UNIT 2  BIOLOGICAL BASIS OF HUMAN HEREDITY

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Learning Objectives

After reading this unit, you will be able to:

- understand cell, its structure and other cellular components;
- discuss mitotic and meiotic cellular divisions and the differences between them; and
- explain the genetic basis of human variation.

2.1  INTRODUCTION

Earlier biologists and geneticists viewed heredity and inheritance in a different way, some of which are presented here to widen your understanding in this unit. Galton’s theory of blending inheritance states that the hereditary characteristics of the parents are irreversibly mixed in the progeny. Weismann (1892) put forth his theory of germplasm inheritance according to which germplasm was considered immortal and formed the bridge of life passing from generation to generation. The blood theory of inheritance states that blood acts as a vehicle for the transmission of characters from parents to offspring. All these views have been rendered void after Mendel’s discovery of laws of inheritance. Currently, the principle of chromosomal theory of inheritance is the valid concept to understand heredity.

Hereditary mechanisms keep populations similar and stable from generation to generation. But we know populations do change over time. Such changes may be understood by studying the factors that alter the hereditary mechanisms of populations.

William C. Boyd
2.2 ORGANIZATION OF VARIOUS CELLULAR COMPONENTS

Historical Background

Robert Hook (1665) observed the cell for the first time with the help of his primitive microscope. The material that he observed was a piece of cork. This structure of cell is now known as the unit of life. There is really no ‘typical’ cell in which we can see all the features of the cell. Living things are composed of material structural units called cells. A cell is the fundamental unit of structure and function in an organism. It is that unit of organism which is delimited by plasma membrane and is capable of self-reproduction (Loewy and Siekevitz, 1963). Sir Frederick Gowland Hopkins called cells as theaters of life. All cells carry out the same biological function. They perform metabolic and reproductive functions and maintain cellular integrity for our life. Cells combine to form colonies (Functional Association) and form tissues (Facultative Association).

Cell Theory

The cell theory is a concept proposed by Schwann and Schleiden (1838-39) and Rudolf Virchow (1858). This theory states that:

- All organisms are made up of cells.
- Cells are organisms.
- Cells arise from pre-existing cells.
- The activities of organisms are the outcome of individual cells.

Cell Types

Living organisms on earth provide us high degree of cellular diversity in reference to cell types. There are two principle cell types’ namely unicellular simple prokaryotes and multi cellular complex eukaryotes. The former shows the absence of well-organized nucleus and nuclear membrane and the latter shows the presence of them. The examples of prokaryotes (e.g. bacterial cell) and of eukaryotes (e.g. human) are listed below:

- Reproductive cells e.g. sperm, egg.
- Somatic cells e.g. nerve cells.
- Intestinal cells e.g. mucosa.
- Columnar epithelial cells e.g. gut.
- Goblet cells e.g. lumen of gut.
- Connective tissue cells e.g. collagen fibre.
- Muscle cells e.g. smooth muscle cell.
- Unicellular organisms e.g. amoeba.
- Prokaryotic cell e.g. bacterium.
- Eukaryotic plant cell e.g. onion peel cell.
- Eukaryotic cell e.g. human cheek epithelial.
Cell Structure

The cell consists of three principle components. They are: 1) Plasma membrane 2) Cytoplasm and 3) Nucleus, and all of them are combinely known as protoplasm. The nucleus controls all the activities of the cell (Fig. 2.1). Besides this, the cytoplasm possesses many organelles and inclusions. For example, endoplasmic reticulum and mitochondrion are organelles while vacuoles and vesicles are inclusions. The cell has two types of membranes: 1) cytoplasmic membrane which regulates internal environment and 2) internal membrane which encloses organelles and perform metabolic functions such as mitochondrial ATP synthesis. There are many organelles present inside the cell. The nucleus and chromosomes take active part in the hereditary transmission of characters so we will examine them in greater detail in the following.

Fig 2.1: Diagrammatic representation of cell structure showing differences in animal and plant cells (Source: Gupta (1974)).

The Nucleus

Nucleus is the most vital part of the cell. It controls all the activities of cell and can be called as manager of the cellular factory. It was first discovered by Robert Brown in 1831. It is defined as any formation surrounded by cytoplasm from which chromosomes arise during cell division. Nucleus is present in all cells. However, it is absent in human red blood corpuscles (RBC) and in some lens cells.

