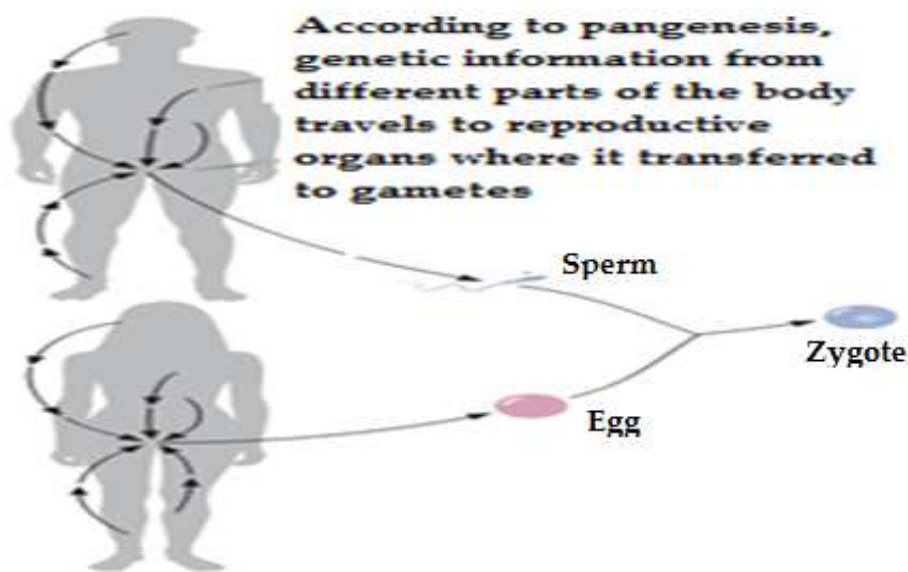


Figure 2a: Pangenesis Concept

2.1.3. The preformation theory

According to preformationism, inside the egg or sperm there exists a fully formed miniature adult, a homunculus, which simply enlarges in the course of development. Preformationism meant that all traits were inherited from only one parent from the father if the homunculus was in the sperm or from the mother if it was in the egg.

Although many observations suggested that offspring possess a mixture of traits from both parents, preformationism remained a popular concept throughout much of the seventeenth and eighteenth centuries (Fig 2c).

2.1.4. Blending theory of inheritance

Another early notion of heredity was blending inheritance, which proposed that offspring are a blend, or mixture, of parental traits. This idea suggested that the genetic material itself blends, as blue and yellow pigments blend to make green paint. Once blended genetic differences could not be separated out in future generations, just as green paint cannot be separated out into blue and yellow pigments. Some traits do appear to show blending inheritance; however, we realize today that individual genes do not blend.



Figure 2c: Preformationism

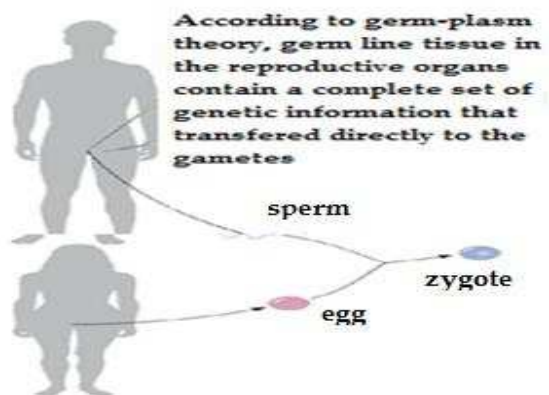


Figure 2b: Germ- plasm theory

2.1.5. Cell theory

Building on the work of Matthias Jacob Schleiden (1804-1881) and Theodor Schwann (1810-1882) proposed the concept of the cell theory in 1839. According to this theory: all life is composed of cells, cells arise only from preexisting cells, cell is the fundamental unit of structure and function in living organisms. Walther Fleming in 1879 observed the division of chromosomes and published excellent description of mitosis and by 1885 it was generally recognized that the nucleus contained the hereditary information.

2.1.6. Germ-plasm theory

Weismann (1834–1914) proposed the germ plasm theory, which holds that the cells in the reproductive organs carry a complete set of genetic information that is passed to the egg and sperm (**Fig 2b**). Generally, each of pre-Mendelian theories are summarized as the following (**Table 1**).

Table 1: Table showing the differences between pre-Mendelian theories

Concept	Proposed	Remark
Pangenesis	Genetic information travels from different parts of the body to reproductive organs.	Incorrect
Inheritance of acquired characteristics	Acquired traits become incorporated into hereditary information.	Incorrect
Preformationism	Miniature organism resides in sex cells, and all traits are inherited from one parent.	Incorrect
Blending inheritance	Genes blend and mix	Incorrect
Germ-plasm theory	All cells contain a complete set of genetic information.	Correct
Cell theory	All life is composed of cells, and cells arise only from cells.	Correct
Mendelian inheritance	Traits are inherited in accord with defined principles.	Correct

2.2. Mendel's Theory of Heredity

Mendel's crucial publication in 1866 on experiments with pea plants revealed the principles of heredity. The significance of his conclusions was recognized and other biologists immediately began to conduct similar genetic studies on mice, chickens, and other organisms. The results of these investigations showed that many traits indeed follow Mendel's rules.

2.2.1. Mendel's hybridization experiments and results

2.2.1.1. Hybridization experiments with garden pea

Mendel's approach to the study of heredity was on pea (*Pisum sativum*) plant which offered clear advantages for genetic investigation due to the precautions. These precautions are: Organism selected for the experiment should be homozygous, for crossing only those parents should be selected who possess contrasting characters, at one time only one character should be investigated, for the experiment the organism should be available in plenty and it should have short life-cycle and record of observations should be clear and complete.

Mendel carried out his experiment on large number of varieties of peas because these varieties differed in various traits and were genetically pure. With this variation, Mendel used seven characteristics of pea plants such as Seed shape (Smooth and Wrinkle), Cotyledon color (Yellow and Green), Seed coat color (Colored and White), Pod type (Hard and Soft), Pod color (Yellow and Green), Flower position (Axillary and Terminal) and Stature (Tall and dwarf). During this he focused on those that exist in two easily differentiated forms, such as white versus gray seed coats, round versus wrinkled seeds and inflated versus constricted pods (Fig 3).

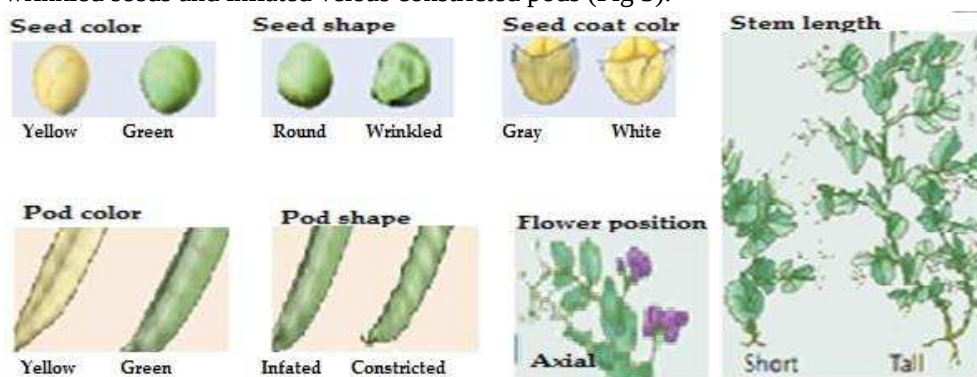


Figure 3: Different seven contrasting traits of pea plant Mendel used in his experiment

During cross fertilization of two pea plants containing contrasting traits he used to prevent self-fertilization of the crop because pea plant can be fertilized by both cross

and self-fertilization. Here is a method he followed (**Fig 4**).

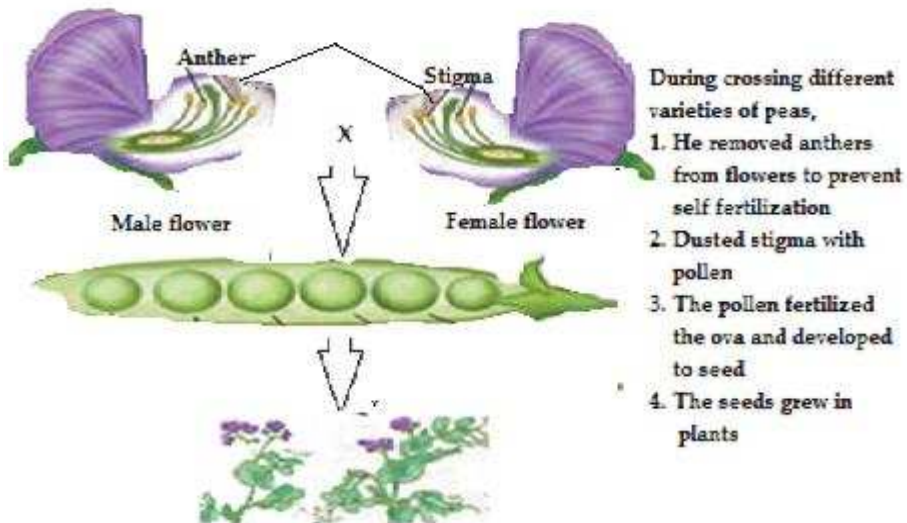


Figure 4: Methodology Mendel used to prevent self-fertilization

2.2.1.2. Results of the hybridization works

Mendel carried out his experiment by crossing two distinct individuals with different characteristics then they are mated or crossed to each other, this is called a hybridization experiment and the offspring are referred to as hybrids. During this he determined numbers of traits undergo crosses.

2.2.1.3. Monohybrids cross

Mendel began by studying monohybrid crosses those between parents that differed in a single characteristic. In one experiment, Mendel crossed a pure-breeding (homozygous) pea plant for round seeds with one that was pure-breeding for wrinkled seeds. The first generation of a cross is the P (parental) generation and the offspring from the parents in the P generation are the F (filial 1) generation. He found F1 generation that they expressed only one of the phenotypes present in the parental generation i.e., all the F1 seeds were round. Mendel carried out 60 such crosses and always obtained this result. He also conducted reciprocal crosses: in one cross, pollen (the male gamete) was taken

from a plant with round seeds and, in its reciprocal cross; pollen was taken from a plant with wrinkled seeds and he got the same result for reciprocal crosses i.e., all the F1 were round.

2.2.1.4. Deduction of principles and laws governing heredity

Based up on the result observed, firstly Mendel concluded as each plant must therefore possess two genetic factors encoding a character now called alleles are designated with letters, the allele for round seeds is usually represented by “R” and the allele for wrinkled seeds by “r”, the plants in the Parental generation of Mendel’s cross possessed two identical alleles i.e., “RR” in the round-seeded parent and “rr” in the wrinkled-seeded parent. Secondly he concluded that two alleles in each plant separate when gametes are formed, and one allele goes into each gamete. When two gametes (one from each parent) fuse to produce a zygote, the allele from the male parent unites with the allele from the female parent to produce the genotype of the offspring. Thirdly his conclusion was derived the concept of dominance i.e., traits that appeared unchanged in the F1 heterozygous offspring Mendel called dominant, and those traits that disappeared in the F1 heterozygous offspring he called recessive. When dominant and recessive alleles are present together, the recessive allele is masked or suppressed. His fourth conclusion was that the two alleles of an individual plant separate with equal probability into the gametes. When plants of the F1 (with genotype Rr) produced gametes, half of the gametes received the R allele for round seeds and half received the r allele for wrinkled seeds. The principle of segregation states that each individual diploid organism possesses two alleles for any particular characteristic. These two alleles segregate (separate) when gametes are formed, and one allele goes into each gamete. Furthermore, the two alleles segregate into gametes in equal proportions

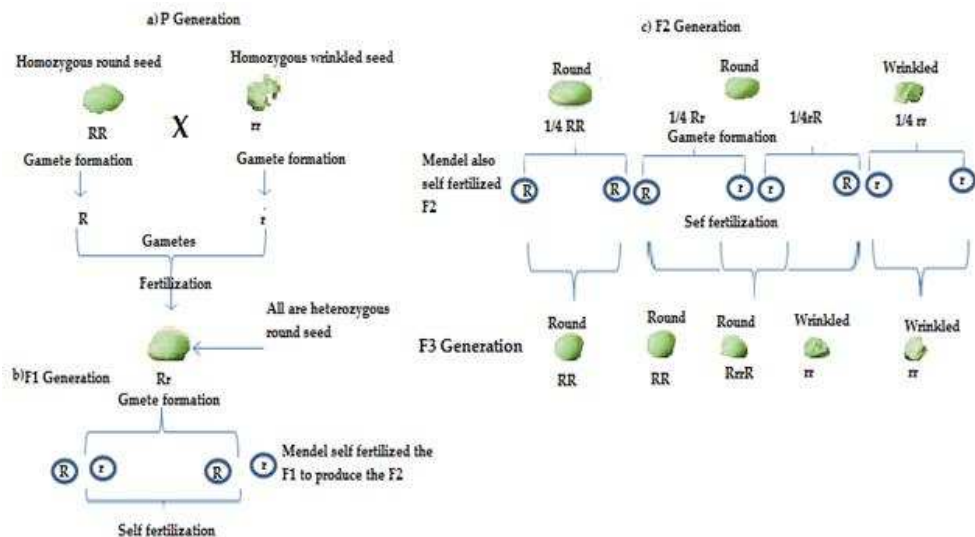


Figure 5: Mendel's monohybrid crosses revealed the principles of segregation and the concept of dominance

2.2.1.5. How can we predict genetic cross?

Punnett Square: Punnett square is one of Mendel's tools in conducting his experiments on pea plants to develop a way to predict the outcome of crosses between plants with different phenotypes which is constructed by drawing a grid putting the gametes produced by one parent along the upper edge and the gametes produced by the other parent down the left. It can be used to determine the results of a genetic cross. For example the homozygous round(RR) seed crossed with homozygous wrinkled(rr) seed as on Fig 5 can be arranged on the following punnet square(**Tab 2.**).

Table 2: Monohybrid crosses by using punnet square method

Parents	R	R	F1 X F1		R	r	F2 X F2		R	R	R	r	
r	Rr	Rr		R	RR	Rr		R	RR	RR	Rr	rr	r
r	Rr	Rr		r	Rr	rr		r	Rr	Rr	Rr	rr	r

Probability: probability is another method for determining the outcome of a genetic cross. It expresses the likelihood of the occurrence of a particular event or number of times that a particular event occurs, divided by the number of all possible outcomes.

Example(1), the probability of one king of heart card from 52 cards containing only one king of hearts is $1/52$, because there is only one card that is the king of hearts (one event) and there are 52 cards that can be drawn from the deck (52 possible outcomes). Example (2), the probability of rolling a six-sided die and getting a four is $1/6$, because the die has six sides and any one side is equally likely to end up on top. So, in this case, understanding the nature of the event the shape of the thrown die allows us to determine the probability.

The Testcross: Test cross is another useful tool for analyzing genetic crosses where one individual of unknown genotype is crossed with another individual with a homozygous recessive genotype for the trait in question. For example, suppose for a tall pea plant with no information about its parents because tallness is a dominant trait in peas so that the plant could be either homozygous (TT) or heterozygous (Tt). To determine its genotype by performing a testcross, if the plant were homozygous (TT), a testcross would produce all tall progeny (TT X tt = all Tt) and if the plant were heterozygous (Tt), half of the progeny would be tall and half would be short (Tt X tt = $1/2$ Tt and $1/2$ tt). When a testcross is performed, any recessive allele in the unknown genotype is expressed in the progeny.

2.3. Cross Involving Higher Level of Hybridity and Ratio

2.3.1. Dihybrid crosses

Mendel crossed varieties of peas that differed in two characteristics (dihybrid) cross. For example, when two varieties of pea plants round yellow (RRYY) crossed with wrinkled green (rr yy), the seeds of all the first filial (F1) progeny were round yellow (RrYy). He then self-fertilized the F1 with F1 and obtained the following progeny in the F2: 9: 3:3:1 ratio; i.e. $9/16$ of the progeny were round yellow, $3/16$ was wrinkled yellow, $3/16$ was round green and $1/16$ was wrinkled green. In this case there is also the law of segregation and independent assortment (**Fig 6**).

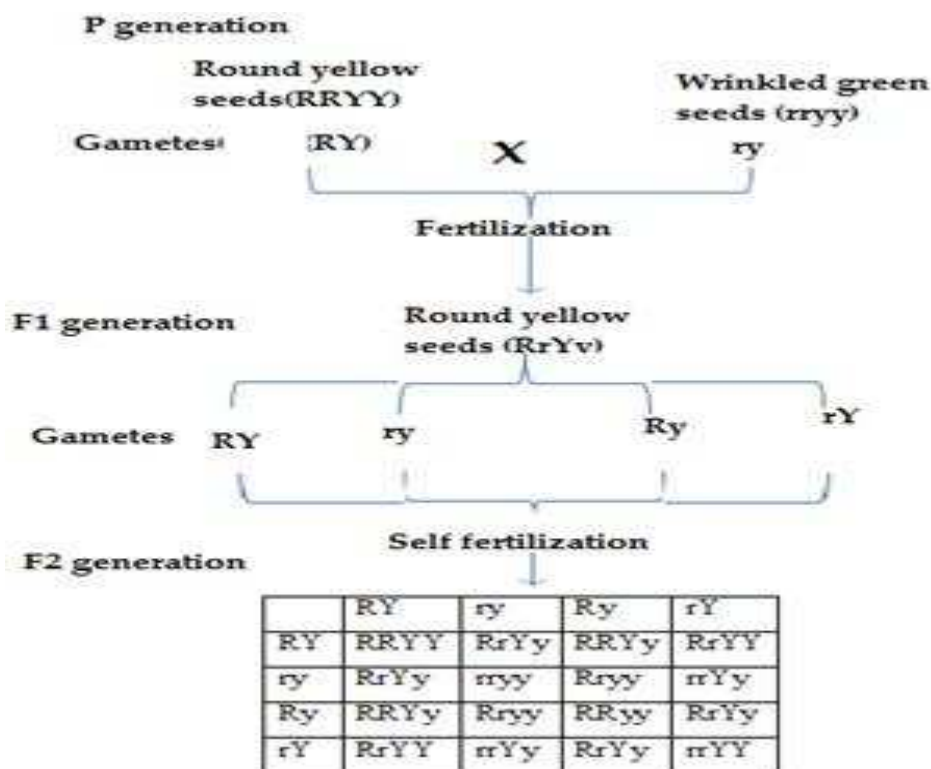


Figure 6: Mendelian dihybrid crossing showing 9:3:3:1 ratio on F2 generation

For the dihybrid it is possible to use probability and branch diagram. Let's examine Mendel's dihybrid cross between two heterozygous round yellow pea plants (Rr Yy X Rr Yy) by considering each characteristic separately (*Fig 7*).

2.3.2. Multi hybrids cross

To illustrate the advantage of the probability method for more than tri-hybrid, consider the cross between organisms possessing five characteristics as an example AaBbccDdEe X AaBbCcddEe. If it is required to know the probability of obtaining offspring with the genotype aabbccdde, determining the probability of this cross by a Punnett Square might be takes to solution for months. However, it can be quickly figured out to obtain the probability of the offspring by breaking this cross into a series of single-locus crosses (*Table 3*).

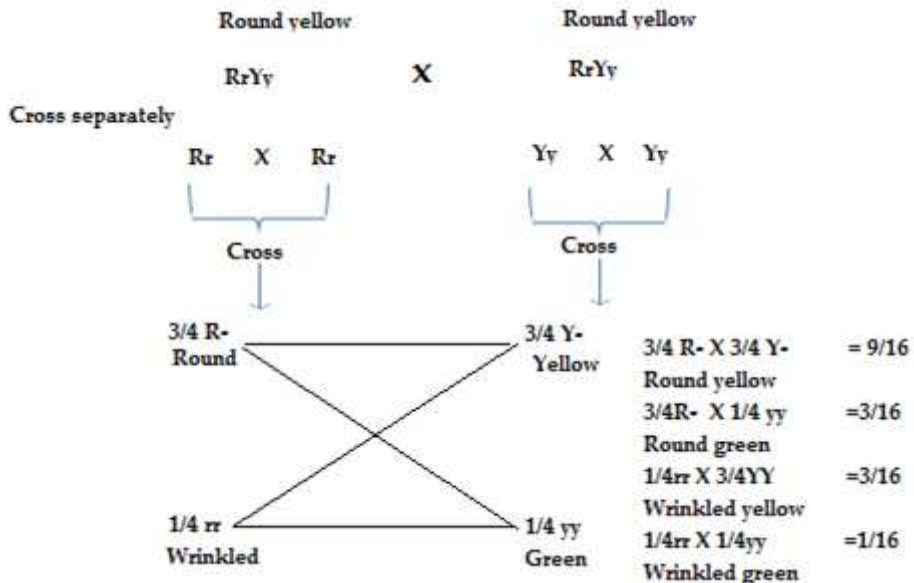


Figure 7: A branch diagram used to determine the proportion of offspring

Table 3: Alleles of multi-hybrid cross carried out separately

Progeny cross	Genotype	Probability
Aa X Aa	aa	¼
Bb X Bb	bb	¼
Cc X Cc	cc	¼
Dd X dd	dd	¼
Ee X Ee	ee	¼

The probability of an offspring from this cross having genotype aabbccdde is now easily be obtained by using the multiplication rule: $\frac{1}{4} \times \frac{1}{4} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{4} = 1/256$. This show a cross including several characteristics can be worked by breaking the cross down into single-locus crosses and using the multiplication rule to determine the proportions of combinations of characteristics.

REVIEWING THE KEY CONCEPTS

- People have understood the hereditary nature of traits and have practiced genetics for thousands of years before the rise of Mendel.
- Theory of pangenesis: says specific particles (later called gemmules) carry

information from various parts of the body to the reproductive organs.

