# THE CELL

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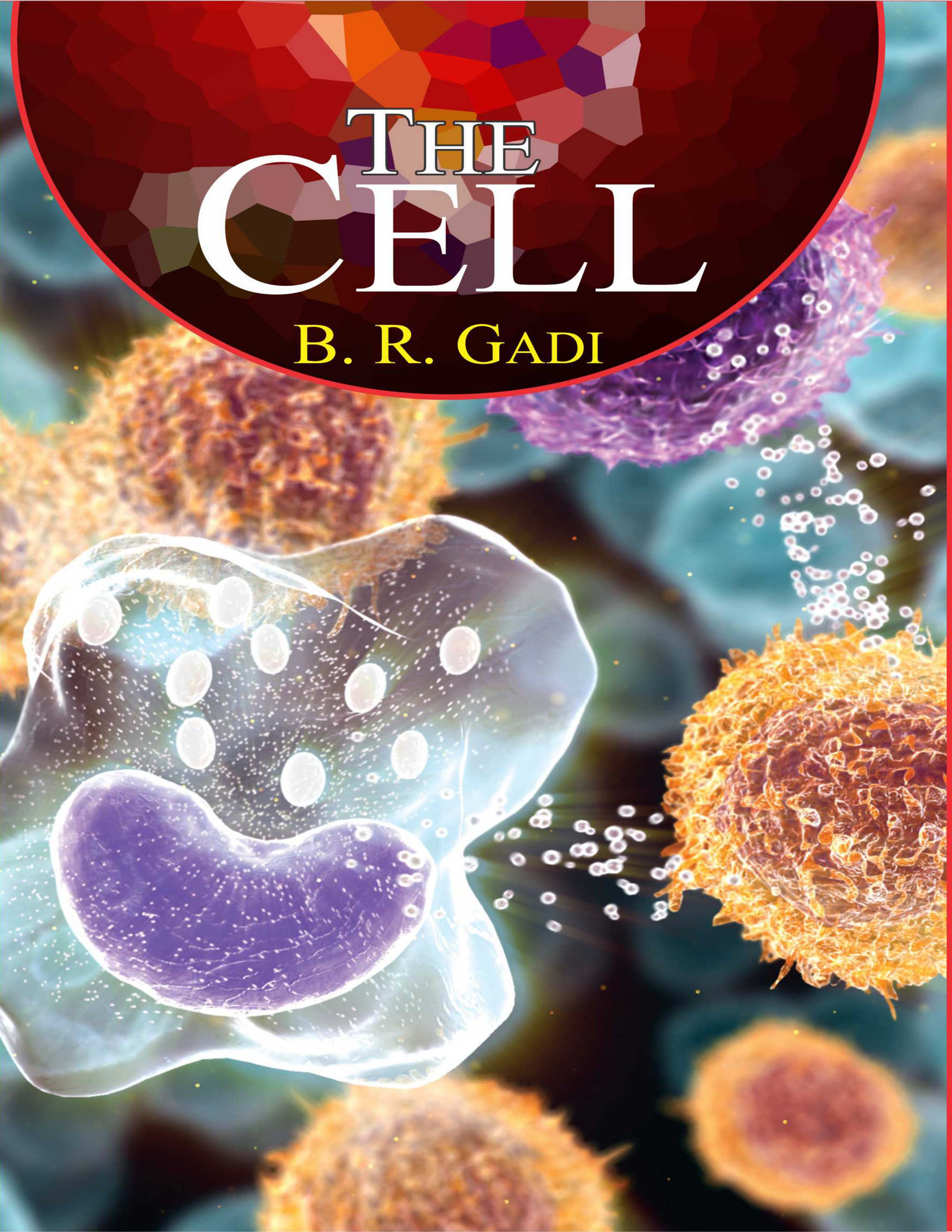

CHAPTER 1

# Cell, Cell Theory, Molecular Biology: Historical Development

## INTRODUCTION

The Cell theory, or cell doctrine, states that all organisms are composed of similar units of organization, called cells. The concept was formally articulated in 1839 by Schleiden and Schwann and has remained as the foundation of modern biology. The idea predates other great paradigms of biology including Darwin's theory of evolution (1859), Mendel's laws of inheritance (1865), and the establishment of comparative biochemistry (1940).