The nucleus is bounded by a double layer of membranes called nuclear membrane. A thread like material can be seen within nucleus called chromatin which consists of DNA and proteins. The nucleus is filled with a transparent substance called nuclear sap in which nucleolus and chromatin threads remain enclosed.
The nucleus consists of nucleolus proteins and nucleic acids. The nucleic acids are of two types - DNA (deoxyribonucleic acid and RNA (ribonucleic acid). DNA is present in chromatin network and RNA is present in nucleolus.

The most significant role of the nucleus is to store and transmit hereditary information from generation to generation of cells.

**The Chromosomes**

Chromosomes are self-reproducing thread like structures located inside the nucleus. The word chromosome (chromo = colour, soma = body) means coloured bodies. They can be easily stained with dyes. Hofmeister in 1848 discovered chromosomes. They are the vehicles of heredity and serve as our horoscope. The chromosome number varies from species to species. But it remains constant between the members of the same species.

Humans have 46 chromosomes in 23 pairs: 22 pairs are called autosomes and one pair is the sex chromosomes X and Y. These chromosomes are divided into 7 (A-G) groups as per Denver-London System of classification. From cyto genetic point of view, males are characterized by (22 autosomes + XY) and females are characterized by 22 autosomes + XX. The presence of barr body is characteristic of females and sex determination in humans. Males with 22 autosomes + XY are heterogametic producing two types of gametes, while females with 22 autosomes + XX are homogametic producing one type of gamete (Fig. 2.2).

![Fig. 2.2: Sex determination (Source: Sabanayagam, 1990).](image)

The principle of chromosomal basis of hereditary transmission clearly states that genes we have with their unique features form an integral part of the chromosome of each cell. Sexual reproduction mediates the transmission of chromosomes (genes) from generation to generation. The chromosomal
constitution of an individual, a species or race is called karyotype which is an arrangement of chromosomes according to their size and position of centromere.

There are 4 types of chromosomes (Fig. 2.3): metacentric, sub-metacentric, acrocentric (with satellites), acrocentric (without satellites) and telocentric (absent in man). However, acentric chromosomes without centromere can also be found.

![Human chromosomes, one member of each homologous pair, shown in groups A to G, and in numerical order of Denver London classification. Banding pattern indicated. The sex chromosomes X and Y are shown in groups C and G, respectively (Source: Bhatnagar et al., 1977).](image)

**The Cell Cycle**

Living organisms are characterized by two important features, growth and reproduction. Each cell grows to a definite size and then it undergoes self-reproduction to give daughter cells.

There are two phases/periods in the life of a cell. They are N (inter phase or period of non-division) and M (phase or period of division). The longest phase in cell cycle is the inter phase (89 hours). The cycle shows 4 distinct phases.
Introduction to Human Genetics

G\textsubscript{1} Phase $\rightarrow$ S – Phase $\downarrow$

M-Phase

$\leftarrow$ G\textsubscript{2} Phase

G\textsubscript{1} - Gap (1\textsuperscript{st} Growth)
S = Synthesis
G\textsubscript{2} = 2\textsuperscript{nd} Growth
M = Mitosis

The M phase consists of the following two sub phases.
Karyokinesis – division of nucleus into two daughter nuclei.
Cytokinesis – division of cytoplasm into two daughter cells.

2.3 CELL DIVISION

Organisms show two types of cell division viz., mitosis and meiosis. Following is the brief account of cell divisions with their genetic significance.

2.3.1 Mitosis

Mitosis is essentially somatic cell division and was first discovered by Fleming in 1879. It is defined as that cell division which gives rise to two identical daughter cells, each with nucleus containing the same amount of DNA and same genes as the parent cell. Mitosis is necessary for growth and reproduction of all living organisms.

Following are the types of mitosis.
Intra nuclear mitosis: It occurs within the nucleus (cell division).
Extra nuclear mitosis: It occurs outside nucleus but in cytoplasm.
Endomitosis: Chromosomes multiply without cell division e.g. polytene chromosome.

*Mechanism of Mitosis*

The mitotic division takes place in following two stages.
Karyokinesis – the division of nucleus into two daughter nuclei
Cytokinesis – division of cytoplasm into two daughter cells.

The former cell division takes place in four stages. They are prophase, metaphase, anaphase and telophase (Figs. 2.4, 2.5). We will examine in brief these changes in each phase.

1) Prophase – It is the first phase of mitosis in which chromosomes become short and thick; each chromosome is formed of two chromatids and are connected by centromere.
2) Metaphase – Chromosomes are arranged in the equatorial plane and chromosomal fibers are formed.

3) Anaphase – The chromatids of each chromosome are separated to form two daughter chromosomes which move to opposite poles of the cell.