- Theory of the inheritance of acquired characteristics: says traits acquired in a person's lifetime become incorporated into that person's hereditary information and are passed on to offspring.
- The preformation theory: inside the egg or sperm there exists a fully formed miniature adult, a homunculus, which simply enlarges in the course of development. Preformationism meant that all traits were inherited from only one parent from the father if the homunculus was in the sperm or from the mother if it was in the egg.
- Blending theory of inheritance: says offspring are a blend, or mixture, of parental traits.
- Cell theory: Matthias Jacob Schleiden (1804-1881) and Theodor Schwann (1810-1882) proposed the concept of the cell theory in 1839 which says all life is composed of cells, cells arise only from preexisting cells and cell is the fundamental unit of structure and function in living organisms.
- Germ-plasm theory: Weismann (1834-1914) proposed that cells in the reproductive organs carry a complete set of genetic information that is passed to the egg and sperm.
- Mendel's Theory of Heredity: Mendel's crucial publication in 1866 on experiments with pea plants revealed the principles of heredity.
- Mendel conducted his experiment on seven characteristics of pea plant of their monohybrid crosses and dihybrid crosses, and he deduced the ratio of offspring at each generation. The method used in this cross was punnet square method, probability method and test cross method. However, when organisms containing poly traits are required to be crossed, since segregation and independent assortment of their gametes fuse with each other with equal probability, determining the probability of offspring their respective alleles should be crossed with each other separately then by using multiplication rule the corresponding genotype would be calculated.

COMPREHENSION QUESTIONS

1. *Why Mendel used test cross do you think?*
2. *If you are given to cross organisms containing multi traits for example: AAbbCcDDee X AaBBcCddEE, what would be the probability of AaBbccDDEe to be*

obtained?

3. *What does it mean segregation?*

4. *Why multi hybrid crosses are complex than monohybrids and di-hybrids.*

CHAPTER 3

THE CYTOLOGICAL BASIS OF HEREDITY



Cytology, branch of biology concerned with the study of the structure and function of cells as individual units, supplementing histology, which deals with cells as components of tissues. It is concerned with the structure and activities of the various parts of the cell and cell membrane; the mechanism of cell division; the development of sex cells, fertilization, and the formation of the embryo; cell disorders such as those occurring in cancer; cellular immunity; and the problems of heredity. Recently, new procedures have been introduced by which the living cell can be observed and studied by equipment like *phase-contrast microscope* (provides a means of studying the living cell in action without the use of dyes), Micro-dissection, microinjection, and microchemistry furnish (methods for drawing off minute amounts of living protoplasm through tubes a half micrometer in diameter and subjecting them to analysis). Cytology is important in modern medicine, especially in the diagnosis of diseases by examination of the cells occurring in the various body fluids. The determination of the number and proportion of the different types of cells in the blood, by a blood count, is important in diagnosing acute infections and other diseases. Variations in the size and shape of the red blood cell for example indicate the presence of i (if the cell is half-moon shaped); *pernicious anemia* (if it is very large) or *iron-deficiency anemia* (if it is very small). The type of disease may also be determined through cytology, as, for example, in distinguishing the various types of meningitis by examination of the cells present in the cerebrospinal fluid.

Cells are of two basic types (eukaryotic and prokaryotic cells) where the genetic information (chromosomes) of organisms contained whether in nucleus, mitochondria, chloroplast or freely in cytoplasm depending up on the type of organism. Genes, who are the fundamental unit of heredity within a cell located on chromosomes and are come in multiple forms called alleles which confer phenotypes (**See Fig 8**). So how this chromosome is inherited? Before we are going to see their heredity let we see their

structure, number, homologue, morphology and etc.

3.1. Chromosome Structure

Chromosomes are thin and difficult to observe by naked eye but before cell division they condense further into thick, readily observed structures by the use of advanced microscope. At this time it can be observed that functional chromosome has three essential elements i.e. centromere, pair of telomeres, and origins of replication (**Fig 9**).

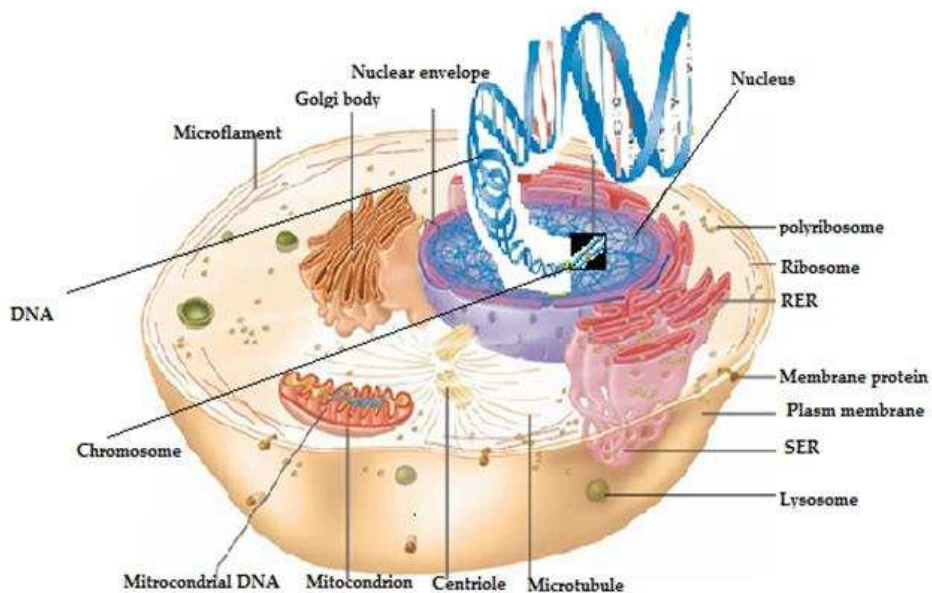


Figure 8: Arrangement of genes on a chromosome found in a cell

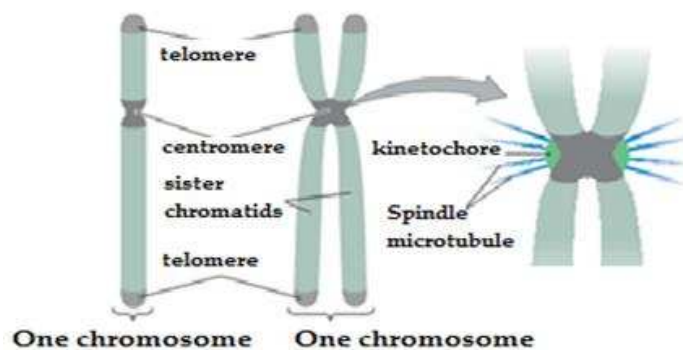


Figure 9: Structure of chromosome with its essential elements

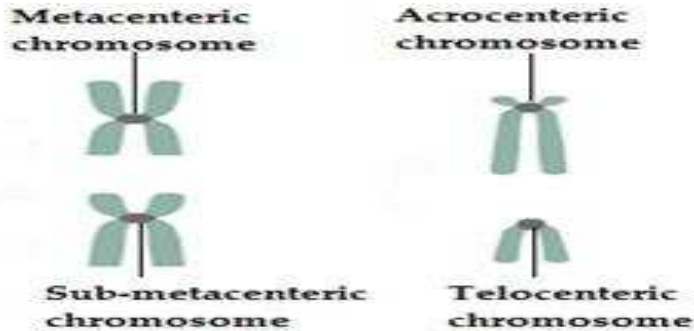


Figure 10: types of chromosome based on the location of chromosome

The centromere: The Centromere is the attachment point for spindle micro tubules the filaments responsible for moving chromosomes in cell division which appears as a constricted region. Before cell division, a multi protein complex called the kinetochore assembles on the centromere; later, spindle microtubules attach to the kinetochore. Chromosomes lacking a centromere cannot be drawn into the newly formed nuclei. On the basis of the location of the centromere, chromosomes are classified into four types: metacentric, sub metacentric, acrocentric and telocentric.

Telomeres: Telomeres are the natural ends or tips of a whole linear chromosome that protect and stabilize the chromosome ends and provide chromosome stability. Telomeres also participate in limiting cell division and may play important roles in aging and cancer.

Origins of replication: Origins of replication are the sites where DNA synthesis begins and are not easily observed by microscopy. In preparation for cell division, each chromosome replicates, making a copy of it. These two initially identical copies, called sister chromatids, are held together at the centromere. Each sister chromatid consists of a single molecule of DNA.

3.2. Cell Cycle

Cell cycle is the stage through which a cell passes from one division to the next is critical to genetics because through the cell cycle, the genetic instructions for all characteristics are passed from parent to daughter cells. A new cycle begins after a cell

has divided and produced two new cells. Each new cell metabolizes, grows, and develops. At the end of its cycle, the cell divides to produce two cells, which can then undergo additional cell cycles. Progression through the cell cycle is regulated at key transition points called checkpoints. The cell cycle consists of two major phases, mitosis and meiosis phase in which both of them preceded by Interphase phase

3.2.1. Interphase

Interphase is the period between cell divisions, in which the cell grows, develops, and functions. DNA is being synthesized, RNA and proteins are being produced, and hundreds of biochemical reactions necessary for cellular functions are taking place. Interphase includes several checkpoints, which regulate the cell cycle by allowing or prohibiting the cells division. Defects in checkpoints can lead to unregulated cell growth, as is seen in some cancers. Interphase is divided into three sub-phases i.e. gap one (*G1*) *phase*, synthesis (*S*) *phase* and gap two (*G2*) *phase*. In *G1* the cell grows, and proteins necessary for cell division are synthesized. Near the end of *G1*, a critical point termed the *G1/S* checkpoint holds the cell in *G1* until the cell has all of the enzymes necessary for the replication of DNA. After this checkpoint has been passed, the cell is committed to divide and then enters the *S* phase (for DNA synthesis) in which each chromosome duplicates. If DNA synthesis is blocked by drugs or by mutagenic substances the cell will not be able to undergo mitosis. After the *S* phase the cell enters *G2* (*gap2*) in which several additional biochemical events necessary for cell division take place. The important *G2/M* checkpoint is reached near the end of *G2* and the cell is ready to divide and enters the *M* phase. Before reaching the *G1/S* checkpoint, cells may exit from the active cell cycle in response to regulatory signals and pass into a non-dividing phase called *G0*, which is a stable state during which cells usually maintain a constant size (*See Fig11*).

3.2.2. Mitotic phase

Mitotic phase is the period of active cell division where nuclear division and cytokinesis or cytoplasmic division takes place. Sister chromatids separate and the cell undergo division. Mitotic phase divided into six stages: prophase, anaphase, prometa phase, telophase, Metaphase and Cytokinesis

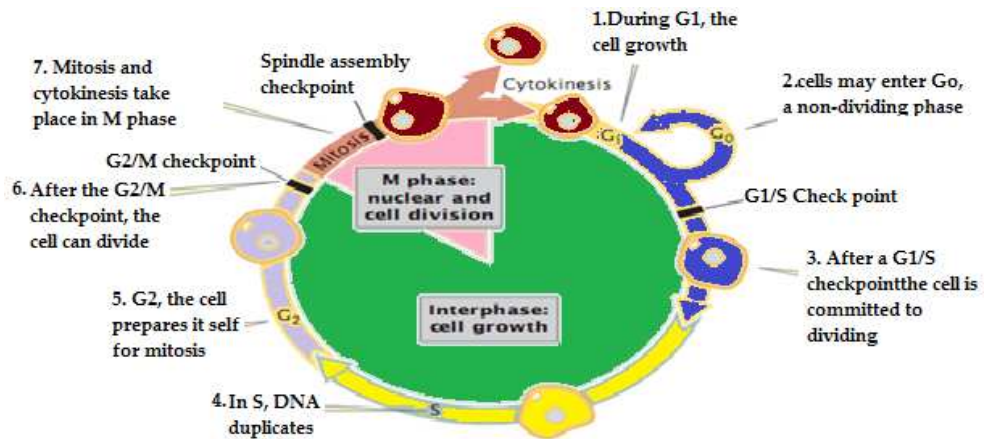


Table 11: The cell cycle consists of interphase and mitosis phase

Prophase: During prophase chromosomes become visible under a light microscope because it was duplicated in the preceding S phase. Each chromosome possesses two chromatids attached at the centromere. The mitotic spindle, an organized array of microtubules that move the chromosomes in mitosis is formed.

Pro-metaphase: At this stage the nuclear membrane starts to breakdown and spindle microtubules enter the nuclear region. The ends of certain microtubules make contact with the chromosomes and anchors to the kinetochore of one of the sister chromatids. A micro-tubule from the opposite centrosome then attaches to the other sister chromatid. One important property of microtubules is that it can lengthen and shorten, pushing and pulling the chromosomes to opposite poles of nucleus.

Metaphase: The chromosomes become arranged on the metaphase plate, between the two centrosomes. During this a spindle-assembly checkpoint ensures that each chromosome is aligned on the metaphase plate and attached to spindle fibers from opposite poles. The spindle-assembly checkpoint is able to detect even a single pair of chromosomes that are not properly attached to microtubules.

Anaphase: The connection between sister chromatids breaks down and the sister chromatids separate during this stage. Chromosomes move toward opposite spindle poles due to the disassembly of tubulin molecules at both the kinetochore end (called the end) and the spindle end of the spindle fiber. Tubulin is protein subunits that connect the chromosomes to the spindle poles. Special proteins called molecular

motors disassemble tubulin molecules from the spindle and generate forces that pull the chromosome toward the spindle pole.

Telophase: is when the arrival of the chromosomes at the spindle poles and nuclear membrane re-forms around each set of chromosomes, producing two separate nuclei within the cell. The chromosomes relax and lengthen, once again disappearing from view. In many cells, division of the cytoplasm called cytokinesis is simultaneous with telophase.

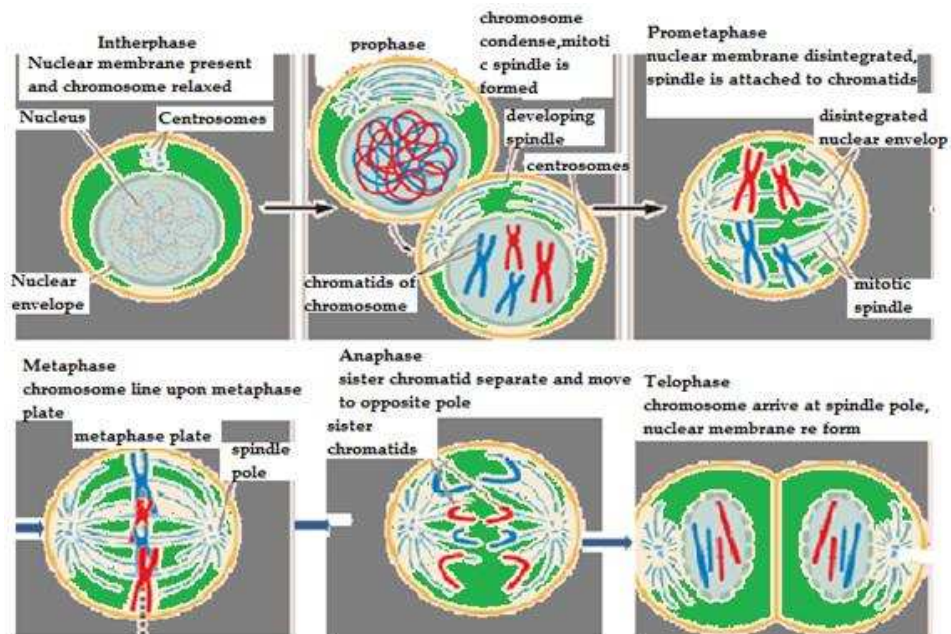


Figure 12: Phases of mitosis and action in each phase

Table 4: General feature of cell cycle

Stage	Major feature
G0 phase	Stable, non-dividing period of variable length
Interphase	
G1 phase	Growth and development of the cell; G1/S checkpoint
S phase	Synthesis of DNA
G2 phase	Preparation for division; G2/M checkpoint
M phase	
Prophase	Chromosomes condense and mitotic spindle forms
prometaphase	Nuclear envelope disintegrate, and spindle microtubules anchor to kinetochores
metaphase	Chromosomes align on the metaphase plate; spindle assembly check point
Anaphase	Sister chromatids separate; becoming individual chromosomes that migrate towards spindle pole
telophase	Chromosomes arrive at spindle poles, the nuclear envelope reforms and the condensed chromosome relax.
cytokinesis	Cytoplasm divides cell wall forms in plant cells.

3.2.3. Meiosis

Meiosis is preceded by an interphase stage gap one (G1), synthesis (S) and gap two (G2) phases. It consists of two that includes distinct processes: meiosis I and meiosis II. Division at the end of meiosis I is termed as the reduction division because the number of chromosomes per cell is reduced by half. The second division, which comes at the end of meiosis II, is sometimes termed the equational division.

Meiosis I: Meiosis I has sub-phases like that of mitosis i.e. prophase I, metaphase I, anaphase I and telophase I. Prophase I is a lengthy stage, divided into five sub-stages: *leptotene* (the chromosomes contract and become visible), *Zygotene* (the chromosomes continue to condense; homologous chromosomes pair up and begin synapsis, each homologous pair of synapsed chromosomes consists of four chromatids called a bivalent or tetrad), *Pachytene* (the chromosomes become shorter and thicker, crossing over takes place in which homologous chromosomes exchange genetic information), *Diplotene* (the centromeres of the paired chromosomes move apart in the two homologs remain attached at each chiasmata) and *Diakinesis* (chromosome condensation continues, chiasmata move toward the ends of the chromosomes so the homologs remain paired only at the tips. Near the end of prophase I, the nuclear membrane breaks down and the spindle forms, setting the stage for metaphase I).

Metaphase I: Metaphase is initiated when homologous pairs of chromosomes align

along the metaphase plate. A microtubule from one pole attaches to one chromosome of a homologous pair and a microtubule from the other pole attaches to the other member of the pair.

Anaphase I: During separation of homologous chromosomes takes place, the two chromosomes of a homologous pair are pulled toward opposite poles. Although the homologous chromosomes separate, the sister chromatids remain attached and travel together.

Interkinesis: This stage is the period between meiosis I and meiosis II where the nuclear membrane re-forms around the chromosomes clustered at each pole, the spindle breaks down and the chromosomes relax.

Meiosis II: similar to meiosis I meiosis II has different sub-phases i.e. prophase II, anaphase II, metaphase II, telophase II and cytokinesis. *Prophase II* (during this phase the events of interkinesis are reversed, the chromosomes re-condense, the spindle re-forms, and the nuclear envelope once again breaks down). *Metaphase II* (chromosomes are line up on metaphase plate). *Anaphase II* (The kinetochores of the sister chromatids separate and the chromatids are pulled to opposite poles, each chromatid is now a distinct chromosome). *Telophase II* (the chromosomes arrive at the spindle poles, a nuclear envelope re-forms around the chromosomes, the cytoplasm divides, the chromosomes relax and are no longer visible).

Table 5: Major events in each stages of meiosis

stage	Major events
Meiosis I	
Prophase I	Chromosome condense, homologous chromosome synapse, crossing over takes place, the nuclear envelop break down, mitotic spindle forms
Metaphase I	Homologous pairs of chromosomes line upon the metaphase plate
Anaphase I	The two chromosomes of each homologous pairs separate and move toward opposite poles
Telophase I	Chromosomes arrive at the spindle poles
Cytokinesis	The cytoplasm divides to produce two cells, each having half the original numbers of chromosomes
interkinesis	In some types of cells the spindle breaks down, chromosomes relax, and nuclear envelop reforms, but no DNA synthesis takes place
Meiosis II	
Prophase II	Chromosomes condense, the spindle forms and nuclear envelop disintegrates
Metaphase II	Individual chromosome line up on metaphase plate
Anaphase II	Sister chromatids separate and move as an individual chromosomes toward the spindle poles
Telophase II	Chromosome arrive at the spindle poles, the spindle breaks down and nuclear envelop re forms
cytokinesis	The cytoplasm divides

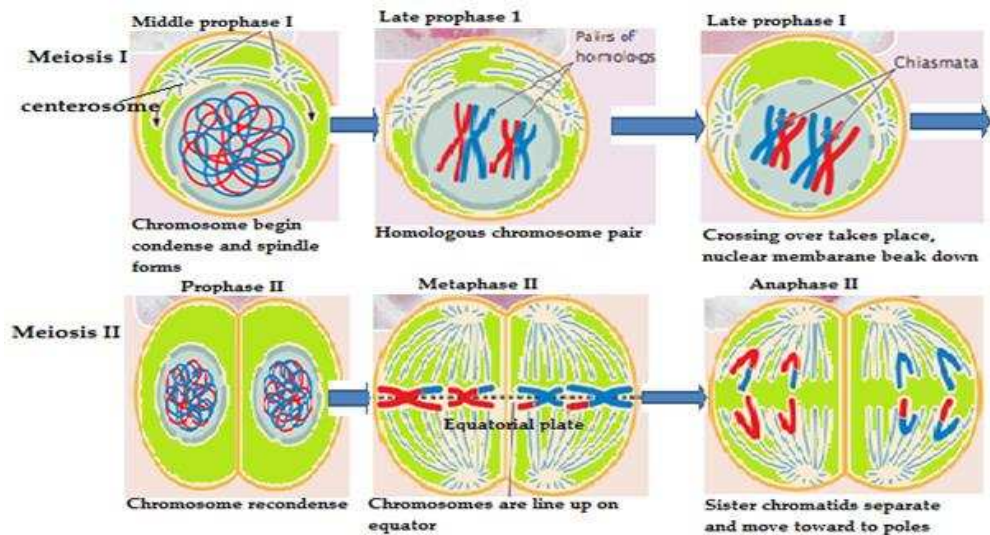


Figure 13: Phases of Meiosis and action in each phase

Crossing over is the basis for intra chromosomal recombination which takes place in prophase I, creating new combinations of alleles on a chromatid. It refers to the exchange of genes between non-sisters chromatids (chromatids from different homologous chromosomes). Due to recombination of chromosome crossing over create genetic variation. For example, consider the following two pairs of alleles which abbreviated Aa and Bb. Assume that one chromosome possesses the A and B alleles and its homolog possesses the a and b alleles. When DNA is replicated in the S phase, each chromosome duplicates, and so the resulting sister chromatids are identical.