Ultrastructural research and modern molecular biology have added many tenets to the cell theory, but it remains as the preeminent theory of biology. The Cell Theory is to Biology as Atomic Theory is to Physics.

### Earlier Development of Cell Theory

#### *Anaximander*

A member of the Greeks in the sixth century B.C. who resided on the Ionian Islands. He is credited with coming up with the primary thoughts of evolution. His perspective was that creatures from the sea were forced to come ashore, thereby evolving into land creatures.

### *Plato*

Plato did not directly aid in the progress of biological thinking. His view was not experimental, but more philosophical. Many of his students went on to influence the progression of biological studies in the field of classification.

### *The Atomists*

The most noted of this group of Greek philosophers was Democritus (460 - 370 B.C.). He followed Anaximander's view of evolution. Democritus is credited as being the father of atomic theory which connects directly to biology. One important theory of his was simply that if you have nothing, nothing may be created out of it.

### *Aristotle*

Aristotle (384 - 322 B.C.) was known for his experimental approach and numerous dissections. He was drawn to animal classification in order to discover aspects of connection between the soul and the human body. Some of his animal classifications still stand today. One of his famous thoughts is a foreshadowing of Mendelian genetic concepts:

> *"It is evident that there must be something or other really existing, corresponding to what we call by the name of Nature. For a given germ does not give rise to any random living being, nor spring from any chance one, but each germ springs from a definite parent and gives rise to a predictable progeny. And thus it is the germ that is the ruling influence and fabricator of the offspring."*

## The Dark Ages

Following the Greeks, there was a downfall in scientific thought. This decline is usually attributed to the Christian Church, and the power shift to the "*barbaric*" tribes.

### *Leonardo Da Vinci, Rene Descartes, and William Harvey*

These three scientific figures, thought not all living during the same time period, can be accredited with much of the advancement of anatomical thought following the Dark Ages, such as discovering the circulation of blood.

### *The Microscope*

This instrument opened up new doors in the field of biology, by allowing scientists to gaze into a new world: the cellular world. Galileo is credited with the invention of the microscope. Two of the main pioneers in microscope usage were Athanasius Kircher and Antonie von Leeuwenhoek.

### *Robert Hooke*

This English naturalist (1635 - 1703) coined the term *cell* after viewing slices of cork through a microscope. The term came from the Latin word *cella* which means *storeroom* or *small container*. He documented his work in the *Micrographia*, written in 1665.

### *Jean-Baptiste De Lamarck*

The majority of this Frenchman's work (1744 - 1829) dealt with animal classification and evolution. He is credited with taking steps towards the creation of the cell theory with this saying: *"Every step which Nature takes when making her direct creations consists in organizing into cellular tissue the minute masses of viscous or mucous substances that she finds at her disposal under favorable circumstances."*

## Formulation of the Cell Theory

In 1838, **Theodor Schwann** and **Matthias Schleiden** were enjoying after-dinner coffee and talking about their studies on cells. It has been suggested that when Schwann heard Schleiden describe plant cells with nuclei, he was struck by the similarity of these plant cells to cells he had observed in animal tissues. The two scientists went immediately to Schwann's laboratory to look at his slides. Schwann published his book on animal and plant cells (Schwann, 1839) the next year, a treatise devoid of acknowledgments of anyone else's contribution, including that of Schleiden (1838). He summarized his observations into three conclusions about cells:

1. The cell is the unit of structure, physiology, and organization in living things.
2. The cell retains a dual existence as a distinct entity and a building block in the construction of organisms.
3. Cells form by free-cell formation, similar to the formation of crystals (spontaneous generation).

We know today that the first two tenets are correct, but the third is clearly wrong. The correct interpretation of cell formation by division was finally promoted by others and formally enunciated in Rudolph Virchow's powerful dictum, "*Omnis cellula e cellula*" (all cells only arise from pre-existing cells).