4) Telophase – It is the last stage in cell division in which chromosomes uncoil and lengthen, nucleolus appears, spindle fibers are dissolved into cytoplasm and two daughter nuclei are formed.

Fig. 2.4: Some early stages of mitosis (after King, 1965) (Source: Verma and Agarwal, 1982).
Genetic significance of Mitosis

The mitotic cell division ensures equitable distribution of nucleus and cytoplasm between the daughter cells. The number of chromosomes in the parent cell is the same in daughter cells. Therefore, the structural, functional and hereditary potentialities of both daughter cells are same as that of the parent.

2.3.2 Meiosis

Meiosis cell division was discovered by Farmer in 1905. It is also called as reduction division or reproductive division because the diploid (2n) chromosomes are reduced to haploid (n). It occurs only in reproductive (germ) cells. The cell in which meiosis takes place is called meiocytes. It is more complex than mitosis. Meiosis has two stages as follows.

1) Heterotypic division (First Meiotic Division): The diploid cell is divided into 2 haploid cells.

2) Homotypic division (Second Meiotic division): During this, the two haploid cells of 1st division divide into 4 haploid cells. The daughter cells are similar to parent cell in chromosome number.
The important point to note here that during the first meiotic division, the centromere does not divide causing the reduction in the number of chromosomes. During second meiotic division, the centromeres divide and not the chromatids.

Meiosis – First stage (Prophase) is represented in the Fig. 2.6 and is comprised of 5 different stages as follows.

1) First Prophase
   
   i) Leptotene – The diploid chromosome appear in the nucleus.
   
   ii) Zygotene – The identical chromosomes come close to each other and undergo pairing whole length. This is called synopsis. The paired chromosomes become Bivalent condition.
   
   iii) Pachytene – The bivalent chromosomes coil around one another and get shortened, chromosomes are haploid.
   
   iv) Diplotene: The longitudinal split of chromosome give rise to 2 chromatids.
   
   v) Diakinesis: Chromosomes coil and become further short. They remain distributed in the Nucleus.

Fig. 2.6: The mechanism of distribution of chromosomes during meiosis first (after King, 1965) (Source: Verma and Agarwal, 1982).
Further stage of Meiotic division is known as Meiosis II and is represented in Figure 2.7. In addition to First Prophase, Meiosis consists of the following stages.

1) First Metaphase: Nuclear membrane disappears, nucleolus vanishes, nuclear spindle develops and bivalent chromosomes move towards equatorial plane. Each chromosome has 2 centromeres and attached to spindle fibers.

2) First Anaphase: The two pairs now get separated and move to opposite poles.

3) First Telophase: Two daughter nuclei each with a pair of chromatids formed at the poles. The nuclei are haploid.

4) Second Metaphase: The paired chromatids are widely separated and point of attachment is at centromere.

5) Second Anaphase: The chromatids separate in opposite poles.

6) Second Telophase: 4 daughter nuclei are formed each with haploid (N) number of chromosomes.

Fig. 2.7: The different stages of meiosis (after King, 1965) (Source: Verma and Agarwal, 1982).

Genetic significance of Meiosis

1) Gametes are produced by meiosis and are essential units of sexual reproduction.

2) Meiosis reduces diploid (2n) chromosomes characteristic of somatic cells to the haploid number (n) characteristic of gametes.
3) Meiosis prevents in the duplication of chromosomes in the zygote which otherwise would be abnormal.

4) The constant number of chromosomes is maintained by meiosis in a given species.

5) Meiosis provides new combination of genetic material due to crossing over. The hereditary factors (genes) from males and females get mixed causing genetic variations among species. Variations are the principle source for evolution.

6) Meiotic drive refers to disturbance in 1:1 sex ratio.

### 2.4 MAJOR DIFFERENCES BETWEEN MITOSIS AND MEIOSIS

The following are some of the major differences between mitosis and meiosis.