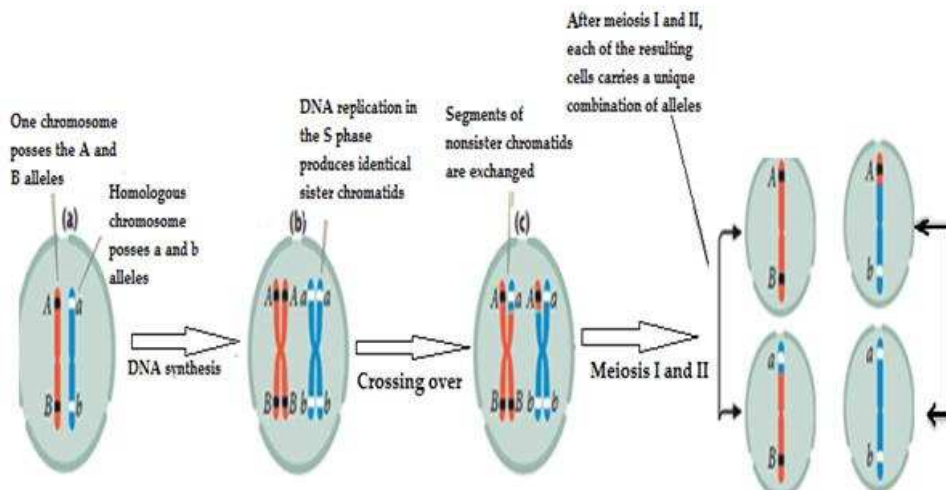


Figure 14: Crossing over produces genetic variation

Generally, the differences between mitosis and meiosis are explained (see table 6c in the appendix)

3.2.4. Cohesin makes chromosome intact

Homologous and sister chromatids to be paired by a molecule called Cohesin (a protein that holds the chromatids together). Joining and separation of chromatids and homologous chromosomes is established in the S phase and persists through G2 and early mitosis. In anaphase of mitosis, cohesin along the entire length of the chromosome is broken down by an enzyme called separase which allow the sister chromatids to separate. It is important to note that the forms of cohesin used in mitosis and meiosis differ. At the beginning of meiosis, the meiosis-specific cohesin is found along the entire length of chromosomes arms. This cohesin also acts on the chromosome arms of homologs at the chiasmata, binding two homologs together at their ends. In anaphase I, cohesin along the chromosome arms is broken, allowing the two homologs to separate however cohesin at the centromere is protected by a protein called shugoshin. Because of this protective action by shugoshin, the centromeric cohesin remains intact and prevents the separation of the two sister chromatids during anaphase I of meiosis. Shugoshin is subsequently degraded and at the end of meta-phase II, the centromeric cohesion no longer protected by shugoshin breaks down, allowing the sister chromatids to separate in anaphase II, just as they do in mitosis.

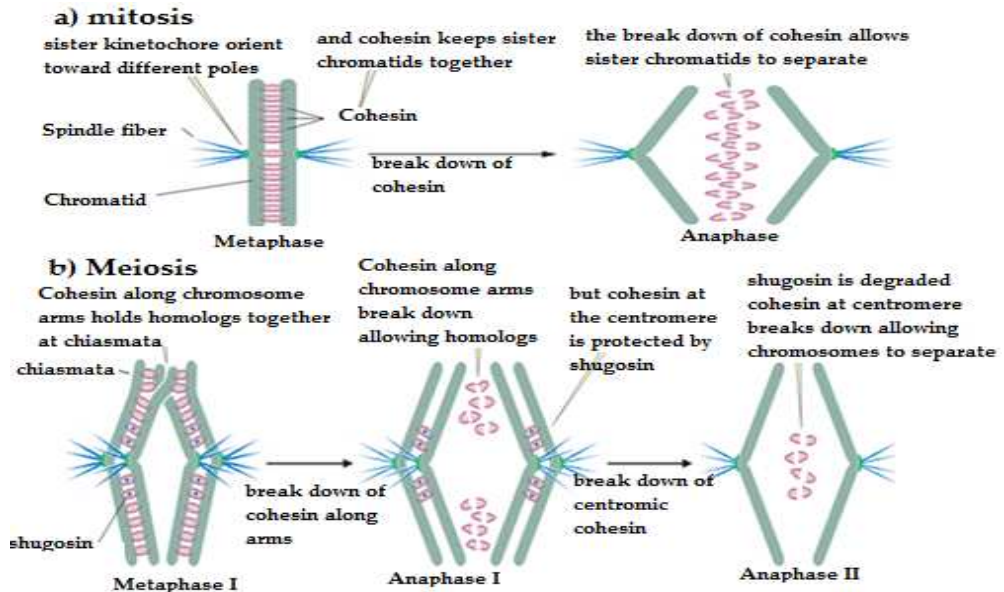


Figure 16: Cohesin force that maintain homologous chromosome and sister chromatid to intact

3.2.5. Meiosis in the life cycle of animals and plants

3.2.5.1. Meiosis in animals

In animals two type processes are there i.e. spermatogenesis (in males) and oogenesis (in females). *Spermatogenesis* is a process of the production of gametes in a male animal takes place in the testes. Diploid germ cells divide mitotically to produce diploid cells called spermatogonia in which each spermatogonium can undergo repeated rounds of mitosis, giving rise to numerous additional spermatogonia. Alternatively, a spermatogonium can initiate meiosis and enter into prophase I called a primary spermatocyte which still diploid because the homologous chromosomes have not yet separated. Each primary spermatocyte completes meiosis I and giving rise to two haploid secondary spermatocytes that then undergo meiosis II to produce two haploid spermatids. Thus, each primary spermatocyte produces a total of four haploid spermatids, which mature and develop into sperm. *Oogenesis* is a process of the production of gametes in a female animal within the ovaries.

Diploid germ cells divide mitotically to produce oogonia which undergo repeated rounds of mitosis or they can enter into meiosis. When they enter prophase I, these still-diploid cells are called primary oocytes. Each primary oocyte completes meiosis I and divides. At this point, the process of oogenesis begins to differ from that of spermatogenesis. In oogenesis, cytokinesis is unequal i.e. most of the cytoplasm is distributed to one of the two haploid cells, the secondary oocyte. The smaller cell, which contains half of the chromosomes but only a small part of the cytoplasm, is called the first polar body (it may or may not divide further). The secondary oocyte completes meiosis II, and again, cytokinesis is unequal most of the cytoplasm passes into one of the cells. The larger cell, which acquires most of the cytoplasm, is the ovum (the mature female gamete). The smaller cell is the second polar body which usually disintegrates. Only the ovum is capable of being fertilized then, produces a single mature gamete from each primary oocyte.

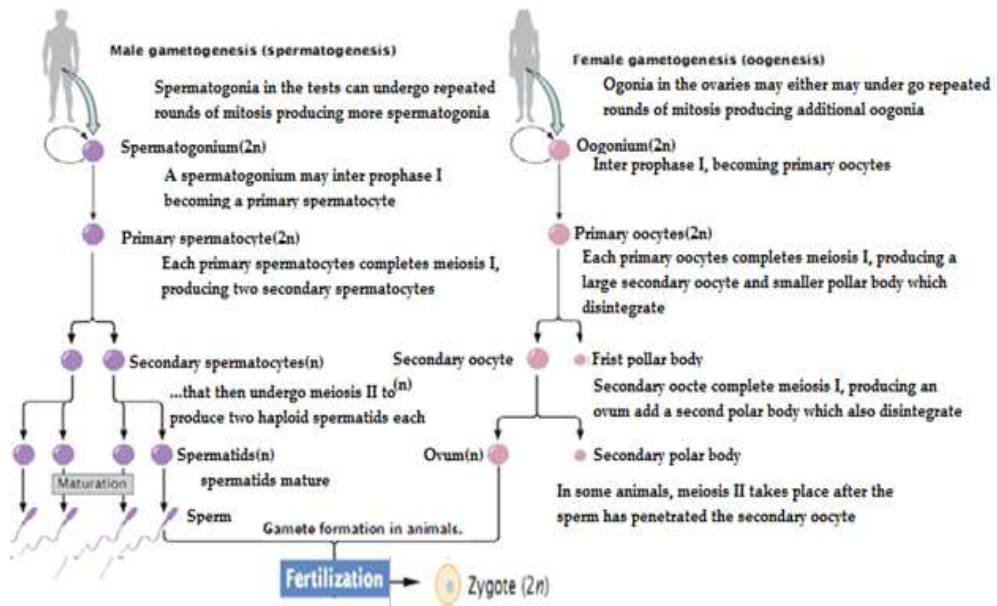


Figure 17: Processes of spermatogenesis and oogenesis in human

3.2.5.2. Meiosis in plants

Most plants have a complex life cycle that includes two distinct generations: **diploid sporophyte** and the **haploid gametophyte** where the life cycle is sometimes called **alternation of generations**. During alternation of generation life cycle, the immediate

products of meiosis are called spores which undergo one or more mitotic divisions to produce gametes. The processes in plants and animals are basically the same: in both, meiosis leads to a reduction in chromosome number, producing haploid cells. However, in some plants, both male and female reproductive structures are found in the same flower; in other plants, they exist in different flowers. In either case, the male part of the flower (stamen) contains diploid reproductive cells called microsporocytes, each of which undergoes meiosis to produce four haploid microspores. Each microspore divides mitotically, producing an immature pollen grain consisting of two haploid nuclei. One of these nuclei called the tube nucleus directs the growth of a pollen tube. The other termed the generative nucleus divides mitotically to produce two sperm cells.

The pollen grain, with its two haploid nuclei, is the male gametophyte and the female part of the flower (ovary) contains diploid cells called mega sporocytes each of which undergoes meiosis to produce four haploid megaspores only one of which survives. The nucleus of the surviving megaspore divides mitotically three times producing a total of eight haploid nuclei that make up the female gametophyte (the embryo sac). Division of the cytoplasm then produces separate cells one of which becomes the egg. When the plant flowers i.e the stamens open and release pollen grains, pollen lands on a flower's stigma, a sticky platform that sits on top of a long stalk called the style. At the base of the style is the ovary where if a pollen grain germinates, it grows a tube down the style into the ovary. The two sperm cells pass down this tube and enter the embryo sac in which one of the sperm cells fertilizes the egg cell and producing a diploid zygote which develops into an embryo. The other sperm cell fuses with two nuclei enclosed in a single cell giving rise to a $3n$ (triploid) endosperm which stores food that will be used later by the embryonic plant. These two fertilization events are termed double fertilization.

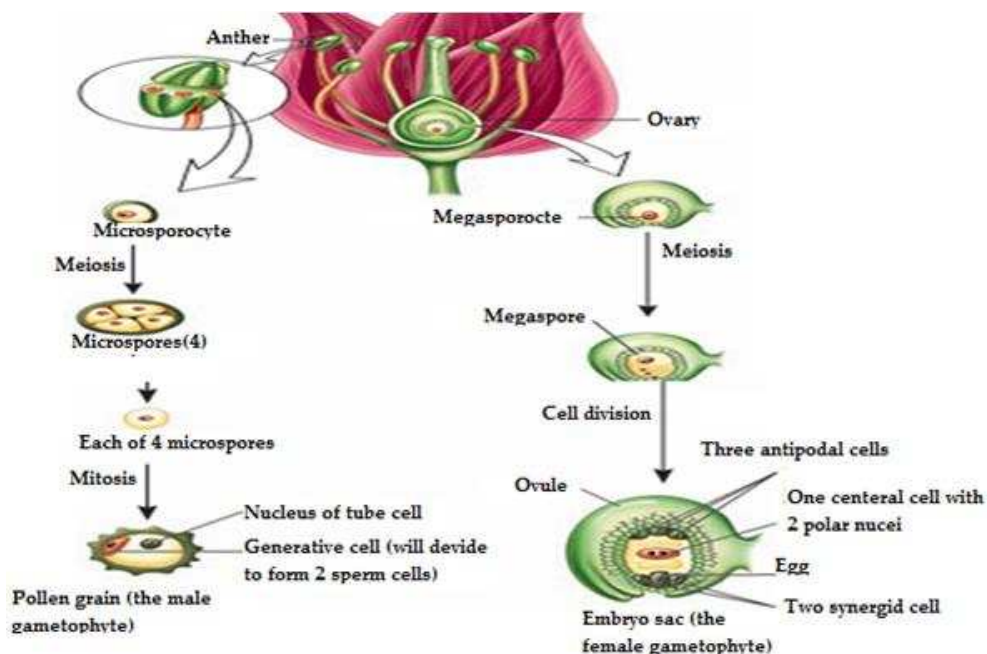


Figure 18: Microsporocyte and megasporocyte formation in meiosis

REVIEWING THE KEY CONCEPTS

- Branch of biology concerned with the study of the structure and function of cells as individual units, supplementing histology, the mechanism of cell division; the development of sex cells, fertilization, and the formation of the embryo and cell disorders is called cytology.
- Genes which are the fundamental unit of heredity within a cell located on chromosomes and are come in multiple forms called alleles which confer phenotypes.
- Chromosomes are thin and difficult to observe it by naked eye but before cell division they condense further into thick, readily observed structures by the use of advanced microscope. The structure of chromosome has centromere, origin of replication and telomeres.
- Based on the position of centromere chromosomes are divided in to centromeric, metacentric, sub-metacentric and telomeric chromosomes.
- The stage through which a cell passes from one division to the next is critical to genetics because through the cell cycle. This cell cycle has different stages i.e.

interphase in which another sub-stages Gap1, Synthesis(S) and gap 2 are included. After the completion of interphase cell recommended to divide by either of the two cell divisions i.e. mitosis and meiosis. During cell division, three proteins are play great role i.e. cohesin, separase and shugoshin.

- Multicellular organisms that can reproduce sexually like animals and plants follow types of cell division like meiosis. In animals sperm is formed by the process of spermatogenesis and egg is formed by oogenesis. However, in plants sperm is formed by micro-sporogenesis and egg is formed by the process of mega-sporogenesis.

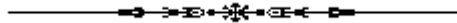
COMPREHENSION QUESTIONS

1. What are the three sub-stages of interphase?
 2. Please differentiate the difference between cohesin, separase and shugoshin?
 3. What would be if crossing over do not takes place between the arms of homologous chromosome do you think?
 4. What is the use of origin of replication during cell division?
 5. Which one of the following structure is diploid?
- A) Microspore B) Egg C) Megaspore D) Microsporocytes

CHAPTER 4

PROBABILITY AND STATISTICAL

TESTING IN GENETICS



Mendel's work, laws of inheritance used to predict the outcome of genetic crosses in agriculture, for example, in plants and animals where breeders are concerned with the types of offspring their crosses will produce. Probability calculations are used in genetic problems to predict the outcome of crosses. To compute probability, we use three mathematical operations known as the sum rule, the product rule, and the binomial expansion equation. These methods allow us to determine the probability that a cross between two individuals will produce a particular outcome.

Multiplication rule: It states that the probability of two or more independent events occurring together is calculated by multiplying their independent probabilities. For example: the probability of rolling one die and obtaining a four is $1/6$. To calculate the probability of rolling a die twice and obtaining 2 fours, we can apply the multiplication rule. The probability of obtaining a four on the first roll and second roll is $1/6$; so the probability of rolling a four on both is $1/6 \times 1/6 = 1/36$. The key indicator for applying the multiplication rule is the word and; in the example just considered, we wanted to know the probability of obtaining a four on the first roll and a four on the second roll. For the multiplication rule to be valid, the events whose joint probability is being calculated must be independent the outcome of one event must not influence the outcome of the other. For example, the number that comes up on one roll of the die has no influence on the number that comes up on the other roll; so these events are independent.

Addition rules: it states that the probability of any one of two or more mutually exclusive events is calculated by adding the probabilities of these events. For example: to obtain the probability of throwing a die once and rolling either a three or a four, we

would use the addition rule, adding the probability of obtaining a three ($1/6$) to the probability of obtaining a four (again, $1/6$), or $1/6 + 1/6 = 2/6 = 1/3$. The key indicators for applying the addition rule are the words either and or. For the addition rule to be valid, the events whose probability is being calculated must be mutually exclusive, meaning that one event excludes the possibility of the occurrence of the other event. For example, you cannot throw a single die just once and obtain both a three and a four, because only one side of the die can be on top. In such mutually exclusive events, the Punnett square is easier to understand and just as quick for simple monohybrid crosses. However, for tackling more complex crosses concerning genes at two or more loci, the probability method is both clearer and quicker than the Punnett square.

4.1. The Binomial Expansion and Probability

When probability is used, it is important to recognize that there may be several different ways in which a set of events can occur. When two parents heterozygous for albinism mate for example ($Aa \times Aa$), the probability of their having a child with albinism (aa) is $1/4$ and the probability of having a child with normal pigmentation (AA or Aa) is $3/4$. Suppose we want to know the probability of this couple having three children all three with albinism. In this case, there is only one way in which they can have three children with albinism i.e. their first child has albinism and their second child has albinism and their third child has albinism. Here, we simply apply the multiplication rule: $1/4 \times 1/4 \times 1/4 = 1/64$. *But what is the probability of this couple having three children, one with albinism and two with normal pigmentation?* This situation is more complicated. Because the first child might have albinism, whereas the second and third are unaffected. The probability of this sequence of events is $1/4 \times 3/4 \times 3/4 = 9/64$. Alternatively the first and the third child might have normal pigmentation, whereas the second has albinism. The probability of this sequence is $3/4 \times 1/4 \times 3/4 = 9/64$. Finally, the first two children might have normal pigmentation and the third albinism. The probability of this sequence is $3/4 \times 3/4 \times 1/4 = 9/64$. Because either the first sequence or the second sequence or the third sequence produces one child with albinism and two with normal pigmentation, we apply the addition rule. The probabilities: $9/64 + 9/64 + 9/64 = 27/64$. If we want to know the probability of this couple having five children, two with albinism and three with normal pigmentation, figuring out all the different combinations of children and their probabilities becomes more difficult. This task is made easier if we apply the binomial expansion as a form $(p+q)^n$ where “p” is the

probability of one event, “q” is the probability of the alternative event, and “n” is the number of times the event occurs.

Accordingly, to figuring the probability of two out of five children with albinism: let P= the probability of a child having albinism (1/ 4) and q= the probability of a child having normal pigmentation (3/4), the binomial for this situation is $(p+q)^5$ because there are five children in the family (n=5). The expansion is: $(p+q)^5 = p^5 + 5p^4q + 10p^3q^2 + 10p^2q^3 + 5pq^4 + q^5$. Each of the terms in the expansion provides the probability for one particular combination of traits in the children. The first term in the expansion (p^5) equals the probability of having five children all with albinism, because p is the probability of albinism. The second term ($5p^4q$) equals the probability of having four children with albinism and one with normal pigmentation. The third term ($10p^3q^2$) equals the probability of having three children with albinism and two with normal pigmentation, and so forth. To obtain the probability of any combination of events, we insert the values of p and q. So the probability of having two out of five children with albinism is: $10p^2q^3 = 10(1/4)^2(3/4)^3 = 270/1024 = 0.26$. In general, the expansion of any binomial $[(p + q)]^n$ consists of a series of n+1 term. In the

preceding example, n=5; so there are 5+1=6 terms: p^5 , $5p^4q$, $10p^3q^2$, $10p^2q^3$, $5pq^4$, and q^5 . To write out the terms, first figure out their exponents. The exponent of p in the first term always begins with the power to which the binomial is raised, or n. In our example, n equals 5, so our first term is p^5 . The exponent of p decreases by one in each successive term; so the exponent of p is 4 in second term (p^4), 3 in the third term (p^3); and so forth. The exponent of q is 0 (no q) in the first term and increases by 1 in each successive term, increasing from 0 to 5 in our example.

The next is determining the coefficient of each term. The coefficient of the first term is always 1; so, in our example, the first term is $1p^5$ or p^5 . The coefficient of the second term is always the same as the power to which the binomial is raised; in our example this coefficient is 5 and the term is $5p^4q$. For the coefficient of the third term, look back at the preceding term; multiply the coefficient of the preceding term (5 in our example) by the exponent of p in that term (4) and divide by the number of that term (second term or 2). So, the coefficient of the third term in our example is $(5 \times 4) / 2 = 20 / 2 = 10$ and the term is $10p^3q^2$. The others will be done accordingly.

Another way to determine the probability of any particular combination of events is

“n” to use the following formula:

$$\text{Over all probability } (p) = \frac{n!}{s! t!} p^s q^t$$

Where: p=the over all probability of event X with probability p occurring s times and event Y with probability q occurring t times. For our example above, event X would be the occurrence of a child with albinism (1/4) and event Y would be the occurrence of a child with normal pigmentation (3/4); s would equal the number of children with albinism (2) and t would equal the number of children with normal pigmentation (3). The “!” symbol stands for factorial, and it means the product of all the integers from n to 1. In this example n=5; so n! = 5x4x3x2x1. Applying this formula to obtain the probability of two out of five children having albinism is calculated by substituting in the above formula.

Accordingly we can obtain

$$(p) = \left(\frac{n!}{s! t!} \right) p^s q^t \quad (p) = \frac{5!}{2! 3!} \left(\frac{1}{4} \right)^2 \left(\frac{3}{4} \right)^3$$

4.2. Crosses Involving Higher Levels of Hybridity and Concomitant Ratios

When crossing is takes place between two organisms containing contrasting traits, there will expectation then after cross observation is takes place. During this observed ratio may be deviated from the expected ratio. The deviation is nothing but it is due to chance alone (a matter of probability). When two individual organisms of known genotype are crossed, we expect certain ratios of genotypes and phenotypes in the progeny. These expected ratios are based on the Mendelian principles of segregation, independent assortment, and dominance. The ratios of genotypes and phenotypes actually observed among the progeny. However, it may deviate from these expectations. For example, in German cockroaches, brown body color (Y) is dominant over yellow body color (y). If we cross a brown heterozygous cockroach (Yy) with a yellow cockroach (yy), we expect a 1: 1 ratio of brown (Yy) and yellow (yy) progeny. Among 40 progeny, we therefore expect to see 20 brown and 20 yellow offspring. However, the observed numbers might deviate from these expected values; we might in fact see 22 brown and 18 yellow progeny. To evaluate the role of chance in producing deviations between observed and expected values, a statistical test called the

goodness-of-fit chi-square test is used which provides information about how well observed values fit expected values.