## The Modern Tenets of the Cell Theory Include:

1. all known living things are made up of cells.
2. the cell is structural and functional unit of all living things.
3. all cells come from pre-existing cells by division. (Spontaneous Generation does not occur).
4. cells contains hereditary information which is passed from cell to cell during cell division.
5. all cells are basically the same in chemical composition.
6. all energy flow (metabolism and biochemistry) of life occurs within cells.

As with any theory, its tenets are based upon previous observations and facts, which are synthesized into a coherent whole via the scientific method. The Cell Theory is no different being founded upon the observations of many (*Landmarks in the Study of Cells*).

## HISTORICAL DEVELOPMENT

Credit for the first compound (more than one lens) microscope is usually given to **Zacharias Jansen**, of Middleburg, Holland, around the year 1595. Since Jansen was very young at that time, it's possible that his father Hans made the first one, but young Jansen perfected the production. Details about the first Jansen microscopes are not clear, but there is some evidence which allows us to make some guesses about them (Jansen microscopes).

In 1663 an English scientist, **Robert Hooke**, discovered cells in a piece of cork, which he examined under his primitive microscope. Actually, Hooke only observed cell walls because cork cells are dead and without cytoplasmic contents. Hooke drew the cells he saw and also coined the word CELL. The word cell is derived from the Latin word '*cellula*' which means small compartment. Hooke published his findings in his famous work, *Micrographia: Physiological Descriptions of Minute Bodies made by Magnifying Glasses* (1665).

Ten years later **Anton van Leeuwenhoek** (1632-1723), a Dutch businessman and a contemporary of Hooke used his own (single lens) monocular microscopes and was the first person to observe bacteria and protozoa. Leeuwenhoek is known to have made over 500 microscopes, of which fewer than ten have survived to the present day. In basic design, probably all of Leeuwenhoek's instruments were simply powerful magnifying glasses, not compound microscopes of the type used today. Leeuwenhoek's skill at grinding lenses, together with his naturally acute eyesight and great care in adjusting the lighting where he worked, enabled him to build microscopes that magnified over 200 times, with clearer and brighter images than any of his colleagues at that time. In 1673, Leeuwenhoek began writing letters to the newly formed Royal Society of London, describing what he had seen with his lenses.

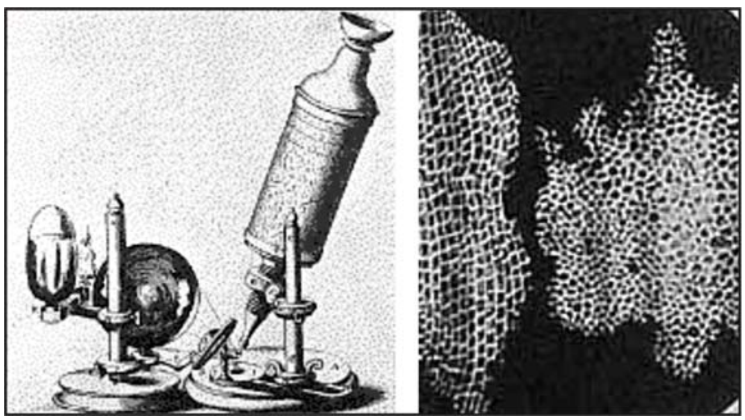

**Fig. 1.1:** (Left) The microscope used by Robert Hooke, (Right) Robert's Hooke's drawing of cork showing compartments (cells).

Between 1680 and the early 1800's it appears that not much was accomplished in the study of cell structure. This may be due to the lack of quality lens for microscopes and the dedication to spend long hours of detailed observation over what microscopes existed at that time. Leeuwenhoek did not record his methodology for grinding quality lenses and thus microscopy suffered for over 100 years.

German natur-philosopher and microscopist, **Lorenz Oken** had been trained in medicine at Freiburg University. He went on to become a renownd philosopher and thinker of the 29$^{th}$ century. It is reported that in 1805 Oken stated that "*All living organisms originate from and consist of cells*"... which may have been the first statement of a cell theory.