<table>
<thead>
<tr>
<th>Mitosis</th>
<th>Meiosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. It is a simple cell division.</td>
<td>1. It is a complex cell division.</td>
</tr>
<tr>
<td>2. It takes place in somatic (body) cells.</td>
<td>2. It takes place in reproductive (germ) cells.</td>
</tr>
<tr>
<td>3. It helps for the growth of organism.</td>
<td>3. It is concerned with reproduction.</td>
</tr>
<tr>
<td>4. It is a single step cell division.</td>
<td>4. It is a multiple step cell division.</td>
</tr>
<tr>
<td>5. It produces two cells.</td>
<td>5. It produces four cells.</td>
</tr>
<tr>
<td>6. Similarity between daughter cells and parent cells is observed.</td>
<td>6. No similarity between daughter cells and parent cells is observed.</td>
</tr>
<tr>
<td>7. Chromosome number of daughter cells is same as parents i.e. if parents are 2N each, the daughter cells are also 2N.</td>
<td>7. Chromosome number of daughter cells is reduced to half i.e. if parents are 2N each, the daughter cells are N each.</td>
</tr>
<tr>
<td>9. Prophase is short and simple.</td>
<td>9. Prophase is long and complex.</td>
</tr>
<tr>
<td>11. No chiasmata and crossing over occurs.</td>
<td>11. Chiasmata is formed due to crossing over of chromosomes.</td>
</tr>
<tr>
<td>13. Centromere position is towards equator and arms towards poles.</td>
<td>13. Opposite situation is observed in meiosis.</td>
</tr>
<tr>
<td>14. The size of chromosomes is thin and large.</td>
<td>14. The size of chromosomes is short and thick.</td>
</tr>
<tr>
<td>15. Telophase occurs.</td>
<td>15. Telophase may be absent.</td>
</tr>
<tr>
<td>16. Karyokinesis (nuclear division) is followed by cytokinesis.</td>
<td>16. Cytokinesis may be absent.</td>
</tr>
</tbody>
</table>
2.5 BIOCHEMICAL BASIS OF CELL DIVISION

The biochemical basis of cell division is not very simple and straight as we believe. It involves various highly sensitive cellular interactions and based on enzymes. Cell biologists are currently involved in unraveling the mystery of cell divisions through intensive current research. Recent advances in cell biology genetics and molecular biology have shown new insights into cell division. All higher organisms possess B₁ type of cyclins. Mitotic cyclins play a vital role in cell division. They are accumulated; activated and destroyed during cell division. When cellular proteins are phosphorylated to high degree the cell enters Mitosis. When they are dephosphorylated the cell leaves Mitosis.

2.6 GENETIC BASIS OF HUMAN VARIATION

Genetic variability is a universal feature of all breeding populations. It forms a pre-requisite condition for evolution.

Human body with all its physical attributes is the product of heredity and environment. Variation is due to heredity and environment says Galton. Variation forms the principal source for evolution. When variation within a population is converted into variation between population evolutions occurs (Lewontin, 1967).

The Mendelian school and Darwinian school differ in their very outlook of variations. The former look at variations upward from the genes, while later looks at variation downward from the phenotype. Variations refer to dynamic study of gene differences in the population to understand evolutionary changes. The greater genetic diversity in man is due to combination of alleles. Besides this, mutations play a vital role in the maintenance of genetic variability.

How Variations originate in the Biological System

We have good constancy in the operation of various biological systems. For example

1) Precise transcription of DNA
2) Precise pattern of chromosome movement
3) Strong sugar–phosphate backbone of DNA that maintains correct transmission of hereditary information.
4) Mitosis ensures identical genetic content in daughter cells

With all the above mechanisms of constancy, biological systems generate new information or combination of new information. At the backdrop of above constancy, all biological systems have to play following two games of chance to play.

1) Errors in the replication of DNA (mutations).
2) Random assortment of chromosomes pair (meiosis).
Types of Variations

A) Phenotypic variation

<table>
<thead>
<tr>
<th>Continuous variation</th>
<th>Discontinuous variation</th>
<th>Quasi Semi Continuous Variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Quantitative variation)</td>
<td>(Qualitative variation)</td>
<td></td>
</tr>
<tr>
<td>e.g. height, weight</td>
<td>e.g. blood groups, hair colour, skin colour</td>
<td>e.g. ridges on fingers, number of teeth</td>
</tr>
</tbody>
</table>

B) Genotypic variation ($V_g$)

It is that portion of phenotypic variation which is entirely due to genes. This is called $H$ (heritability). If $H$ is 100% then all variations are genetic. In other words, it means absence of environmental variation. As environmental variation increases, heritability decreases. The remarkable genetic diversity which sets each person apart is a unique phenomenon in nature. There is a definite genetic basis of this variation. Even among MZ (monozygotic) identical twins variations are bound to occur due to intra-uterine environment. It is often said that there are as many genotypes as many individuals in the world.