Before we learn how to calculate the chi square, it is important to understand what this test does and does not indicate about a genetic cross. First the chi-square test cannot tell us whether a genetic cross has been correctly carried out, whether the results are correct, or whether we have chosen the correct genetic explanation for the results. Second the probability that the difference between the observed and the expected values is due to chance. Third this hypothesis, that chance alone is responsible for any deviations between observed and expected values, is sometimes called the null hypothesis. When the probability calculated from the chi-square test is high, we assume that chance alone produced the difference (the null hypothesis is true) and when the probability is low, we assume that some factor other than chance some significant factor produced the deviation (the null hypothesis is false).

Table 7: calculating expected ratio from observed ratio

Phenotype	Observed	expected
Purple	105	3/4x150
White	45	1/4x150
total	150	

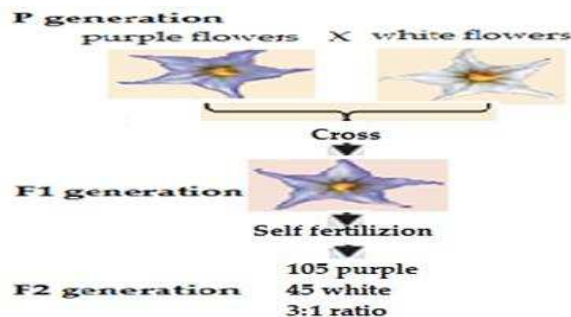


Figure 19: The observed ratio of crossing between purple flower and white flower

$$\chi^2 = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

Where, χ^2 =chi-square, Σ =summation of all the squared differences between observed and expected. See **figure 19** as example. The expected values are obtained by multiplying the expected proportion by the total and the chi-square value is calculated.

The probability associated with the calculated chi-square value is between 0.1 and 0.5 indicating a high probability that the difference between observed and expected values is due to chance. It is not due to other factors which its probability is less than 0.1 as reading from **Table 7**.

$$X^2 = \sum \frac{(O - E)^2}{E}$$

$$X^2 = \sum \frac{(105-112.5)^2}{112.5} + \frac{(45-37.5)^2}{37.5}$$

$$X^2 = \frac{56.25}{112.5} + \frac{56.25}{37.5}$$

$$X^2 = 0.5 + 1.5 = 2$$

Degree of freedom=n-1 where n is number of traits (2). So it is 2-1= 1. By reading the degree of freedom obtained the values of chi-square will be searched where it is located between probability values as shown on the (**Table 8**).

Table 8: Critical values of the chi-square (X²) distribution

	P								
df	0.995	0.975	0.9	0.5	0.1	0.05*	0.025	0.01	0.005
1	0.000	0.000	0.016	0.455	2.706	3.841	5.024	6.635	7.879
2	0.010	0.051	0.211	1.386	4.605	5.991	7.378	9.210	10.597
3	0.072	0.216	0.584	2.366	6.251	7.815	9.348	11.345	12.838
4	0.207	0.484	1.064	3.357	7.779	9.488	11.143	13.277	14.860
5	0.412	0.831	1.610	4.351	9.236	11.070	12.832	15.086	16.750
6	0.676	1.237	2.204	5.348	10.645	12.592	14.449	16.812	18.548
7	0.989	1.690	2.833	6.346	12.017	14.067	16.013	18.475	20.278
8	1.344	2.180	3.490	7.344	13.362	15.507	17.535	20.090	21.955
9	1.735	2.700	4.168	8.343	14.684	16.919	19.023	21.666	23.589
10	2.156	3.247	4.865	9.342	15.987	18.307	20.483	23.209	25.188
11	2.603	3.816	5.578	10.341	17.275	19.675	21.920	24.725	26.757
12	3.074	4.404	6.304	11.340	18.549	21.026	23.337	26.217	28.300
13	3.565	5.009	7.042	12.340	19.812	22.362	24.736	27.688	29.819
14	4.075	5.629	7.790	13.339	21.064	23.685	26.119	29.141	31.319
15	4.601	6.262	8.547	14.339	22.307	24.996	27.488	30.578	32.801

REVIEWING THE KEY CONCEPTS

- Probability calculations are used in genetic problems to predict the outcome of crosses where three mathematical operations known as the sum rule, the product

rule, and the binomial expansion equation.

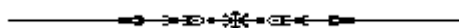
- Multiplication rule is the rule of probability of two or more independent events occurring together is calculated by multiplying their independent probabilities.
- Addition rules states that the probability of any one of two or more mutually exclusive events is calculated by adding the probabilities of these events.
- Binomial expansion is when probability of crosses between two individual is importantly too occurred in several different ways.
- Sometimes when crossing takes place between two organisms containing contrasting traits, there will be expected ratio. However, after cross the observation failed to equal with the expected one. During this observed ratio may be deviated from the expected ratio due to chance alone. This deviation is calculated by chi-square formula i.e. summation of expected ratio from observed ratio to expected ratio.

COMPREHENSION QUESTIONS

1. In a family of seven children, what is the probability of obtaining the following numbers of boys and girls?
 - (a) All boys
 - (c) Six girls and one boy
 - (d) Four boys and three girls
 - (e) Four girls and three boys
2. Assume that red is dominant over white color of certain trees. If pure homozygous red flower crossed with homozygous white you expect that all F1 off-springs are heterozygous red i.e. 1:1 ratio. If after cross you observed 15 heterozygous red and 5 homozygous white out of twenty off-springs.
 - A. Calculate the chi-square test
 - B. what is the range of probability from the calculated chi-square
 - C. what do you decide the deviation is due to chance or due to another factors?

CHAPTER 5

GENE INTERACTIONS AND THE INFLUENCE OF ENVIRONMENT ON GENES EXPRESSION



Principle of segregation and the principle of independent assortment allow us to predict the outcomes of genetic crosses. In this chapter we will see differently expression of alleles of traits during off spring is formed as well as expression of one gene affects the expression genes found on another locus. One of Mendel's important contributions to the study of heredity is the concept of dominance. It is the idea that an individual organism possesses two different alleles for a characteristic but the trait encoded by only one of the alleles is observed in the phenotype. Dominance can be understood in regard to how the phenotype of the heterozygote relates to the phenotypes of the homozygotes. Mendel observed dominance in all of the traits that he chose to study extensively but he was aware that not all characteristics exhibit dominance.

5.1. Types of Dominance

Complete dominance: For example take flower color ranges from red (homozygous genotype A_1A_1) produces red flower pigment to white (homozygous genotype A_2A_2) produces no pigment resulting in white flowers. If the heterozygote A_1A_2 produces the same amount of pigment as the A_1A_1 homozygote, resulting in red, then the A_1 allele displays complete dominance over the A_2 allele i.e. red is dominant over white. If, on the other hand, the heterozygote produces no pigment results in flowers with the same color as the A_2A_2 homozygote (white), then the A_2 allele is dominant over red(**Fig 20**).

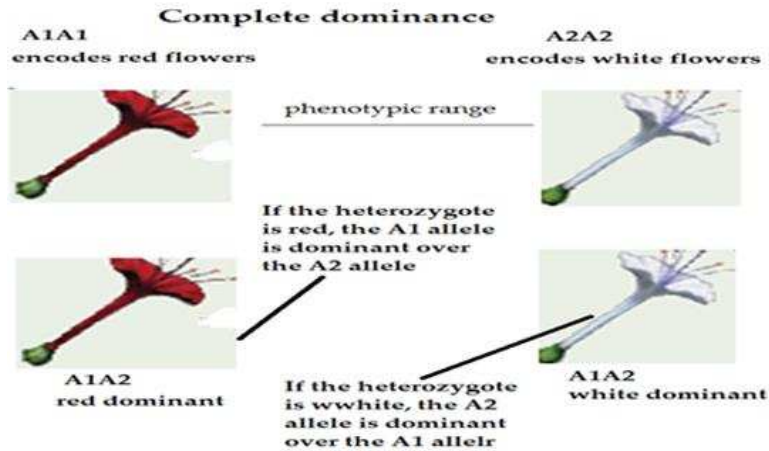


Figure 20: Complete dominance formation during crosses between red flowers and white flowers

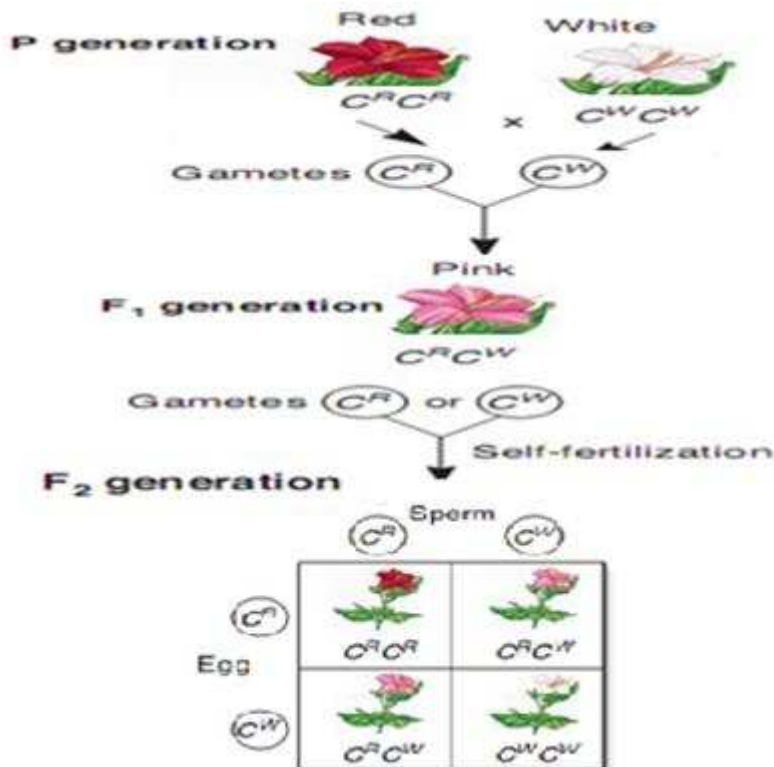


Figure 21: Incomplete dominance fall between the two homozygous traits

In-complete dominance: When the heterozygote falls in between the phenotypes of

the two homozygotes the dominance is said to be incomplete. For example when two different homozygotes (CWCW and CRCR) are crossed, the resulting heterozygote, CRCW, has an intermediate phenotype of pink flowers. In this case, 50% of the functional protein encoded by the allele is not sufficient to produce a red phenotype. That means the incomplete one is neither red nor white in color, it is intermediate between the two.

Overdominance: Over dominance occurs when heterozygotes have superior traits. As we have seen, the environment plays a key role in the out-come of traits. For certain genes, heterozygotes may display characteristics that are more beneficial for their survival in a particular environment. Such heterozygotes may be more likely to survive and reproduce. For example, a heterozygote may be larger, disease-resistant, or better able to withstand harsh environmental conditions. The phenomenon in which a heterozygote has greater reproductive success compared with either of the corresponding homozygotes is called overdominance, or heterozygote advantage. For example, human allele that causes sickle cell disease in homozygous individuals which is an autosomal recessive disorder in which the affected individual produces an altered form of the protein hemoglobin, which carries oxygen within red blood cells.

Most people carry the *HbA* allele and make hemoglobin A. Individuals affected with sickle cell disease are homozygous for the *HbS* allele and produce only hemoglobin S. This causes their red blood cells to deform into a sickle shape under conditions of low oxygen concentration. The sickling phenomenon causes the life span of these cells to be greatly shortened to only a few weeks compared with a normal span of 4 months, and therefore, anemia results. In addition, abnormal sickled cells can become clogged in the capillaries throughout the body, leading to localized areas of oxygen depletion. Such an event, called a crisis, causes pain and sometimes tissue and organ damage. For these reasons, the homozygous *HbSHbS* individual usually has a shortened life span relative to individual producing hemoglobin A. In spite of the harmful consequences to homozygotes, the sickle cell allele has been found at a fairly high frequency among human populations that are exposed to malaria. The protozoan genus that causes malaria, *Plasmodium*, spends part of its life cycle within the *Anopheles* mosquito and another part within the red blood cells of humans who have been bitten by an infected mosquito. However, red blood cells of heterozygotes, *HbAHbS*, are likely to rupture (disagreement) when infected by this parasite, thereby preventing the parasite from propagating. Hence, people who are heterozygous (*HbAHbS*) have better resistance to

malaria than do homozygotes (*HbAHbA*), while not incurring the ill effects of sickle cell disease. Therefore, even though the homozygous (*HbSHbS*) condition is detrimental, the greater survival of the heterozygote has selected for the presence of the HbS allele within populations where malaria is prevalent. When viewing survival in such a region, overdominance explains the prevalence of the sickle cell allele.

Codominance: Codominance is another type of interaction between alleles where phenotype of the heterozygote is not intermediate between the phenotypes of the homozygotes rather; the heterozygote simultaneously expresses the phenotypes of both homozygotes. An example of Codominance is seen in the MN blood types. The MN loci encode one of the types of antigens on red blood cells. At the MN locus, there are two alleles: the L^M allele (encodes the M antigen) and L^N allele (encodes the N antigen). Homozygotes with genotype the $L^M L^M$ express the M antigen on their red blood cells and have the M blood type. Homozygotes with $L^N L^N$ genotype express the N antigen and have the N blood type. Heterozygotes with genotype $L^M L^N$ exhibit codominance and express both the M and the N antigens; they have blood-type MN.

Table 9: Difference between dominance, incomplete dominance and codominance

Type of dominance	Definition
dominance	Phenotype of the heterozygote is the same as the phenotype of one of homozygote
Incomplete dominance	Phenotype of the heterozygote is intermediate (falls within the range) between the phenotypes of the two homozygotes.
codominance	Phenotype of the heterozygote includes the phenotypes of both homozygotes.

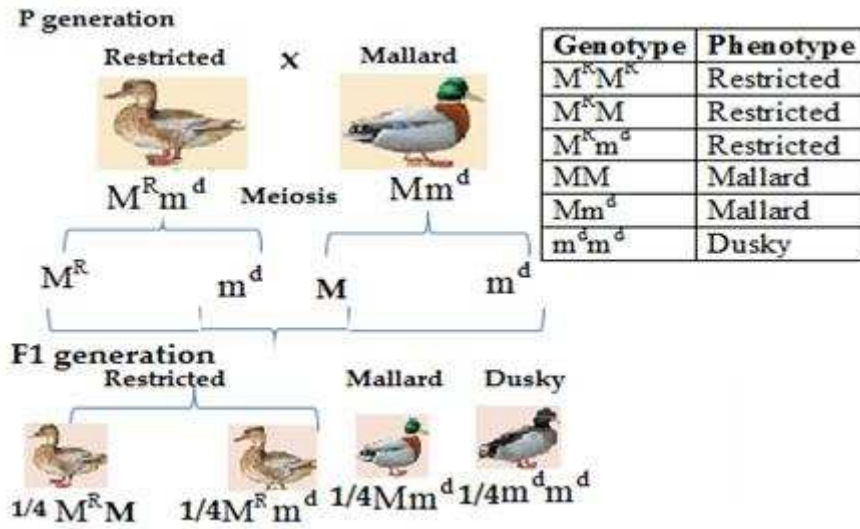
5.2. Penetrance and Expressivity

Penetrance is defined as the percentage of individual organisms having a particular genotype that express the expected phenotype. For example, if we examined 42 people

having an allele for polydactyl and found that only 38 of them were polydactyl, the penetrance would be $38/42 = 0.90$ (90%). Whereas expressivity is the degree to which a character is expressed. In above example, polydactyl exhibits variable expressivity where some polydactyl persons possess extra fingers and toes that are fully functional, whereas others possess only a small tag of extra skin. Incomplete penetrance and variable expressivity are due to the effects of other genes and to environmental factors that can alter or completely suppress the effect of a particular gene. For example, a gene may encode an enzyme that produces a particular phenotype only within a limited temperature range. At higher or lower temperatures, the enzyme does not function and the phenotype is not expressed; the allele encoding such an enzyme is therefore penetrant only within a particular temperature range. Many characters exhibit incomplete penetrance and variable expressivity; thus the mere presence of a gene does not guarantee its expression.

Lethal Alleles: A lethal allele causes death at an early stage of development often before birth and so some genotypes may not appear among the progeny. So, this can create variation of ratio from the Mendel's 3:1 ratio.

Multiple alleles: For some loci, more than two alleles are present within a group of organisms the locus has multiple alleles. The inheritance of characteristics encoded by multiple alleles is no different from the inheritance of characteristics encoded by two alleles, except that a greater variety of genotypes and phenotypes are possible. In general, the number of genotypes possible will be $[(n+1)]/2$ where; n equals the number of different alleles at a locus. See the following example of feather pattern of mallard ducks. One allele, (M) produces the wild-type mallard pattern, the second allele; (M^R) produces a different pattern called restricted, and a third allele, (m^d) produces a pattern termed dusky. In this allelic series, restricted is dominant over mallard and dusky, and mallard is dominant over dusky: $M^R > M > m^d$. The six genotypes possible with these three alleles and their resulting phenotypes are: $[n(n+1)]/2$.



Another multiple-allele system is the three common ABO blood group alleles. The I^A encodes the A antigen, I^B encodes the B antigen, and i , which encodes O (no antigen). We can represent the dominance relations among the ABO alleles as follows: $I^A > i$, $I^B > i$, $I^A = I^B$. The synthesis of these surface antigens is controlled by two alleles designated as I^A and I^B . The i allele is recessive to both I^A and I^B . A person who is homozygous ii has type O blood and does not produce either antigen. A homozygous $I^A I^A$ or heterozygous $I^A i$ individual has type A blood. The red blood cells of this individual contain the surface antigen known as A. Similarly, a homozygous $I^B I^B$ or heterozygous $I^B i$ individual produces surface antigen B. A person who is $I^A I^B$ has the blood type AB and expresses both surface antigens A and B. The phenomenon in which two alleles are both expressed in the heterozygous individual is called *codominance*. In this case the I^A and I^B alleles are codominant to each other. As an example of the inheritance of blood type, see the possible offspring between two parents $I^A \times I^B$ (**Figure: 22**). $I^A I^B$, $I^A i$, $I^B i$, and ii offspring in a 1:1:1:1 ratio. The resulting blood types are AB, A, B, and O, respectively.

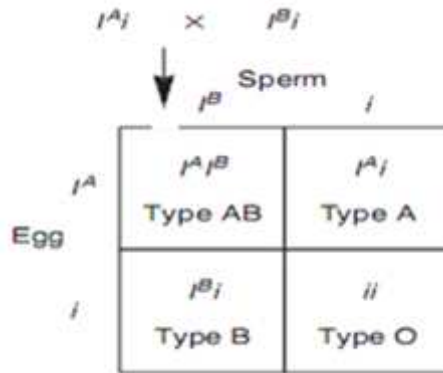


Figure 22: The ABO blood group inheritance pattern

5.3. Gene Interaction with Epistasis

Sometimes the effect of gene interaction is that one gene masks (hides) the effect of another gene at a different locus and the phenomenon is known as epistasis. Researchers now appreciate that essentially all traits are affected by the contributions of many genes. Morphological features such as height, weight, growth rate, and pigmentation are all affected by the expression of many different genes in combination with environmental factors. In our understanding of genetics by considering how the allelic variants of two different genes affect a single trait is known as gene interaction. Epistasis is similar to dominance, except that dominance entails the masking of genes at the same locus (allelic genes). But in epistasis gene at one locus affect the expression of another gene at different locus. In epistasis, the gene that does the masking is called an epistatic gene; the gene whose effect is masked is a hypostatic gene. Epistatic genes may be recessive or dominant in their effects.

Recessive Epistasis: Example look a crosses between Labrador dogs with pure-breeding black retrievers ($BBEE$) and one type of pure-breeding golden retriever ($bbee$) create an F1 generation of dihybrid black retrievers ($BbEe$). Crosses between these F1 dihybrids produce an F2 generation with nine black dogs ($B-E-$), three brown ($bbE-$) and four gold ($--ee$). Note that there are only three phenotypic classes because three $B-ee$ and the one $bbee$ combined to produce golden phenotypes due to the expression of recessive ee alleles. So the ratio is 9:3:4. Because the ee genotype completely masks the influence of the other gene for coat color, you cannot tell by

looking at a golden Labrador what its genotype is for the black or brown (B or b) gene (See Fig 23).

P	Black (BBEE)	Yellow (bb ee)			
Gametes	BE	be			
F1	Black (BbEe)	X	Black (BbEe)		
	BE	Be	bE	be	
F2	BE	BBEE	BBEe	BbEE	BbEe
	Be	BBEe	BBee	BbEe	Bbee
	bE	BbEE	BbEe	bbEE	bbEe
	be	BbEe	Bbee	bbEe	bbee
9 B-E- (Black)					
3 bbE- (Brown)					
4 - - ee (Yellow)					

Figure 23: A dihybrid cross showing recessive epistasis

Dominant Epistasis I: Epistasis in which the dominant allele of one gene hides the effects of another gene is called dominant epistasis. For example in a cross between the white F1 dihybrids (AaBb X AaBb), the F2 phenotypic ratio is 12 white: 3 yellow: 1 green. The 12 includes two genotypic classes: 9A-B- and 3aaB-. Another way of looking at this same phenomenon is that dominant epistasis restores the 3:1 ratio for the dominant epistatic phenotype (12 white) versus all other phenotypes (4 green plus yellow). See the following Table 24.

P	AABB	aabb			
Gametes	AB	ab			
	AaBb	AaBb			
	AB	Ab	aB	ab	
F2	AB	AABB	AABb	AaBB	AaBb
	Ab	AABb	AAbb	AaBb	Aabb
	aB	AaBB	AaBb	AaBB	aaBb
	ab	AaBb	Aabb	aaBb	aabb
12: 9A-B-white					
3aaB-white					
3 A-bb yellow					
1 aabb green					

Figure 24: A dihybrid crosses showing dominant epistasis I

Dominant epistasis II: Another dominant epistasis is the cross between white leghorn

and white Wyandotte's chickens where the F₂ generation resulting from this dihybrid cross produced offspring with the ratio of white birds to birds with color is 13:3. This is because at least one copy of A and the absence of B is needed to produce color (Table 25).