Around 1833 **Robert Brown** reported the discovery of the nucleus. Brown was a naturalist who visited the colonies of Australia from 1801 through 1805, where he cataloged and described over 1,700 new species of plants. Brown was an accomplished technician and an extraordinarily gifted observer of microscopic phenomena.

It is upon the works of Hooke, Leeuwenhoek, Oken, and Brown that Schleiden and Schwann built their Cell Theory. It was the German professor of botany at the University of Jena, Dr. M. J. Schleiden, who brought the nucleus to popular attention, and to asserted its all-importance in the function of a cell. **Theodor Schwann**, professor of physiology in the University of Louvain, Schwann was puzzling over certain details of animal histology, which he could not clearly explain. He had noted a strange resemblance of embryonic cord material, from which the spinal column develops, to vegetable cells. Schwann recognized a cell-like character of certain animal tissues. Adopting the same designation, Schwann propounded what soon became famous as the **Cell Theory**.

The cell doctrine reached its present-day eminence in 1896 with the publication of E. B. Wilson's **The Cell in Development and Heredity**, which was an accumulation of what was known about the roles of cells in embryology and chromosomal behavior.

## DEVELOPMENT OF MOLECULAR BIOLOGY AND BIOCHEMISTRY

Molecular Biology is the branch of biology that spans biophysics and biochemistry. It involves the study of the molecular building blocks of life, such as nucleic acids and proteins.

Biophysics is the interdisciplinary study of biological phenomena and problems, using the principles and techniques of physics. The science of biophysics developed after World War II, stimulated in part by the application of nuclear physics to biological systems, including the investigation of radiation effects on living matter. In the course of these studies, physicists were introduced to biologists and biological problems, and biophysics evolved as a new scientific field.

Nucleic acids are extremely complex molecules produced by living cells and viruses. Their name comes from their initial isolation from the nuclei of living cells. Certain nucleic acids, however, are found not in the cell nucleus but in cell cytoplasm. Nucleic acids have at least two functions: to pass on hereditary characteristics from one generation to the next, and to trigger the manufacture of specific proteins. How nucleic acids accomplish these functions is the object of some of the most intense and promising.

Nucleic acids are responsible for storing and transferring genetic information. They are enormous molecules made up of long strands of subunits, called bases that are arranged in a precise sequence. These are "*read*" by other components of the cell and used as a guide in making proteins.

Biochemistry is the study of the substances found in living organisms, and of the chemical reactions underlying life processes. This science is a branch of both chemistry and biology; the prefix bio- comes from *bios*, the Greek word for *life*. The chief goal of biochemistry is to understand the structure and behavior of biomolecules. These are the carbon-containing compounds that make up the various parts of the living cell and carry out the chemical reactions that enable it to grow, maintain and reproduce itself, and use and store energy.

A vast array of biomolecules is present in the cell. The structure of each biomolecule determines in what chemical reactions it is able to participate, and hence what role it plays in the cell's life processes. Among the most important classes of biomolecules are nucleic acids, proteins, carbohydrates, and lipids.

### *Genetic Engineering*

Genetic Engineering, alteration of an organism's genetic, or hereditary, material to eliminate undesirable characteristics or to produce desirable new ones. Genetic engineering is used to increase plant and animal food production; to diagnose disease, improve medical treatment, and produce vaccines and other useful drugs; and to help dispose of industrial wastes. Included in genetic engineering techniques are the selective breeding of plants and animals, hybridization (reproduction between different strains or species), and recombinant deoxyribonucleic acid (DNA).

The first genetic engineering technique, still used today, was the selective breeding of plants and animals, usually for increased food production. In selective breeding, only those plants or animals with desirable characteristics are chosen for further breeding. Corn has been selectively bred for increased kernel size and number and for nutritional content for about 7,000 years. More recently, selective breeding of wheat and rice to produce higher yields has helped supply the world's ever-increasing need for food.

## Molecular Biology

Molecular biology, which spans biophysics and biochemistry, has made the most fundamental contributions to modern biology. Much is now known about the structure and action of nucleic acids and protein, the key molecules of all living matter. The discovery of the mechanism of heredity was a major breakthrough in modern science. Another important advance was in understanding how molecules conduct metabolism, that is, how they process the energy needed to sustain life.