Genes (hereditary factors) play a very important role in causing variation. At cellular level, DNA has a definite role to play in genetics as shown in the following diagram.

```
DNA --- Replication --- DNA --- DNA
     \              \              |
      rRNA        mRNA        tRNA
     \              \              \  |
      Translation Proteins
```

Genes are located in linear fashion on the chromosomes which are made up of DNA and proteins. Thus DNA segments are genes. It is the germ cells which carry genes from one generation to another. Life itself is an eternal journey from cell to cell.

The gene is made up of 4 functional units namely Codon, Recon, Muton and Cistron. Gene is a segment of DNA molecule that codes polypeptide.

2.7 SUMMARY

This unit provides a comprehensive picture on various aspects, heredity, inheritance, biological and genetic basis of transmission of hereditary characters in man. Besides this, this unit is endowed with good coverage of all basic points in reference to cell, cell structure, cell types, structural components of cell, mitosis and meiosis their major differences and genetic basis of human variation.
<table>
<thead>
<tr>
<th><strong>Glossary</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotype</td>
<td>Observable hereditary characteristic of an individual.</td>
</tr>
<tr>
<td>Genotype</td>
<td>Characteristic present in an individual.</td>
</tr>
<tr>
<td>Karyokinesis</td>
<td>Division of nucleus.</td>
</tr>
<tr>
<td>Cytokinesis</td>
<td>Division of cytoplasm.</td>
</tr>
<tr>
<td>Diploid</td>
<td>The double state of all chromosomes in somatic cells (2N).</td>
</tr>
<tr>
<td>Somatic cells</td>
<td>Cells of the body.</td>
</tr>
<tr>
<td>Reproductive cells</td>
<td>Germ cells e.g. egg, sperm.</td>
</tr>
<tr>
<td>Homogametic</td>
<td>Produce one type of gametes (females).</td>
</tr>
<tr>
<td>Heterogametic</td>
<td>Two types of gametes are produced (males).</td>
</tr>
<tr>
<td>Gene</td>
<td>A segment of DNA that codes for one polypeptide.</td>
</tr>
<tr>
<td>Prokaryotes</td>
<td>Unicellular primitive organisms.</td>
</tr>
<tr>
<td>Eukaryotes</td>
<td>Multicellular organisms.</td>
</tr>
<tr>
<td>Karyotype</td>
<td>The chromosome set of a somatic cell. It is also called idiograph.</td>
</tr>
<tr>
<td>Locus</td>
<td>The site of location of the gene on chromosome.</td>
</tr>
<tr>
<td>Centromere</td>
<td>The constricted portion of the chromosome.</td>
</tr>
<tr>
<td>Chromatid</td>
<td>One of the two identical longitudinal half of chromosome.</td>
</tr>
<tr>
<td>Crossing over</td>
<td>Exchange of genetic material between two homologous chromosomes during meiosis.</td>
</tr>
<tr>
<td>Codon</td>
<td>A triplet of 3 successive bases in a DNA or RNA molecule that code for single amino acid.</td>
</tr>
<tr>
<td>Cistron</td>
<td>The smallest structural and functional unit of the gene which specifies the coding of a</td>
</tr>
<tr>
<td></td>
<td>particular polypeptide.</td>
</tr>
<tr>
<td>Muton</td>
<td>Smallest sub unit of cistron that brings mutation in the genetic material, as small as</td>
</tr>
<tr>
<td></td>
<td>one nucleotide pair.</td>
</tr>
<tr>
<td>Recon</td>
<td>The smallest unit of sub unit of cistron that is capable of recombination equals one</td>
</tr>
<tr>
<td></td>
<td>nucleotide pair.</td>
</tr>
<tr>
<td>Allele</td>
<td>An alternate form of a gene occurring at a locus.</td>
</tr>
<tr>
<td>Meiotic drive</td>
<td>Refers to disturbance in 1:1 sex ratio.</td>
</tr>
<tr>
<td>Acentric chromosome</td>
<td>Chromosomes without centromere.</td>
</tr>
</tbody>
</table>
**Suggested Readings**


**Sample Questions**

1) What is the difference between prokaryotes and eukaryotes in their cell structure?

2) What is cell theory? Who proposed it? Explain the theory.

3) What is the composition of a gene? How many functional units are present in it?

4) Explain transcription, translation and replication with reference to DNA.

5) Define mitosis. Briefly comment on various stages of cell division.

6) Define meiosis and list various stages involved in this cell division.

7) What are the major differences between mitosis and meiosis. What is genetic significance of cell division.

8) What is karyotype?

9) What are the three principle components of a cell? Elaborate.

10) Explain in brief various earlier theories of heredity and inheritance.