P	White leghorn(AABB) X White wyandote(aabb)				
Gametes	AB		ab		
F ₁ (all white)	AaBb		X	AaBb	
F ₂	AB	Ab	aB	ab	
	AB	AABB	AABb	AABB	AaBb
	Ab	AABb	AAbb	AaBb	Aabb
	aB	AaBB	AaBb	aaBB	aaBb
	ab	AaBb	Aabb	aaBb	aabb
13 9 A-B- white					
3 aaB-					
1 aabb					
3 A-bb colored					

Figure 25: Cross showing epistasis II

REVIEWING THE KEY CONCEPTS

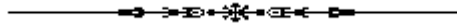
Dominance is the idea that an individual organism possesses two different alleles for a characteristic but the trait encoded by only one of the alleles is observed in the phenotype. Dominance can be seen in various ways i.e. complete dominance, incomplete dominance, and codominance and over dominance. The percentage of individual organisms having a particular genotype that express the expected phenotype is penetrance whereas degree to which a character expressed is expressivity. Lethal alleles, multiple alleles, linked genes (will be discussed in chapter 6) and gene interaction with epistasis causes different out come from the expected ratio of Mendel. This is due Lethal alleles also causes difference ratio from that of Mendel due to prematurely abortion of alleles by any kinds of mechanisms. The expression of one gene at one locus influences the expression of another gene at another locus in gene interaction which the outcome can be deviated from the ratio postulated by Mendel. Gene interaction with epistasis can be seen in different ways: recessive epistasis, dominant epistasis I and dominant epistasis II.

COMPREHENSION QUESTION

1. List and discuss types of dominance
2. Why the ratio of recessive epistasis is 9:3:4 when we compare with the ratio Mendel discovered i.e. 9:3:3:1?
3. When crossing alleles of ABO blood group ($I^A i \times I^B i$) the ratio of offspring formed is 1:1:1:1 respectively for $I^A I^B$, $I^A i$, $I^B i$ and ii . Why do you think?
4. List and discuss types of gene interaction with epistasis.

CHAPTER 6

GENE LINKAGE AND CHROMOSOMAL MAPPING



Genes located close together on the same chromosome and belong to the same linkage group are called linked genes. Linked genes travel together in meiosis, eventually arriving at the same destination (the same gamete), and are not expected to assort independently. That means they do not obey the rule of independent assortment according to that of Mendel's principle; rather, they tend to be inherited together. This tendency requires a new approach to understanding their inheritance and predicting the types of offspring produced. A critical piece of information necessary for predicting the results of these crosses is the arrangement of the genes on the chromosomes. Since these genes are inherited together the ratio of progenies is not equal with that of Mendel's independent assortment. For example the following crosses between homozygous purple flower long pollen and red flower round pollen (**Fig 26**). Linked genes are segregated together and crossing over produces recombination between them depending up on the distance between them. Genes that are close together on the same chromosome usually segregate as a unit and are therefore inherited together.

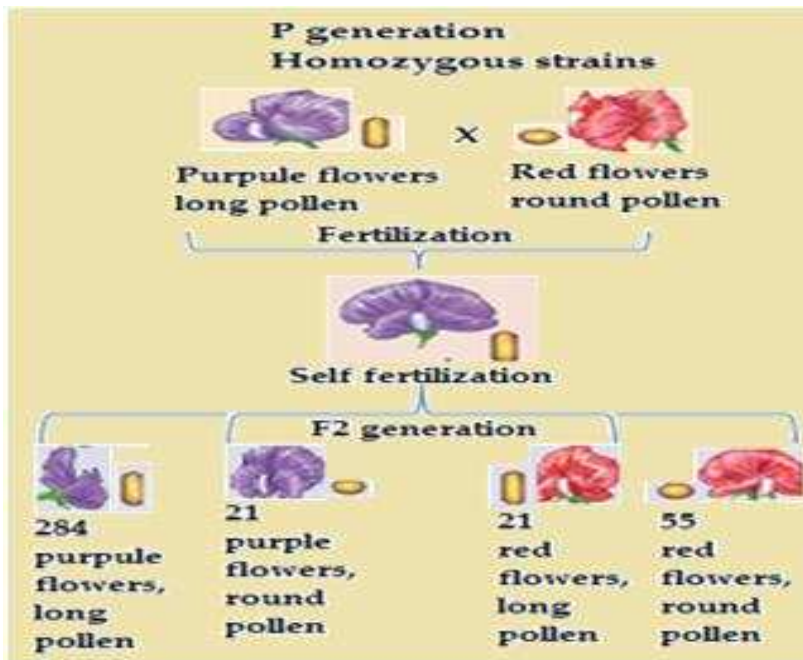


Figure 26: Example of linked gene in crosses of purple and red flowers that the outcome is different from 9:3:3:1

However, genes occasionally switch from one homologous chromosome to the other through the process of crossing over i.e. linkage and crossing over can be seen as processes that have opposite effects. Linkage keeps particular genes together, and crossing over mixes them up. Here look when genes on homologous chromosomes cross over with each other and produce recombination within each individual progeny (Fig 27).

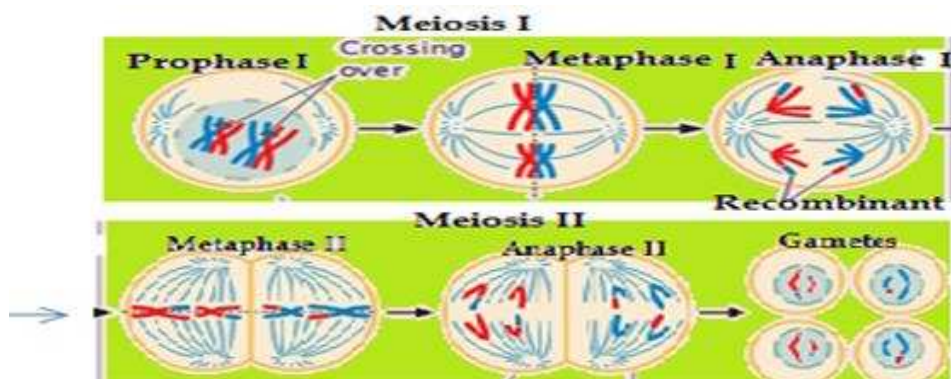


Figure 27: formation of recombinant chromosome in meiosis

Recombination is when one of the F1 progeny reproduces, the combination of alleles in its gametes may differ from the combinations in the gametes from its parents. We can see the progeny based on the recombination i.e., non-recombinant progeny and recombinant progeny. Some genes are very close together on the same chromosome and do not exhibit crossing over as a result there is no recombination after meiosis. Such types of genes are called completely linked genes whereas; some genes are located on the same chromosome on some distance from each other and these genes can undergo crossing over and produce recombination. So, the distance of gene from each other on the same chromosome is more important to know whether crossing over to take place in case of linked genes (**Fig 28**).

Let us see linkage and recombination to a cross between tomato plants that differ in the genes that encode leaf type and plant height. Assume that these genes are linked and that some crossing over takes place between them. When crossing over takes place in the genes for leaf type and height, two of the four gametes produced are recombinants. When there is no crossing over, all four resulting gametes are non-recombinants.

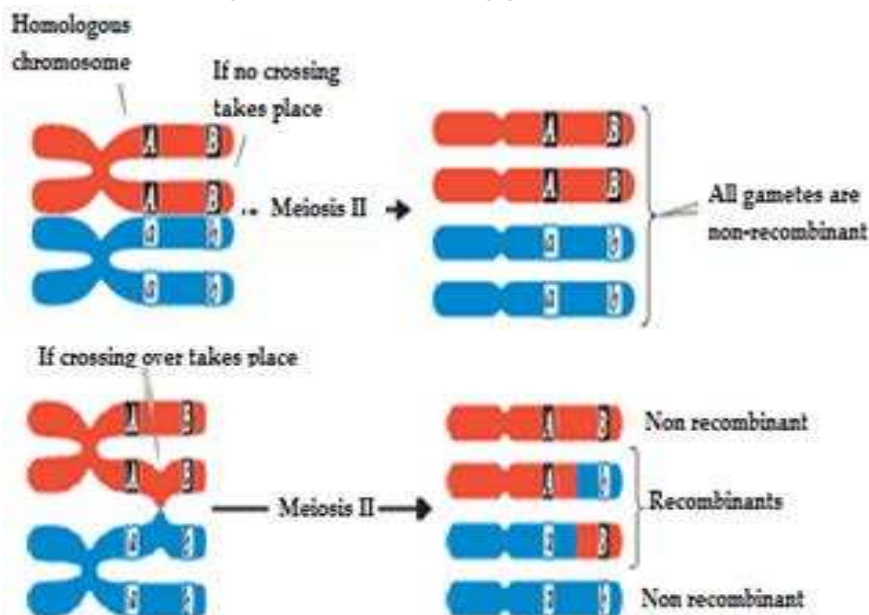


Figure 28: Results of crossing over and non-crossing over in meiosis II

If there are 55 dominant normal leaves and are tall; 53 recessive have mottled leaf and are dwarf and they are non-recombinant progeny because they containing the original combination of traits of the parents. The recombinants are 8 normal leaved and

are dwarf, and 7 are mottle leave and are tall. These plants are recombinant progeny because they are different from that of the parents.

$$\text{Recombinant frequency} = \frac{\text{Number of recombinant progeny}}{\text{Total number of progeny}} \times 100$$

$$\text{That is } \frac{8+7}{55+53+8+7} \times 100 = \frac{15}{123} \times 100 = 12.2\%$$

Thus, 12.2% of the progeny exhibit new combinations of traits resulting from crossing over.

6.1. Phases of Linkage

In crosses for linked genes, the arrangement of alleles on the homologous chromosomes is critical in determining the outcome of the cross. For example consider the inheritance of two genes in the Australian blowfly (*Lucilia cuprina*). In this species, one locus determines the color of the thorax: a purple thorax (p) is recessive to the normal green thorax (p⁺). A second locus determines the color of the puparium: a black puparium (b) is recessive to the normal brown puparium (b⁺). The loci for thorax color and puparium color are located close together on the chromosome. Suppose we test-cross a fly that is heterozygous at both loci with a fly that is homozygous recessive at both. Because these genes are linked, there are two possible arrangements on the chromosomes of the heterozygous progeny fly. First possibility is the dominant alleles for green thorax (p⁺) and brown puparium (b⁺) might reside on one chromosome of the homologous pair, and the recessive alleles for purple thorax (p) and black puparium (b) might reside on the other homologous chromosome: The arrangement in which wild-type alleles are found on one chromosome and mutant alleles are found on the other chromosome, is referred to as the coupling (cis configuration). The second probability is one chromosome might bear the alleles for green thorax (p⁺) and black puparium (b), and the other chromosome carries the alleles for purple thorax (p) and brown puparium (b⁺) is called repulsion or trans configuration (Fig 29).

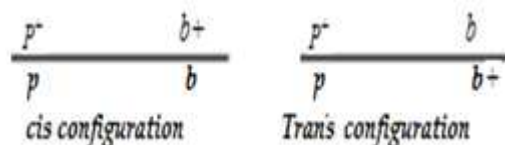


Figure 29: Cis and Trans configuration of alleles on chromosomes

6.2. Gene Mapping with Recombination Frequencies

Physical distances between genes on a chromosome are related to the rates of recombination. Two genes that lie far apart are more likely to undergo a crossover than are two genes that lie close together. Recombination frequencies could provide a convenient way to determine the order of genes along a chromosome and would give estimates of the relative distances between the genes. Chromosome maps calculated by using the genetic phenomenon of recombination are called genetic maps. In contrast, chromosome maps calculated by using physical distances along the chromosome (often expressed as numbers of base pairs) are called physical maps. Distances on genetic maps are measured in map units (m.u.); one map unit equals 1% recombination. Map units are also called centi Morgans (cM), in honor of Thomas Hunt Morgan; 100 centi Morgans equals 1 Morgan. Genetic distances measured with recombination rates are approximately additive. For example let say A, B and C are genes found on a chromosome, if the distance from gene A to gene B is 5 m.u., the distance from gene B to gene C is 10 m.u., and the distance from gene A to gene C is 15 m.u., then gene B must be located between genes A and C. We can draw a simple genetic map for genes A, B, and C, as shown two possible (**Appendix A**). Again if we obtained distances to an additional gene let say D, then we could position A and C relative to that gene. See their recombination frequency of paired genes A and D is 8, B and D is 13, C and D is 23 on a chromosome. From this C and D exhibit the greatest amount of recombination (23); therefore, they must be farthest apart, with genes A and B between them (**Appendix B**).

REVIEWING THE KEY CONCEPTS

Linked genes travel together in meiosis and arriving at the same destination (the same gamete) without assorting independently as a result they do not obey the rule of independent assortment according to that of Mendel's principle; rather, they tend to be inherited together. The distance between these two or more genes determine whether or not crossing over takes place during cell division in meiosis. If some gaps are there between these genes due to crossing over of arms of chromosome containing these genes, genetic recombination is formed in the gametes. This can be calculated by the formula of recombinant frequencies which indicates the percent by which the genetic

makeups of the gametes are recombined. Linked genes can be arranged on a chromosome by either in coupling (cis configuration) in which two genes containing similar character(example the dominant gene with another dominant gene) arranged in one direction, and repulsion(trans configuration)in which genes containing different character(example the dominant gene and recessive gene) are arranged in opposite direction on a chromosome

COMPEREHENSION QUESTION

1. What is map unit and map distance?
2. What recombination frequency indicates?
3. What would be gametes of chromosomes?
 - a. If double crossed over?
 - b. Tripled crossed over?
 - c. No crossed over?
4. Do you think coupling and repulsion of genes on a chromosome have effect on crossing? How?

CHAPTER 7

SEX DETERMINATION AND INHERITANCES RELATED TO SEX



The sexual phenotype of organisms is referred to as sex and most organisms have only two sexual phenotypes: male and female. The fundamental difference between males and females is gamete size (males produce small gametes; females produce relatively larger gametes). Organism's differences in sex allow themselves to reproduce sexually. Sexual reproduction is the formation of offspring that is genetically distinct from their parents. Most often, two parents contribute genes to their offspring and the genes are assorted into new combinations through meiosis. Among most eukaryotes, sexual reproduction consists of two processes that lead to an alternation of haploid and diploid cells: meiosis produces haploid gametes (spores in plants), and fertilization produces diploid zygotes. So, sex determination the mechanism by which sex is established.

7.1. Differentiation between Sex and Autosomal Chromosomes

7.1.1. Chromosomal sex determining system

The chromosome theory of inheritance states that genes are located on chromosomes, which serve as vehicles for the segregation of genes in meiosis. Definitive proof of this theory was provided by the discovery that the sex of certain insects is determined by the presence or absence of particular chromosomes. Stevens and Wilson found for insects, sex in many organisms is determined by a pair of chromosomes (sex chromosomes) which differ between males and females. The non sex chromosomes,

which are the same for males and females, are called *autosomes*. Males produce two different types of gametes with respect to the sex chromosomes, they are said to be the *heterogametic sex*. Females, which produce gametes that are all the same with respect to the sex chromosomes, are homogametic sex. However, sometimes this exact may not be maintained in some organisms due to different factors that hinders number of sex chromosomes of that organisms. *For example, in XX-XO sex determination, the mechanism of sex determination in the grasshoppers studied by McClung. In this system, females have two X chromosomes (XX), and males possess a single X chromosome (XO). The letter O signifies the absence of a sex chromosome. X-bearing sperm unite with X-bearing eggs to produce XX zygotes, which eventually develop as females. Sperm lacking an X chromosome (i.e. OY) unite with X-bearing eggs to produce XO zygotes, which develop into males.*

Another example is *XX-XY sex determination, in many species including some plants, insects, and reptiles, and all mammals (including humans), the cells of males and females have the same number of chromosomes. But the cells of females have two X chromosomes (XX) and the cells of males have a single X chromosome and a smaller Y chromosome (XY). In this system male is the heterogametic sex and the female is the homogametic sex. Other organisms (e.g., duck-billed platypus) have variations of the XX-XY system of sex determination, in which females have five pairs of X chromosomes and males have five pairs of X and Y chromosomes. Although the X and Y chromosomes are not generally homologous, they do pair and segregate into different cells in meiosis because these chromosomes are homologous in small regions called the pseudo-autosomal regions, in which they carry the same genes. In humans, there are pseudo-autosomal regions at both tips of the X and Y chromosomes (Fig 30).*

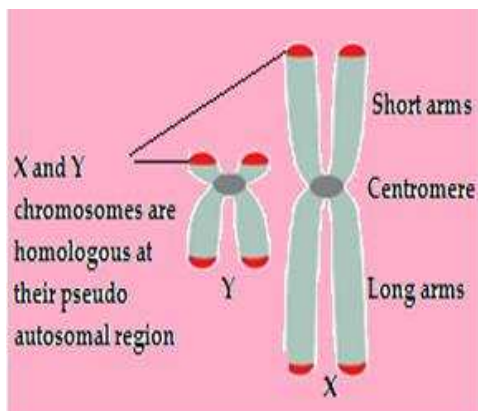


Figure 30: The X and Y chromosomes in humans differ in size and genetic content but homologous only in the pseudo autosomal region

The *third* example is that ZZ-ZW sex determination, in this system, the female is *heterogametic* and the male is *homogametic*. To prevent confusion with the XX-XY system, the sex chromosomes in this system are called Z and W. Females in this system are ZW; after meiosis, half of the eggs have a Z chromosome and the other half have a W chromosome. Males are ZZ; all sperm contain a single Z chromosome. This type of sex determination system is found in birds, snakes, butterflies, some amphibians, and some fishes. The *fourth* type of sex determination is that *genic sex determination* in some plants, fungi, and protozoans where there are no obvious differences in the chromosomes of males and females (there are no sex chromosomes). These organisms have genic sex determination i.e. genotypes at one or more loci determine the sex of an individual plant, fungus, or protozoan. In both genic sex determination and chromosomal sex determination, sex is controlled by individual genes; the difference is that, with chromosomal sex determination, the chromosomes look different in males and females.

7.1.2. Environmental Sex Determination

In a number of organisms sex is determined fully or in part by environmental factors. For example the marine mollusk (*Crepidula fornicate*), also known as the common slipper limpet live in stacks, one on top of another. Each limpet begins life as a swimming larva where the first larva to settle on a solid, unoccupied substrate develops into a female limpet. It then produces chemicals that attract other larvae, which settle

on top of it which develop into males, which then serve as mates for the limpet below. After a period of time, the males on top develop into females and, in turn, attract additional larvae that settle on top of the stack, develop into males, and serve as mates for the limpets under them. Limpets can form stacks of a dozen or more animals; the uppermost animals are always male. This type of sexual development is called *sequential hermaphroditism*. Each individual animal can be both male and female, although not (**Fig 31**). In addition to this mollusks the sexual phenotype of many turtles, crocodiles, and alligators is affected by temperature during embryonic development however they have sex chromosome. In turtles, for example, warm temperatures produce females during certain times of the year, whereas cool temperatures produce males and the reverse is true in alligators.

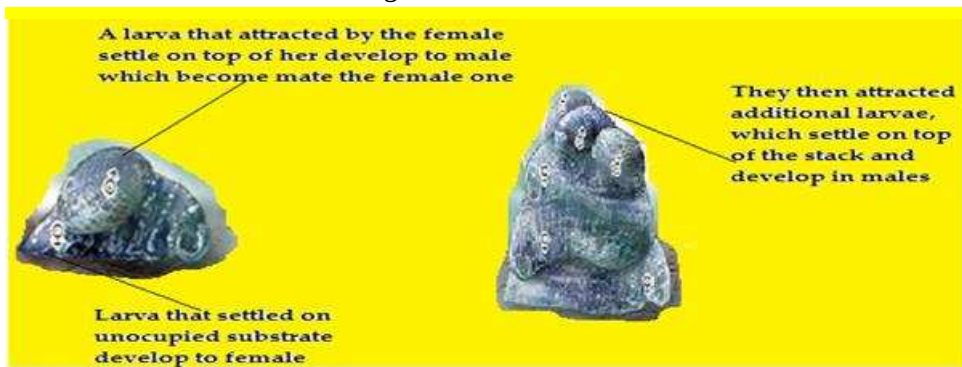


Figure 31: Environmental sex determination of marine mollusk

Table 10: Types of some sex determining system

System	Mechanism		Heterogametic Sex
XX-XO	Females XX	Males X	Male
XX-XY	Females XX	Males XY	Male
ZZ-ZW	Females ZW	Males ZZ	Female
Genic sex determination	No distinct sex chromosomes Sex determined by genes on undifferentiated chromosomes		Varies
Environmental sex determination	Sex determined by environmental factors		None

7.1.3. Sex Determination in Fruit fly (*D. melanogaster*)

Drosophila has eight chromosomes where 3 pairs are of autosomes and 1 pair is of sex chromosomes. Normally, females have two X chromosomes and males have an X chromosome and a Y chromosome. However, the presence of the Y chromosome does not determine maleness in *Drosophila* instead; each fly's sex is determined by a balance between genes on the autosomes and a gene on the X chromosomes is called the genic balance system. The X chromosome contains genes with female producing effects whereas the autosomes contain genes with male producing effects. Consequently, a fly's sex is determined by the X: A ratio (X chromosome: Autosome ratio).

$$\frac{(\text{number of X chromosomes})}{(\text{number of haploid sets of autosomal chromosomes})}$$

X: A ratio is that $\frac{(\text{number of X chromosomes})}{(\text{number of haploid sets of autosomal chromosomes})}$. Here, if X: A ratio is 1 the fly is normal female, if X: A ratio is 0.5 the fly is normal male, if X: A ratio is less than 0.5 the fly is male but weak and sterile called metamales, if X: A ratio is between 1.0 and 0.5 the fly is an intersex (mixture of male and female characteristics) and if the X: A ratio is greater than 1 the fly is female called a metafemale having developmental problems (Table 11).