Cellular biology is closely linked with molecular biology. To understand the functions of the cell - the basic structural unit of living matter - cell biologists study its components on the molecular level. Organismal biology, in turn, is related to cellular biology, because the life functions of multicellular organisms are governed by the activities and interactions of their cellular components. The study of organisms includes their growth and development (developmental biology) and how they function (physiology). Particularly important are investigations of the brain and nervous system (neurophysiology) and animal behavior (ethology).

**Table 1.1:** Landmarks in study of cell biology

| | |
|---|---|
| 1595 | Jansen credited with 1st compound microscope |
| 1626 | Redi postulated that living things do not arise from spontaneous generation. |
| 1655 | Hooke described 'cells' in cork. |
| 1674 | Leeuwenhoek discovered protozoa. He saw bacteria some 9 years later. |
| 1833 | Brown descibed the cell nucleus in cells of the orchid. |
| 1838 | Schleiden and Schwann proposed cell theory. |
| 1840 | Albrecht von Roelliker realized that sperm cells and egg cells are also cells. |
| 1856 | N. Pringsheim observed how a sperm cell penetrated an egg cell. |
| 1858 | Rudolf Virchow (physician, pathologist and anthropologist) expounds his famous conclusion: *omnis cellula e cellula*, that is cells develop only from existing cells [cells come from preexisting cells] |
| 1857 | Kolliker described mitochondria. |
| 1869 | Miescher isolated DNA for the first time. |
| 1879 | Flemming described chromosome behavior during mitosis. |
| 1883 | Germ cells are haploid, chromosome theory of heredity. |
| 1898 | Golgi described the Golgi apparatus. |
| 1926 | Svedberg developed the first analytical ultracentrifuge. |
| 1938 | Behrens used differential centrifugation to separate nuclei from cytoplasm. |

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|---|---|
| 1939 | Siemens produced the first commercial transmission electron microscope. |
| 1941 | Coons used fluorescent labeled antibodies to detect cellular antigens. |
| 1952 | Gey and co-workers established a continuous human cell line. |
| 1953 | Crick, Wilkins and Watson proposed structure of DNA double-helix. |
| 1955 | Eagle systematically defined the nutritional needs of animal cells in culture. |
| 1957 | Meselson, Stahl and Vinograd developed density gradient centrifugation in cesium chloride solutions for separating nucleic acids. |
| 1965 | Ham introduced a defined serum-free medium. Cambridge Instruments produced the first commercial scanning electron microscope. |
| 1976 | Sato and colleagues publish papers showing that different cell lines require different mixtures of hormones and growth factors in serum-free media. |
| 1981 | Transgenic mice and fruit flies are produced. Mouse embryonic stem cell line established. |
| 1987 | First knockout mouse created. |
| 1998 | Mice are cloned from somatic cells. |
| 2000 | Human genome DNA sequence draft. |

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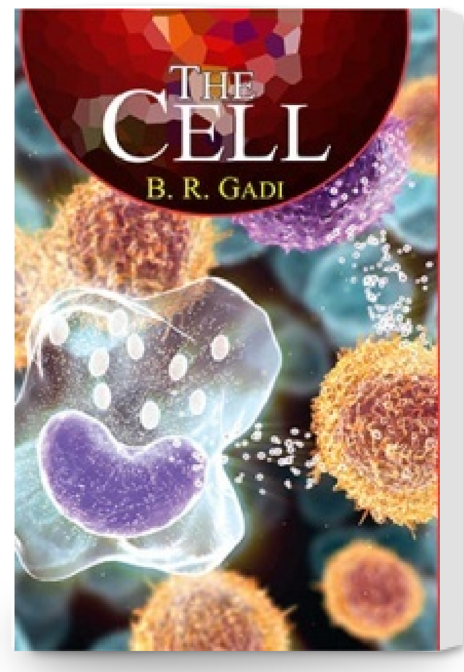


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