Table 11: Sex determination of fruit fly (*D. melanogaster*)

Sex-Chromosome Complement	Haploid Sets of Autosomes	X: A Ratio	Sexual Phenotype
XX	AA	1.0	Female
XY	AA	0.5	Male
XO	AA	0.5	Male
XXY	AA	1.0	Female
XXX	AA	1.5	Metafemale
XXXY	AA	1.5	Metafemale
XX	AAA	0.67	Intersex
XO	AAA	0.33	Metamale
XXXX	AAA	1.3	Metafemale

7.1.4. Sex Determination in Humans

Like *Drosophila*, humans have XX-XY sex determination, but, in humans, the presence of a gene (SRY) on the Y chromosome determines maleness. When the sex chromosomes do not segregate properly in meiosis or mitosis, the phenotypes show abnormal numbers of sex chromosomes. For example, Turner syndrome is a syndrome occurred on female who's one X chromosome is lost (XO). This female has undeveloped secondary characteristics, short, low hairline, relatively broad chest and folds of skin on the neck. However their intelligence is usually normal, most them are sterile. Klinefelter syndrome another syndrome having cells with one or more Y chromosomes and multiple X chromosomes. The cells of most males having this condition are XXY but the cells of a few Klinefelter males are XXXY, XXXXY, or XXYY. Men with this condition frequently have small testes, reduced facial and pubic hair, often taller and sterile. Poly-X females also a condition often referred to as triplo-X syndrome. Few of persons with this syndrome are sterile and many of them menstruate regularly and fertile.

7.2. Sex-Linked Characteristics

Characteristic determined by genes located on the sex chromosomes are said to be sex linked characteristics. Genes on the X chromosome determine X-linked characteristics; those on the Y chromosome determine Y-linked characteristics. Because the Y chromosome of many organisms contains little genetic information, most sex-linked characteristics are X linked. Males and females differ in their sex chromosomes; so the pattern of inheritance for sex-linked characteristics differs from that exhibited by genes located on autosomal chromosomes. An example of X linked characters is X-Linked White Eyes in *Drosophila*. American biologist Thomas Hunt Morgan observed that white eye characteristic is X linked in *D. melanogaster* (**Fig: 32**). Another example is X-linked color blindness in humans' eye color which perceived in light sensing cone cells in the retina. Each cone cell contains one of three pigments blue light, red light and green light which capable of absorbing light of a particular wavelength. The brain mixes the signals from different cone cells to create the wide spectrum of colors that we perceive. Each of the three pigments is encoded by a separate locus i.e. the locus for the blue pigment is found on chromosome 7, and those for the green and the red

pigments lie close together on the X chromosome. The most common types of human color blindness are caused by defects of the red and green pigments. Because the genes encoding the red and the green pigments are located on the X chromosome, red-green color blindness is inherited as an X-linked recessive characteristic (See the cross on **Fig 33**).

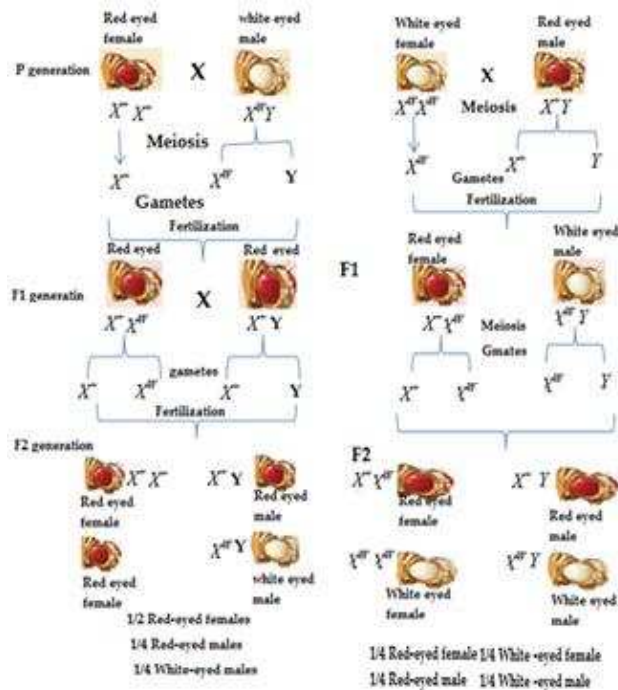


Figure 32: Sex linked character in drosophila

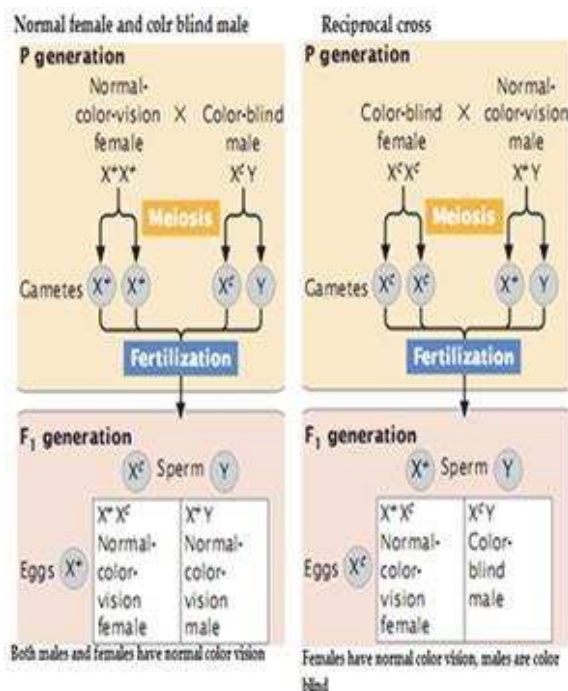


Figure 33: Sex linked character in human

Male determining gene in humans, the Y chromosome is important in producing a male phenotype in all animals. However, scientists discovered a few rare XX males whose cells apparently lack a Y chromosome. *How could a male phenotype exist without a Y chromosome?* Close examination eventually revealed a small part of the Y chromosome attached to another chromosome. This finding indicates that it is not the entire Y chromosome that determines maleness in humans; rather, it is a gene on the Y chromosome. In early development, all humans possess undifferentiated gonads and both male and female reproductive ducts. About *six weeks* after fertilization, a gene on the Y chromosome becomes active. By an *unknown mechanism*, this gene causes the neutral gonads to develop into testes, which begin to secrete two hormones: testosterone and *mullerian inhibiting substance*. Testosterone induces the development of male characteristics, and mullerian-inhibiting substance causes the degeneration of the female reproductive ducts. In the absence of this male determining gene, the neutral gonads become ovaries, and female features develop. The male determining gene in humans, called the *sex determining region Y (SRY) gene*, was discovered in 1990. Definitive proof that *SRY* is the male determining gene came when scientists placed a copy of this gene into XX mice by means of genetic engineering. The XX mice that

received this gene, although sterile, developed into anatomical males. The SRY gene encodes a protein called a transcription factor that binds to DNA and stimulates the transcription of other genes that promote the differentiation of the testes. Although SRY is the primary determinant of maleness in humans, other genes (some X linked, others Y linked, and still others autosomal) also have roles in fertility and the development of sex differences (**Fig 34**). Generally, X-linked traits, for example, are passed from father to daughter but never from father to son, and Y-linked traits are passed from father to all sons.

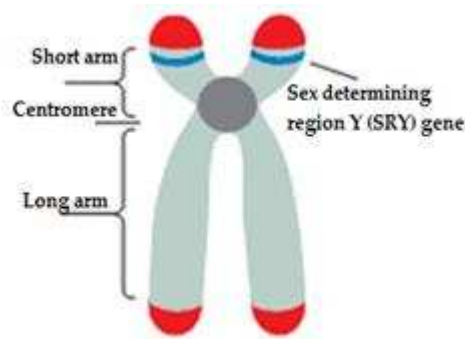


Figure 34: The SRY gene on X chromosome

7.3. Dosage Compensation

In species with XX-XY sex determination, the difference in the number of X chromosomes possessed by males and females presents a special problem in development. Because females have two copies of every X-linked gene and males have only one copy. So that the amount of gene product (protein) encoded by X-linked genes would differ in the two sexes i.e. females would produce twice as much gene product as that produced by males. This difference could be highly harmful because protein concentration plays a critical role in development. In animals this potential problem is solved through dosage compensation, which equalizes the amount of protein produced by X-linked genes in the two sexes. In fruit flies, dosage compensation is achieved by a doubling of the activity of the genes on the X chromosome of the male so that dosage compensation equalizes the amount of protein produced by x-linked genes in males and females.

Table 12: Number of bar bodies in human cells with different complements of sex chromosomes

chromosomes

Sex Chromosomes	Syndrome	Number of Barr Bodies
XX	None	1
XY	None	0
XO	Turner	0
XXY	Klinefelter	1
XXYY	Klinefelter	1
XXX	Klinefelter	2
XXXX	Klinefelter	3
XXX	Triplo-X	2
XXXX	Poly-X female	3
XXXXX	Poly-X female	4

For example darkly staining bodies in the nuclei of cells from female cats known as a Barr body in which one of X chromosome is inactivated. *From the two X chromosomes which one would be inactivated?* If a cell contains more than two X chromosomes, all but one of them is inactivated *randomly*. That means number of inactivated X chromosome shows that number of bar bodies. The **table 12** shows numbers of bar bodies due to inactivated excess X chromosome. Here to answer for the question *how random inactivation of X chromosome takes place*, the mechanism requires two steps. *First*: the cell somehow assesses or how many X chromosomes are present. *Second*: one X chromosome is selected to become the active X chromosome and all others are silenced. Although many details of X-chromosome inactivation *remain unknown*, several genes and sequences that participate in the process have been identified. For example, the gene called *Xist* (X-inactivation-specific transcript) on the X chromosomes intended to become inactivated. When the *Xist* gene is active, it produces an RNA molecule that coats (covers) the X chromosome and inactivates the genes on it, probably by altering chromatin structure. So, if X chromosome intended to become active, other genes repress the activity of *Xist* so that the *Xist* RNA never coats the X chromosome and genes on this chromosome remain active.

7.4. Cytoplasmic Inheritance and Maternal Effect

Not all the genetic material of a cell is found in the nucleus; some characteristics are encoded by genes located in the cytoplasm. For example chloroplasts and mitochondria, contain DNA. The human mitochondrial genome contains about 15,000 nucleotides of DNA, encoding 37 genes when compared with that of nuclear DNA, which contains some 3 billion nucleotides encoding some 20,000 to 25,000 genes. The size of the

mitochondrial genome is very small; nevertheless, mitochondrial and chloroplast genes encode some important characteristics. These characteristics exhibit cytoplasmic inheritance. Cytoplasmically inherited characteristics frequently exhibit extensive phenotypic variation because cells and individual offspring contain various proportions of cytoplasmic genes. Since numbers of mitochondria are in cytoplasm of some organisms, For example from the **Fig 35** mitochondria that have wild-type mtDNA are shown in red and those having mutant mtDNA are shown in blue.

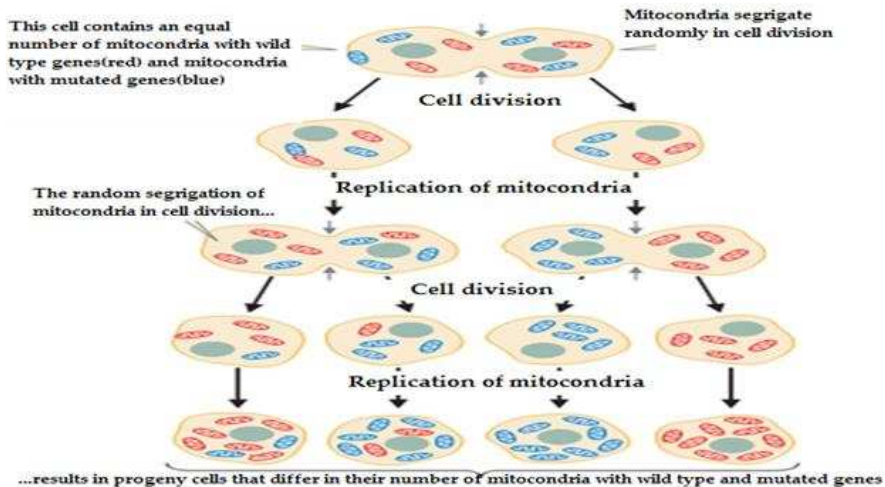


Figure 35: mitochondrial inheritance producing genetic variation in offspring

REVIEWING THE KEY CONCEPTS

Organism's differences in sex which is determined by mechanism of sex determination allow themselves to reproduce sexually, the formation of offspring that is genetically distinct from their parents. These sex determination mechanisms are: Chromosomal Sex determining system which accounts for presence or absence of particular sex chromosomes, X: A Sex Determination in which the number of X chromosome is divided to autosomal chromosome (in this case the ratio of X: A is important to say that organism is male or female), Genic Sex Determination in some plants, fungi, and protozoans where there are no obvious differences in the chromosomes of males and females (where there are no sex chromosomes), genotypes at one or more loci determine the sex of an these organisms, Environmental Sex Determination in which number of organisms sex is determined fully or in part by environmental factors such as chemicals and temperature.

Characteristic determined by genes located on the sex chromosomes are said to be sex linked characteristics that means genes on the X chromosome determine X-linked characteristics; those on the Y chromosome determine Y-linked characteristics. However, numbers of X chromosomes more than number of Y chromosomes for organisms their sex is determined by XX – XY chromosomes. This may cause problem in gene product because twice the XX gene product can be produced than that of XY. This problem is maintained by the process of Dosage Compensation in which all X chromosomes are inactivated randomly except one copy of it as a result gene product (protein) can be equalized. Although the amount of gene content is different, not only chromosomal gene is inherited but also cytoplasmically inherited characteristics frequently exhibit extensive phenotypic variation because cells and individual offspring contain various proportions of cytoplasmic genes.

COMPEREHENSION QUESTION

1. Why do you think cytoplasmic inheritance can cause genetic variation in off springs when you compare with chromosomal inheritance?
2. Why most inherited genes are X-linked gene do you think?
3. What would be occurred organisms if dosage compensation not takes place do you think?
4. Sex determination in fruit fly is determined by XX: XY ratio. True or false?
5. During embryonic stage how many weeks it require SRY gene to be activated and grow to tests after fertilization? By what mechanism? What would be the sex of embryo if X chromosome from mother and X chromosome from father are fertilized? Do you think test is developed after six weeks?

CHAPTER 8

THE GENETIC MATERIAL

The section of a threadlike double-helical molecule called deoxyribonucleic acid, abbreviated as DNA is a genetic material of living organisms. The discovery of genes and the understanding of their molecular structure and function have two of the biggest mysteries of biology: one is 'what makes a species what it is', and the second is 'what causes variation within a species'. The solution of these questions was discovered by Fred Griffith in 1928 when he was done important experiments by transformation that led to the identification of DNA as the genetic material. He was carried out the experiment on different strains of bacteria that causes pneumonia (*Streptococcus pneumonia*). Grift used two types of bacteria: one is virulent (disease-causing) surrounded by a polysaccharide coat which makes the bacterial colony appear smooth(S) when grown on an agar plate. The second is when the virulent forms occasionally mutated to non-virulent forms which lack a polysaccharide coat produce a rough(R) appearing colony. Griffith used to kill these strains by heat and injected mice (Fig 36).

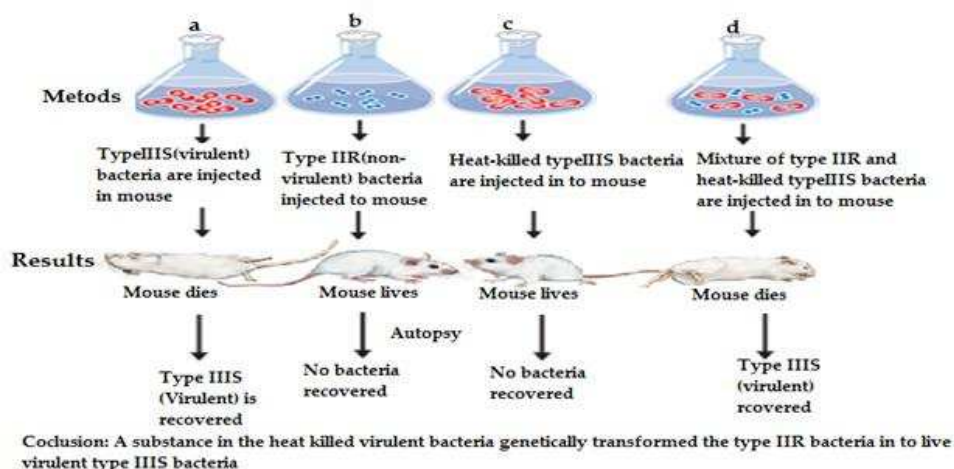


Figure 36: Grifts experiment showing substance that is transformed from one bacterium to another bacteria

From the Grifts' experiment the question is 'what type of substance transformed is Protein, RNA or DNA? To answer this question Colin MacLeod and Maclyn McCarty succeeded in isolating and purifying the transforming substance. They used three enzymes: *trypsin* and *chymotrypsin* which break down proteins, *Ribonuclease* which destroys RNA, and *DNAse* which destroys DNA (**Figure 37**).

8.1. DNA Structure and Replication Mechanism

8.1.1. DNA structure

Structures of DNA are at three levels of increasing complexity; primary, secondary, and tertiary structures. The primary structure of DNA refers to its nucleotide structure and how the nucleotides are joined together by phosphodiester linkages. Nucleotides are the repeating units of DNA, each comprising three parts: sugar, phosphate, and nitrogen containing base.

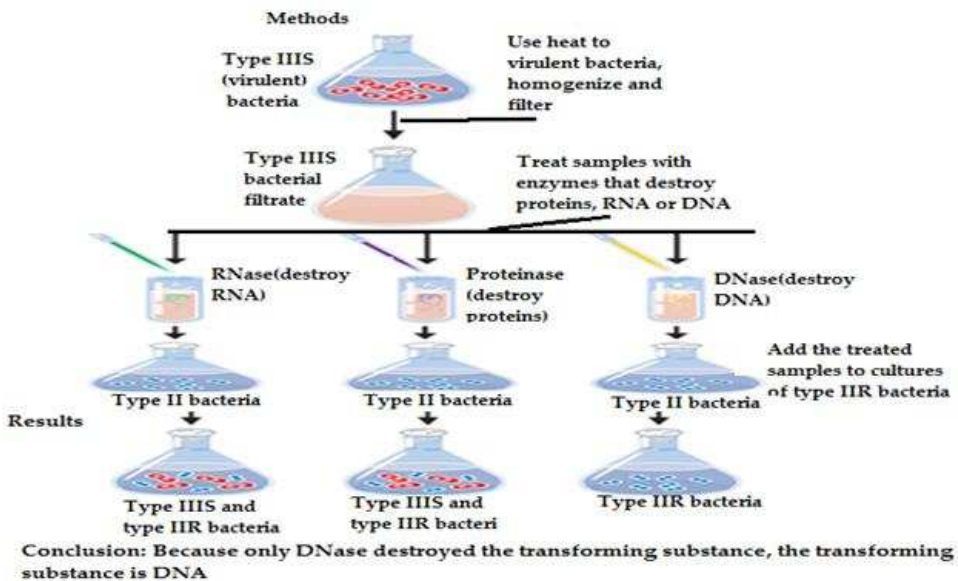
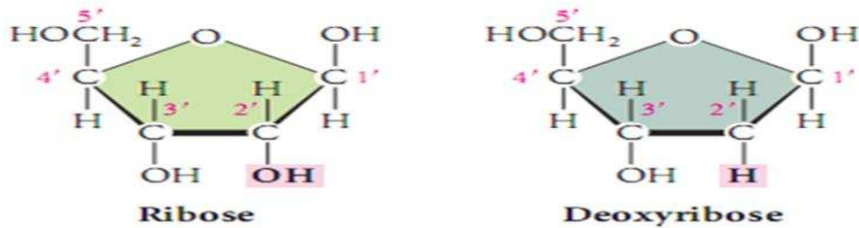


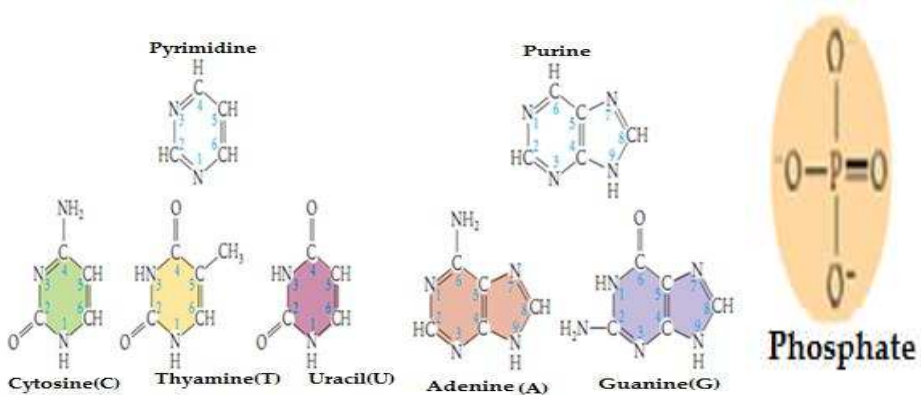
Figure 37: Colin MaLeod and Maclyn McCarty experiment showing as DNA is a transforming substance

Structures of sugars of nucleic acids called pentose sugars having five carbon atoms are different in DNA and RNA. RNA's sugar called *ribose* has a hydroxyl group (OH)

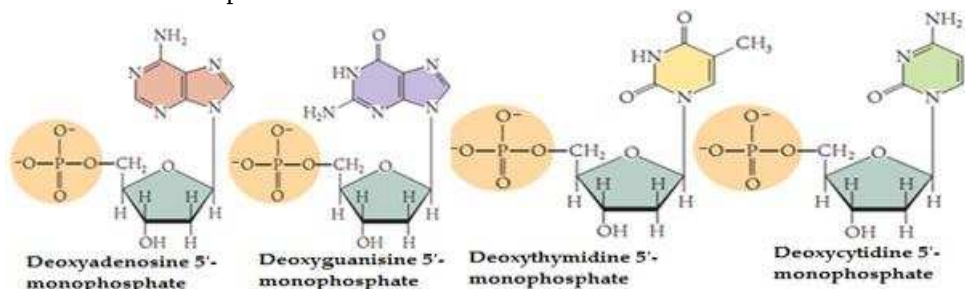
attached to the 2-carbon atom whereas DNA's sugar called *deoxyribose* has a hydrogen atom (H) attached to the 2-carbon atom means that one oxygen atom fewer overall.



Nitrogenous base of a nucleotide is of two types: purine (consists of a six-sided ring attached to a five-sided ring is of two type adenine (A) and guanine (G) or pyrimidine (consists of a six-sided ring only of three types cytosine(C), thymine (T), and uracil (U)). Purines and pyrimidine are linked with each other by hydrogen bonds.



Purines and pyrimidine linked with hydrogen bonds whereas they are linked with sugar by covalent bonds. When sugar binds with nitrogenous base it is called nucleoside when sugar, nitrogenous base and phosphate binds with each other is called nucleotides. Here are some examples of nucleotides.



The secondary structure of DNA refers to three-dimensional configuration and the helical structure of DNA discovered by Watson and Crick. A fundamental characteristic of DNAs secondary structure is that it consists of two polynucleotide strands wound

around each other called double helix. The sugar phosphate linkages are on the outside of the helix, and the bases are stacked in the interior of the molecule. The two polynucleotide strands run in opposite directions (antiparallel), which means that the 5' end of one strand is opposite the 3' end of the other strand. The strands are held together by hydrogen bonds between the bases on opposite strands.

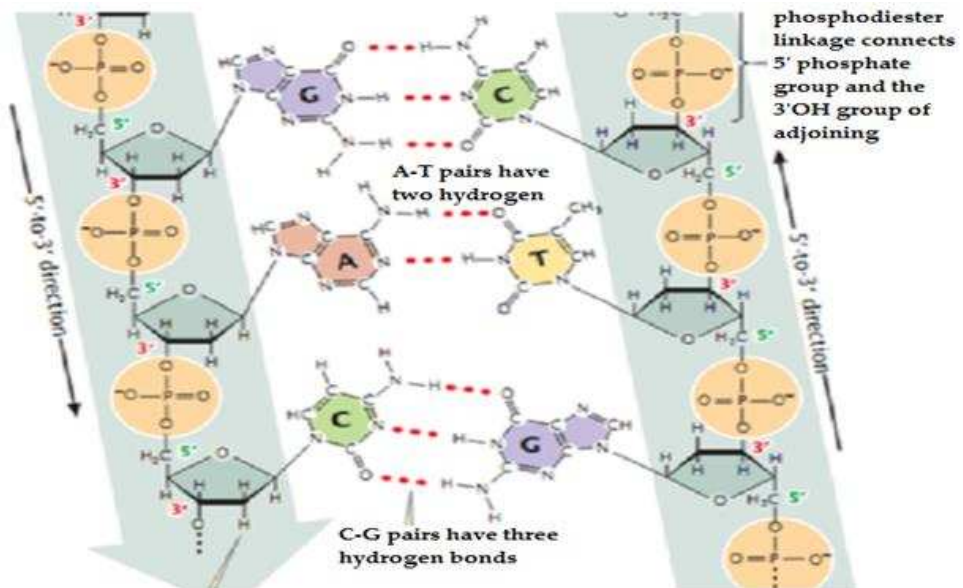


Figure 38: Secondary structure of DNA

DNA is an alpha helix, meaning that it has a right handed, or clockwise coiling direction approximately 10 base pairs per 360 degree rotation of helix so each base pair is twisted 36 degrees relative to the adjacent bases. The base pairs are 0.34 nanometer apart each complete rotation of the molecule encompasses 3.4nanometer. The diameter of the helix is 2nm, and the bases are perpendicular to the long axis of the DNA molecule (**Fig 39a**). Sometime in DNA and RNA, base pairing between nucleotides on the same strand produces special structures such as hairpins. That means sequences within a single strand of nucleotides may be complementary to each other after inverting and can pair by forming hydrogen bonds, producing double-stranded regions. A hairpin consists of a region of paired bases (the stem) and sometimes includes intervening loop (**Fig 39b**).

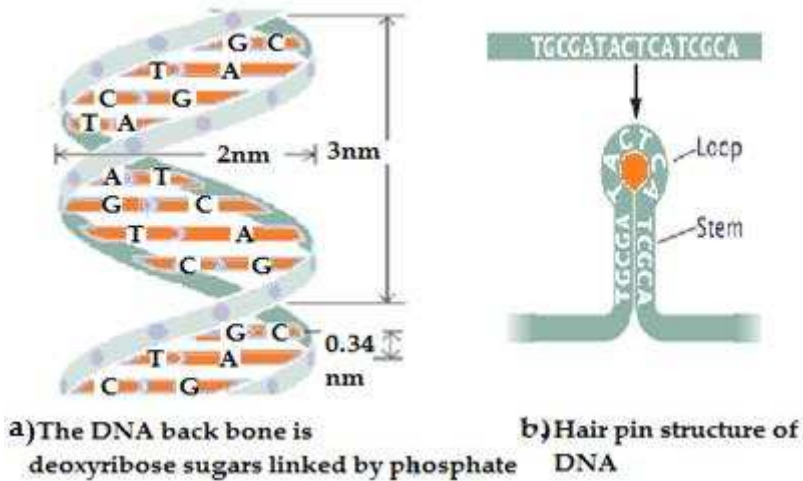


Figure 39: Helix and loop structure of DNA molecule

8.1.2. DNA replication mechanism

There are three fundamental properties of the genetic material: the first is it must be capable of carrying large amounts of information as a result it must vary in structure. The second is ability to replicate faithfully. The third is ability to translate its instructions into the phenotype. During translating instruction, three major pathways of information flow takes place in the cell: replication (information passes from one DNA molecule to other DNA molecules), transcription (information passes from DNA to RNA), and translation (information passes from RNA to protein). This concept of information flow is called the central dogma which states that genetic information passes from DNA to protein in a one way information path way. However in some organisms central dogma is not one way process. For example, retroviruses and some transposable elements transfer information from RNA to DNA (reverse transcription) and in some RNA viruses transfer information from RNA to RNA (**Fig 40**).

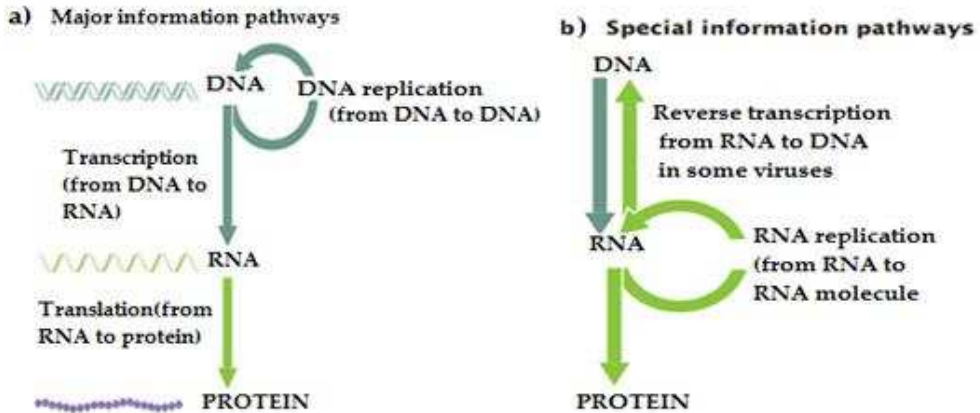


Figure 40: Major information pathways and special information pathways

All DNA Replication takes place in different ways of semiconservative manner differing principally in the nature of the template DNA (whether it is linear or circular). Individual units of replication are called replicons, each of which contains a replication origin where replication starts at the origin and continues until the entire replicon has been replicated. For example, bacterial chromosomes have a single replication origin whereas eukaryotic chromosomes contain many.

8.1.2.1. Bacterial DNA replication

There are two types of bacterial DNA replication: the first is theta replication which takes place in circular DNA of bacteria such as *E. coli*. During this double-stranded DNA begins to unwind at the replication origin generating a loop (replication bubble). The point where the two single nucleotide strands separate from the double-stranded DNA helix, is called a replication fork. If there are two replication forks, one at each end of the replication bubble, the forks proceed outward in both directions in a process called bidirectional replication (**Fig: 41**). The second is rolling-circle replication takes place in some viruses and in the *F factor* (a small circle of extra chromosomal DNA) of *E. coli*. This form of replication is initiated by a break in one of the nucleotide strands that creates a 3' -OH group and a 5' phosphate group. New nucleotides are added to the 3' end of the broken strand, with the inner (unbroken) strand used as a template. As new nucleotides are added to the 3' end, the 5' end of the broken strand is displaced from the template, rolling out like thread being pulled off a spool. The 3'

end grows around the circle, giving rise to the name rolling-circle model (**Fig 42**).

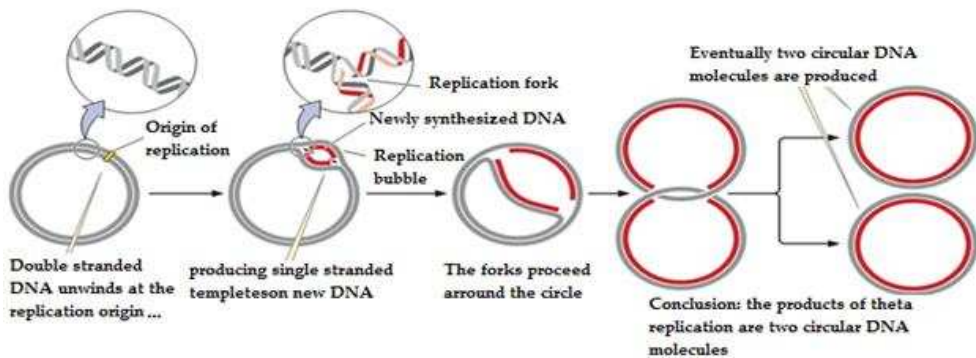


Figure 41: Theta replication of bacterial DNA

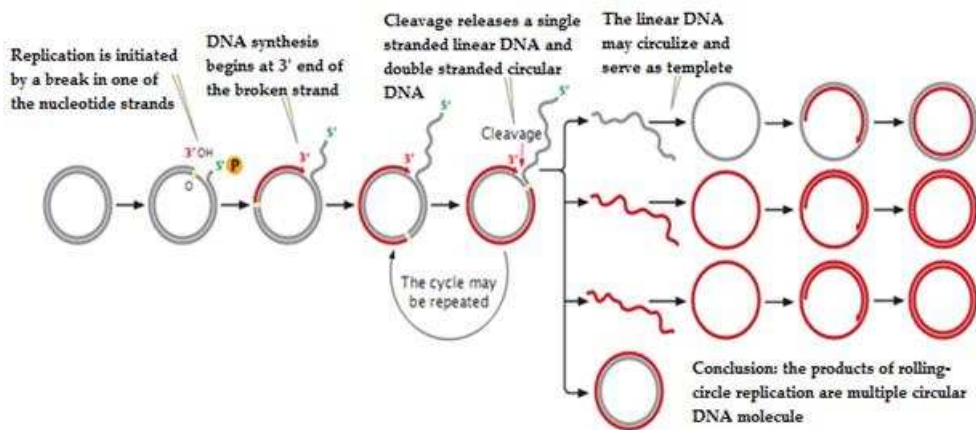


Figure 42: Rolling-circle replication takes place in some viruses and in the F factor of *E. coli*

8.1.2.2. Eukaryotic DNA replication

In eukaryotes linear DNA replication is initiated at thousands of origins where the DNA unwinds and produces a replication bubble. Replication takes place on both strands at each end of the bubble, with the two replication forks spreading outward. Eventually, the replication forks of adjacent replicons run into each other, and the replicons fuse to form long stretches of newly synthesized DNA. During DNA synthesis new nucleotides are joined one at a time to the 3' end of the newly synthesized strand by *DNA polymerases* (the enzymes that synthesize DNA). So, new

DNA strands always elongate in the same 5' to 3' direction. As the DNA unwinds, the template strand that is exposed in the 3' to 5' direction allows the new strand to be synthesized continuously in the 5' to 3' direction. This new strand, which undergoes continuous replication, is called the leading strand. The newly made from 5' to 3' strand that undergoes discontinuous replication is called the lagging strand. The discontinuous replication of DNA forms Okazaki fragments (the short lengths of DNA produced by the lagging strand) which are linked together to create a continuous new DNA molecule by the aid of ligase enzyme (**Fig 43**).

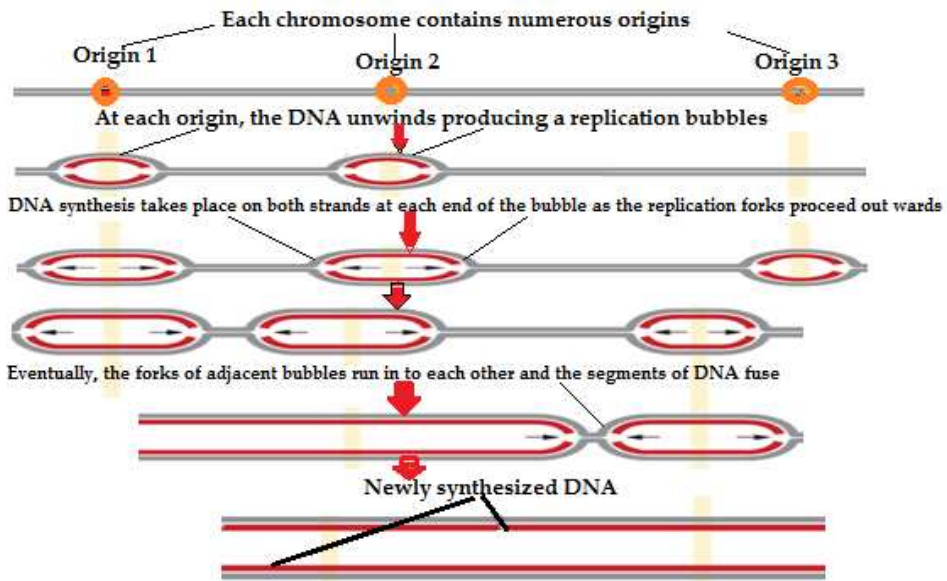


Figure 43: the products of eukaryotic DNA replication are two linear DNA molecules

Replication takes place in various stages: Initiation, Elongation and termination. All these stages are carried out by different enzymes in both prokaryotes and eukaryotes however some deviation is there. These enzymes are: initiator protein (Binds to origin and separates strands of DNA to initiate replication), DNA helicase (unwinds DNA at replication fork), Single-strand-binding protein (attached to single stranded DNA and prevent secondary structures from forming), DNA gyrase (moves ahead of the replication fork, making and resealing breaks in the double helical DNA to release the torque that builds up as a result of unwinding at the replication fork), DNA primase (synthesis a short RNA primer to provide a 3' -OH group for the attachment of DNA nucleotides), DNA polymerase III (Elongates a new nucleotide strand from the 3'-

OH group provided by the primer), DNA polymerase I (Removes RNA primers and replaces them with DNA), and DNA ligase (joins Okazaki fragments by sealing nicks in the sugars- phosphate back bone of newly synthesized DNA (**Fig 45**).

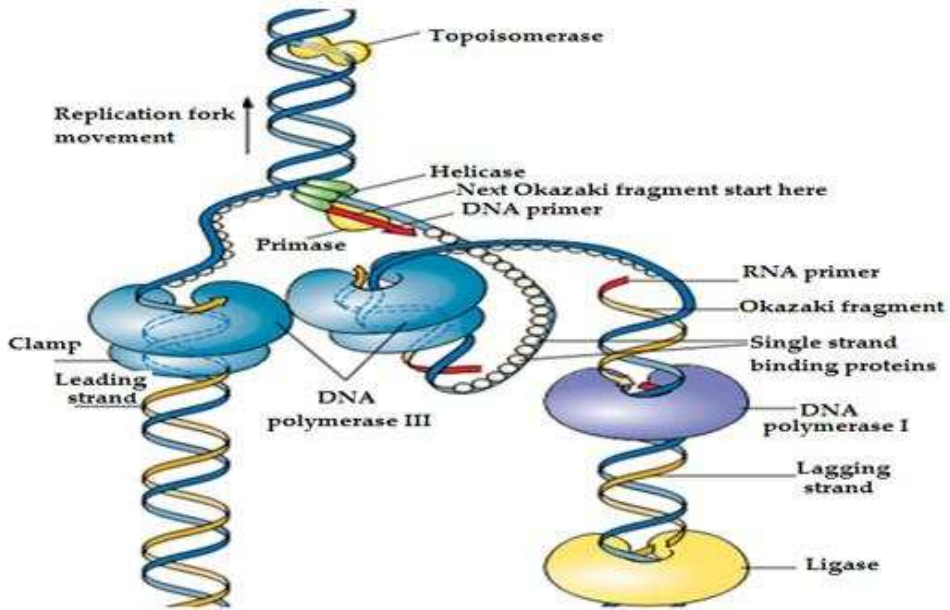


Figure 44: Eukaryotic DNA replication model

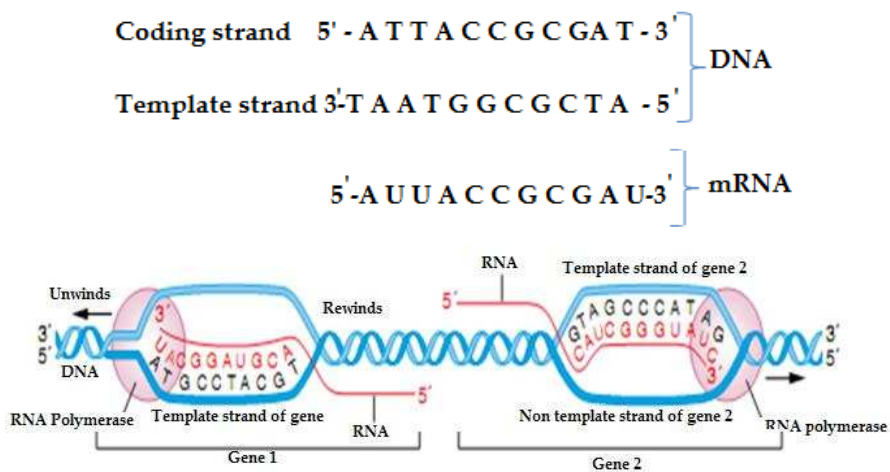
8.1.2.3. RNA Structure

Like DNA, RNA is a polymer consisting of nucleotides joined together by phosphodiester bonds. However, there are differences in their structures. The DNA nucleotides contain deoxyribose sugars lacking free hydroxyl group making DNA is more stable molecule. In DNA, thymine is one of the two pyrimidines. DNA consists of two strands joined by hydrogen bonding between complementary bases. However, the RNA nucleotides have ribose sugars with a free hydroxyl group on the 2' -carbon atom of the ribose sugars which makes RNA is degraded rapidly under alkaline conditions. Instead of thymine in the DNA, RNA has uracil and single stranded.

8.1.3. DNA Transcription

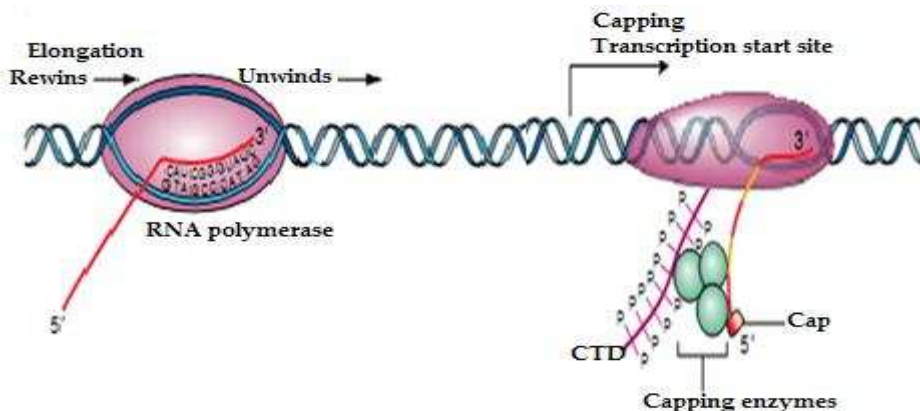
All cellular RNAs are synthesized from DNA templates through the process of

transcription which requires three major components: DNA template, the raw materials (substrates) needed to build a new RNA molecule; and the transcription apparatus, consisting of the proteins necessary to catalyze the synthesis of RNA. Transcription relies on the complementary pairing of bases step by step. First, the two strands of the DNA double helix separate and one of the separated strands acts as a template for RNA synthesis. Next, ribonucleotides synthesized elsewhere in the cell form stable pairs with their complementary bases in the template. Each ribonucleotide is positioned opposite its complementary base by *RNA polymerase* and starts to grow always in the 5' to 3' direction means that the template strand must be oriented 3' to 5'. As an RNA polymerase molecule moves along the gene, it unwinds the DNA double helix ahead of it and rewinds the DNA that has already been transcribed. As the RNA molecule progressively lengthens, the 5' end of the RNA is displaced from the template as the transcription bubble closes behind the polymerase. Consequently, the nucleotide sequence in the RNA must be the same as that in the non-template strand of the DNA, except that the T's are replaced by U'. This non-template strand is said to be coding strand because its sequence is similar to that of mRNA except T is replaced by U.



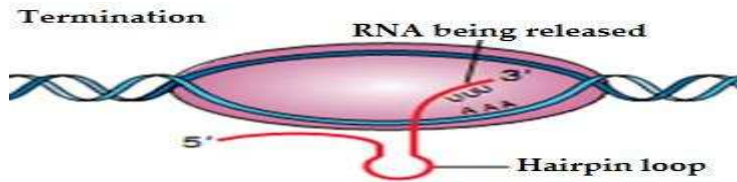
There are three distinct stages of transcription: initiation, elongation and termination. The process of transcription is similar in prokaryotes and eukaryotes however there are some differences. In the initiation prokaryotes, *RNA polymerase* usually binds to a specific DNA sequence called a promoter region located close to the start of the transcribed region. Then unwinds the DNA double helix and begins the synthesis of an RNA molecule. The first transcribed base is always at the same location, designated the initiation site. However, in eukaryotes three different polymerases is *RNA polymerase I* (transcribes rRNA genes), *RNA polymerase II* (transcribes all protein-coding genes, for

which the ultimate transcript is mRNA) and *RNA polymerase III* (transcribes the small functional RNA genes such as the genes for tRNA, some snRNAs, and 5S rRNA). Here many proteins are bind at a promoter before RNA polymerase II begins synthesizing of RNA. Some of these proteins called general transcription factors (GTFs) bind before RNA polymerase II binds. The GTFs are designated TFIIA, TFIIB, and so forth (for transcription factor of RNA polymerase II). Promoters are located on the 5' side (upstream) of the transcription start site and the sequence TATA is often located about 30 base pairs (-30 bp) from the transcription start site. This sequence, called the TATA box, is the site of the first event in transcription (the binding of the TATA binding protein (TBP). TBP is part of the TFIID complex, which is one of the six GTFs which bound to the TATA box it attracts other GTFs and the RNA polymerase II core to the promoter thus forming the pre initiation complex. After transcription has been initiated, RNA polymerase II dissociates from most of the GTFs to elongate the primary RNA transcript. Some of the GTFs remain at the promoter to attract the next RNA polymerase core. In this way, multiple RNA polymerase II enzymes can be synthesizing transcripts from a single gene at one time. RNA synthesis is in the nucleus and then transported to cytoplasm for translation after it has been modified in several way. After initiation elongation continues until RNA polymerase recognizes special nucleotide sequences that act as a signal for chain termination. RNA of eukaryotes must undergo further processing such as the addition of a cap at the 5' end, the addition of a 3' tail of adenine nucleotides (polyadenylation), and splicing to eliminate introns (**Appendix C**). Before it can be translated the cap has two functions. First, it protects the RNA from degradation and secondly, the cap is required for translation of the mRNA.



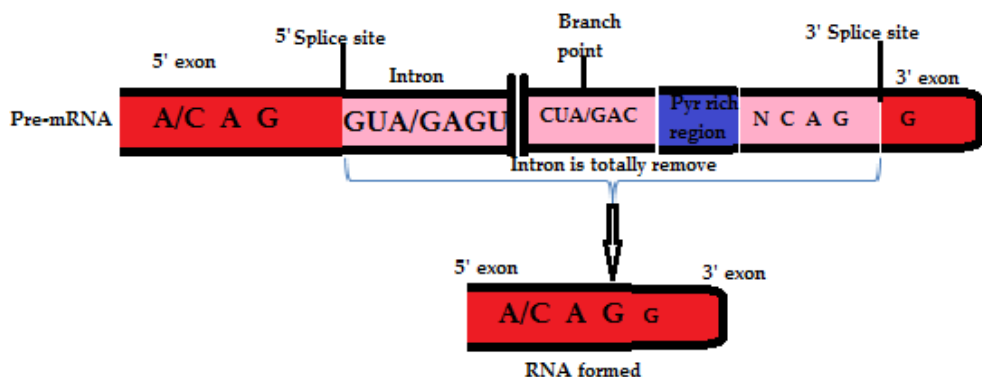
RNA elongation continues until the conserved sequence, AAUAAA or AUUAAA, near the 3'. To this cut end, a stretch of 150 to 200 adenine nucleotides called a

polyadenylation signal tail is added. The transcription of an individual gene is terminated beyond the protein-coding segment of the gene, creating a 3' untranslated region (3' UTR) at the end of the transcript called termination site



8.1.3.1. RNA splicing (the removal of introns)

Eukaryotic genes contain introns, segments of unknown function that do not code for polypeptides. Introns are present not only in protein-coding genes but also in some rRNA and even tRNA genes. They are removed from the primary transcript while RNA is still being synthesized and after the cap has been added, but before the transcript is transported into the cytoplasm. The removal of introns and the joining of exons are called splicing which brings together the coding regions, the exons so that the mRNA now contains a coding sequence that is completely collinear with the protein that it encodes. The number and size of introns varies from gene to gene and from species to species.



8.1.3.2. The genetic code

Genetic code is the triplet base sequences of mRNA that responsible for the reading of

anticodon (triplet sequences of amino acids) during translation. If an mRNA molecule is read from one end to the other, only one of four different bases, A, U, G, or C, can be found at each position. Since a codon is a triplet letters, $4 \times 4 \times 4 = 64$ words are possible.

Table 13: Sequences of amino acid

		Second letter				
		U	C	A	G	
First letter	U	UUU } Phe UUC UUA } Leu UUG	UCU } Ser UCC UCA UCG	UAU } Tyr UAC UAA Stop UAG Stop	UGU } Cys UGC UGA Stop UGG Trp	U C A G
	C	CUU } Leu CUC CUA CUG	CCU } Pro CCC CCA CCG	CAU } His CAC CAA } Gln CAG	CGU } Arg CGC CGA CGG	U C A G
	A	AUU } Ile AUC AUA AUG Met	ACU } Thr ACC ACA ACG	AAU } Asn AAC AAA } Lys AAG	AGU } Ser AGC AGA } Arg AGG	U C A G
	G	GUU } Val GUC GUA GUG	GCU } Ala GCC GCA GCG	GAU } Asp GAC GAA } Glu GAG	GGU } Gly GGC GGA GGG	U C A G
						Third letter

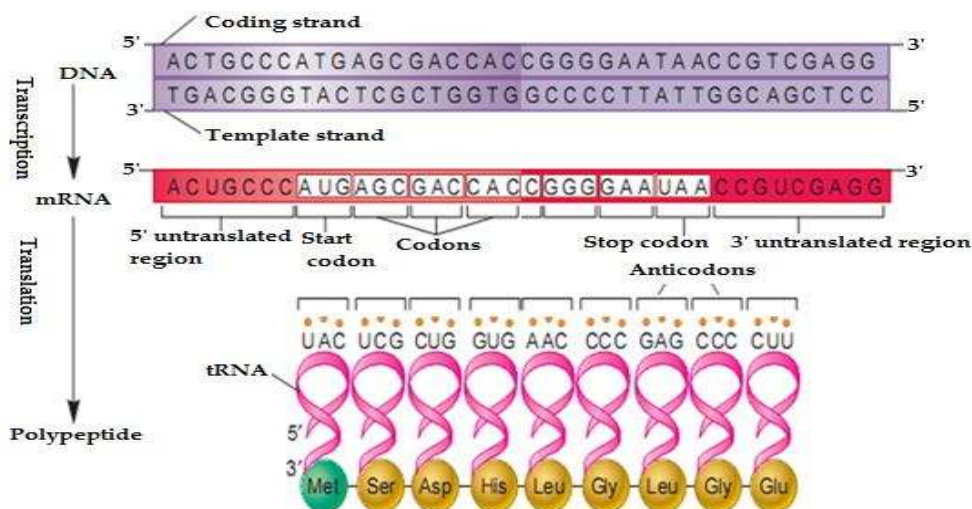
This means more than 20 enough words to describe the amino acids. The genetic code is degenerate; each of the 64 triplets must have some meaning within the code. For this to be true some of the amino acids must be specified by at least two or more different triplets, one amino acid can be coded by more than two or more codons (**Table:13**).

8.1.4. Translation (protein biosynthesis)

The process of synthesizing protein from mRNA where, the genetic code within mRNA is used to make a polypeptide with a specific amino acid sequence is said translation. The ability of mRNA to be translated into a specific sequence of amino acids relies on the genetic code. The sequence of three bases in most codons specifies a particular amino acid termed as sense codons. The process of translation can be divided into three phases: initiation, elongation, and termination. The codon AUG, which specifies methionine, is used as a start codon; is usually the first codon that begins a polypeptide sequence. The AUG codon can also be used to specify additional methionine within the coding sequence. Finally, three codons UAA, UAG, and UGA known as stop codons are used to end the process of translation. They are also known as termination

or nonsense codons.

Anticodons are three-nucleotide sequences carried by transfer RNA (tRNA) molecules that are complementary to codons in mRNA. Transfer RNA (tRNA) molecules are the adapters that translate the three-nucleotide codon in the mRNA into the corresponding amino acid, which is brought to the ribosome in the process of translation. So, the ribosomal RNAs (rRNAs) are the major components of ribosomes, which are large macromolecular complexes that assemble amino acids to form the protein whose sequence is encoded in a specific mRNA.



Any change in reading frame of mRNA codons changes the sequence of polypeptide sequence of a protein resulting mutation in an organism.

8.2. Gene and Chromosome Mutation

Information in DNA is the starting point of gene expression that the cell transcribes that information into mRNA and then translates the mRNA information into protein. Mutations that alter the nucleotide pairs of DNA may modify any of the steps or products of gene expression i.e. mutations in a genes coding sequence may alter the gene product. Mutation can be caused by the substitution, addition and deletion of base pairs.

8.2.1. Types of mutations

Mutation can be seen as mutation in a gene's coding sequence and mutations outside the coding sequence. Mutations in a gene's coding sequence are: ***Silent mutations***; it can change a codon into a mutant codon that specifies exactly the same amino acid. The majority of silent mutations change the third nucleotide of a codon, the position at which most codons for the same amino acid differ. For example, a change from GCA to GCC in a codon would still yield alanine in the protein product because silent mutations do not alter the amino acid it has no effect on any of the phenotypes influenced by the gene. ***Missense mutations***; are mutations that change a codon into a mutant codon that specifies a different amino acid. Two types of missense mutation, one is conservative missense mutation where the substituted amino acid has chemical properties similar to the one it replaces, and then it may have little or no effect on protein function. For example, a mutation that alters a GAC codon for aspartic acid to a GAG codon for glutamic acid is a conservative substitution because both amino acids have acidic R groups. The second type of missense mutation is non-conservative missense mutations that cause substitution of an amino acid with very different properties and have more noticeable consequences. For example, a change of the same GAC codon for aspartic acid to GCC, a codon for alanine (an amino acid with an uncharged, nonpolar R group), is an example of a non-conservative substitution. ***Nonsense mutations*** are that mutations change an amino acid specifying codon to a premature stop codon. They are therefore result in the production of proteins smaller than those encoded by wild-type alleles of the same gene. The shorter, truncated proteins lack all amino acids between the amino acid encoded by the mutant codon and the C terminus of the normal polypeptide. As a result the mutant polypeptide will be unable to function if it requires the missing amino acids for its activity. ***Frame shift mutation*** is the results from the insertion or deletion of nucleotides within the coding sequence (the series of codons specifying the amino acids of the gene product). If the number of extra or missing nucleotides is not divisible by 3, the insertion or deletion will skew the reading frame downstream of the mutation. As a result, frame shift mutations cause unrelated amino acids to appear in place of amino acids critical to protein function.

Types of mutation in a gene's coding sequences

Wild type mRNA	5' GCU GGA GCA CCA GGA CAA GAU GGA 3'
Wild type polypeptide	N Ala Gly Ala Pro Gly Gln Asp Gly C
Silent mutation	GCU GGA GCC CCA GGA CAA GAU GGA Ala Gly Ala Pro Gly Gln Asp Gly
Missense mutation	GCU GGA GCA CCA AGA CAA GAU GGA Ala Gly Ala Pro Arg Gln Asp Gly
Nonsense mutation	GCU GGA GCA CCA GGA UAA GAU GGA Ala Gly Ala Pro Gly Stop GAU GGA
Frame shift mutation	GCU GGA GCC ACC AGG ACA AGA UGG Ala Gly Ala Thr Arg Thr Arg Trp

Mutations outside the coding sequence are occurred in outside of coding sequence because gene expression depends on several signals other than the actual coding sequence, changes in any of these critical signals can disrupt the process. For example, promoters and termination signals in the DNA of a gene instruct RNA polymerase where to start and stop transcription. Changes in the sequence of a promoter that make it hard or impossible for RNA polymerase to recognize the site diminish or prevent transcription. Mutations in a termination signal can diminish the amount of mRNA produced and thus the amount of gene product.

REVIEWING THE KEY CONCEPTS

DNA is a genetic material of living organisms that discovered by Fred Griffith in 1928 when he conducted his experiment on injection of two strains of bacteria to mouse, and Colin MacLeod and Maclyn McCarty when they used three enzymes, DNase that degrade DNA, proteinase which degrade protein and RNase which degrade RNA molecule. DNA can be seen in three structures, primary (nucleotide formation in one strands of DNA molecule), secondary (the hydrogen bonding of nitrogenous bases in the one strand and the another strand to form alpha helical double strands of DNA molecule) and tertiary (is when the long single strand of DNA molecule turn over its own strand and make complement with it) structure. DNA replication is the copy of DNA strand in semiconservative mechanism in which different types of enzymes are involved. It has three stages initiation, elongation and termination. Form of DNA replication in prokaryotes and eukaryotes is different incase prokaryote DNA

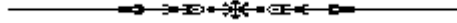
replication takes place in two ways: theta replication and rolling-circle replication where origin of replication is low. However, in eukaryotes replication is carried out in linear form at different site where origins of replication are present.

Transcription is the conversion of genetic information carried by DNA molecule to RNA molecules in which the process has three steps: initiation, elongation and termination also. During transcription various types of RNA molecules are formed. They can be mRNA, tRNA, rRNA and etc. These types of RNA molecules are important during the formation of protein on ribosome by the process of translation. Since information in the RNA molecule is read by anticodon by tRNA, any mutation or change in the sequence of DNA or RNA molecule produce incorrect gene product at the end. These mutations can be formed in coding sequence or in noncoding sequence i.e. starting signals or terminating signals on a DNA molecule.

COMPEREHENSION QUESTION

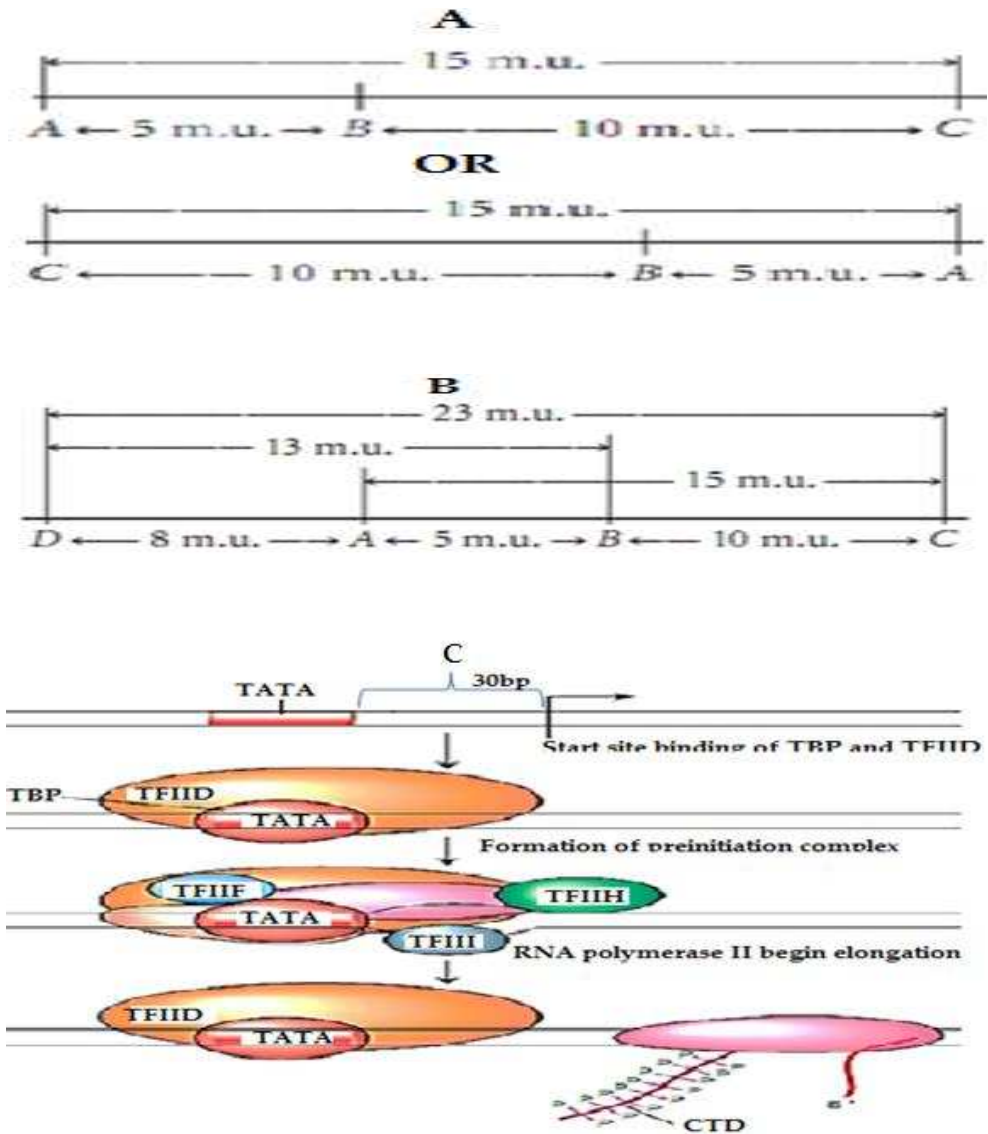
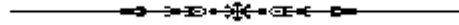
1. From the central dogma, which step is more complicated do you think? Replication or transcription
2. What is importance of RNA splicing?
3. What are the functions of mRNA, rRNA and tRNA?
4. How Okazaki fragments are linked together do you think?
5. How theta and rolling-circle replication is different from each other?
6. Why origin of replication in bacterial DNA is less than that of eukaryotic is do you think?
7. Which type of mutation has no effect from the following lists?
 - a). missense mutation
 - b). silent mutation
 - c). frame shift mutation
 - d). nonsense mutation

REFERENCES



- Benjamin A. Pierce (2012). Genetics: A Conceptual Approach. 4th Edition. *Southwestern University*
- Lizabeth A. Allison (2007). Fundamental of molecular Biology. Department of Biology, College of William and Mary Williamsburg, USA.
- Eberhard Passarge (2007). Color Atlas of Genetics. Third edition, revised and updated.
- Robert J. Brooker (2012). Concepts of genetics. 1st edition. PP: 430- 764
- Brooker, Robert J (2012). Genetics: analysis and principle. 4th edition. pp:430-766
- Leland Hartwell, Leroy Hood, Michael L. Goldberg, Ann E. Reynolds and Lee M. Silver (2011). Genetics: from genes to genomes 4th edition. PP: 430-458
- Jeremy W. Dale and Simon F. Park (2003). Molecular Genetics of Bacteria. 4th Edition. PP: 434
- G/Michael Blackburn, Michael J. Gait, David Loakes and David M. Williams (2006). Nucleic Acids in Chemistry and Biology. 3rd Edition
- Russ Hodge (2009). Genetics and evolution: The Molecules of Life DNA, RNA, and Proteins
- Chris R. Calladine, Horace R. Drew, Ben F. Luisi and Andrew A. Travers (2004). Understanding DNA: The Molecule & How It Works. 3rd Edition.
- Robert F. Weaver (2011). Molecular biology. 5th ed. PP: 506- 543.
- William S. Klug, Michael R. Cummings and Charlotte Spencer (2006). Concepts of genetics. 8th edition. PP: 430-574.
- Robert Schleif (1993). Genetics and Molecular Biology. 2nd Edition

APENDICIES



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Table 6: Comparison of mitosis, meiosis I and meiosis II

Event	mitosis	Meiosis I	Meiosis II
Cell division	Yes	Yes	Yes
Chromosome reduction	No	Yes	No
Genetic variation produced	No	Yes	No
Crossing over	No	Yes	No
Random distribution of maternal and paternal chromosomes	No	Yes	No
metaphase	Individual chromosome line up	Homologous pairs line up	Individual chromosome line up
Anaphase	Chromatids separate	Homologous chromosomes separate	Chromatids separate

Two types of genotype Rr are located on homologous chromosome

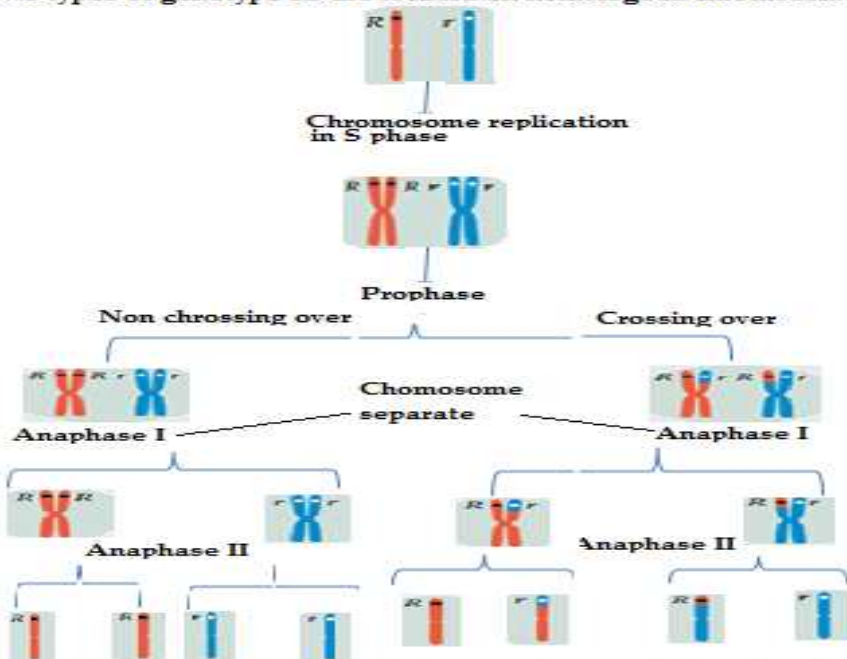


Figure: 15. How crossing over and non crossing over takes place during meiosis

The aim of this book is to show brief concept of genetics based on selected ideas and related facts.

Additional information is presented in the introduction, with a chronological list of important discoveries and advances in the history of genetics, in an appendix with supplementary data in tables, and in references.

This book is written for two kinds of readers: for students of biology and genetics, as an introductory over view; and for their teachers, as a teaching aid. Other interested individuals will also be able to gain information about current developments and achievements in this rapidly growing field.



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