Ministry of Education and Science of Ukraine
V.N. Karazin Kharkiv National University

MEDICAL BIOLOGY

IN TWO PARTS

PART I

Methodical instructions
for self-preparation of 1st year students of the School of Medicine
in the discipline «Medical biology»

Electronic resource

Kharkiv – 2025

UDC: 57: 61(072)
M 46

Reviewers:

Natalia MITRYAEVA – Doctor of Biology, head of laboratory of radiation oncology State Organization «Grigoriev Institute for Medical Radiology and Oncology of the National Academy of Medical Sciences of Ukraine»;
Ludmila BELYAEVA – Candidate of Biology, Associate Professor of the Department of General Practice – Family Medicine of V.N. Karazin Kharkiv National University.

Approved for distribution in the Internet by the decision of the Scientific and Methodical Council of V.N. Karazin Kharkiv National University
(Protocol № 10 of May 21, 2025)

M 46 **Medical** biology. In two parts. Part I : methodical instructions for independent work of 1st year students of the School of Medicine in the discipline «Medical biology» [Electronic resource] / compil. S. O. Sherstiuk, S. A. Nakonechna, A. B. Zotova, S. I. Panov. – Kharkiv : V.N. Karazin KhNU, 2025. – (PDF 111 p.)

Methodical instructions for independent work of students in the discipline «Medical biology» developed in accordance with the current programs in Medical biology for students of medical faculties of universities. The manual is designed to work with students in preparation for the course «Medical biology». Each topic contains a list of practical skills and control questions. Topics are illustrated with drawings and diagrams that facilitate the perception of the material and promote its better assimilation. The materials allow students to form a correct understanding of the laws of the Medical biology.
For medical students.

UDC: 57: 61(072)

CONTENT

INTRODUCTION

Medical biology is the science of the foundations of human life, which studies the patterns of individual development and morphological adaptation to environmental conditions in connection with its biosocial essence and the influence of molecular genetic, cellular, ontogenetic, population, and environmental factors on human health.

I. The work program of the discipline «Medical biology» is compiled in accordance with the Standard of Higher Education of the second (master's) level of the field of knowledge 22 «Health care», specialty 222 «Medicine», approved by the Order of the Ministry of Education and Science of Ukraine dated 08.11.2021 No 1197, the Law of Ukraine «On Higher Education» No1556-VII dated July 1, 2014 (with amendments and additions); Regulations on the organization of the educational process at V.N. Karazin Kharkiv National University, approved by the decision of the Academic Council of V. N. Karazin Kharkiv National University (minutes of the meeting No 11 of June 21, 2024), educational and professional program and curriculum of the second (master's) level of higher education «Medicine», field of knowledge 22 «Health care» in specialty 222 «Medicine» for 2024-2025, approved by the decision of the Academic Council of School of Medicine of Kharkiv V. N. Karazin National University (minutes of the meeting No. 7/1 dated April 10, 2024); Statute of V. N. Karazin Kharkiv National University; Code of Values of V. N. Karazin Kharkiv National University and other regulatory normative documents.

II. The program of the discipline is structured into sections. The volume of the student workload is described in ECTS credits - credit credits, which are credited to students upon successful completion of the corresponding section (credit credit). Number of credits: 4. Total number of hours: 120.

III. The course of medical biology is divided into 5 sections:

Section 1. «Cytogenetics».
Section 2. «Classical Genetics».
Section 3. «Molecular Genetics. Mutations».
Section 4. «Medical Genetics. Population Genetics and Evolution».
Section 5. «Human Ecology. Medical Parasitology».

IV. Medical biology as an academic discipline: contains systematized scientific knowledge about the structural and functional organization of living matter and man as its integral component in terms of the needs of modern medicine.

The object of study of medical biology is biological objects and processes that can cause pathological conditions in humans.

The purpose of teaching this academic discipline is:

- to form in higher education students a complete understanding and assimilation of theoretical material on the basic principles and mechanisms of the functioning of the human body as a whole;

- understanding of the processes of a living organism at different levels - from membrane-cellular to systemic, organismal and biogeocenotic;
- acquiring skills in manipulating a living organism and assessing the state of individual systems and the organism as a whole;
- the ability to use acquired skills in clinical practice.

The final program learning outcomes include knowledge of medical biology, which will further form a qualified specialist and will become the main basis for the study of pathophysiological, pathomorphological processes of the body, clinical features and diagnostics of diseases.

The content of the course

Substantial module 1. «Cytogenetics»

Topic 1. Introduction to Medical Biology. Safety rules briefing. General information about the discipline. Credit-rating system of knowledge assessment. Medical biology as a science of the basics of human activity, studying the laws of heredity, variability, individual and evolutionary development and morpho-physiological and social adaptation of the person to environmental conditions in association with its biosocial essence. The current stage of development of general and medical biology. The place of biology in the medical education system. Biology as a science. Light Microscopy. Branches of biology. The essence of life and life forms, the levels of organization of the living. A special place for man in the system of the organic world. Relationship between physicochemical, biological and social phenomena in human life. Methods of biological research. Microscopic method. Optical systems in biological research. Types of microscopes. Light microscope structure. Dry and immersion lenses. Magnification and resolution. Rules of work with a microscope. Setting up illumination in a light microscope. Change of increasing. Rules of drawing. Temporary and permanent preparations for microscopy. Technique for making temporary and permanent preparations.

Topic 2. Cell Structure. Cell theory. Cell structure. Prokaryotes and eukaryotes, plant and animal cells, unicellular and multicellular organisms. Viruses. Water. Salts. Macroelements, microelements. Organic compounds. Cell membranes. Diffusion and osmosis. Active and passive transport. Cytoplasm ans cytoskeleton. Cyclosis. Cytoplasmic organelles. Nucleus and nucleoles. Cell as an open system. Assimilation and dissimilation. ATP synthesis. Methods for studying cell structure and function.

Topic 3. Cell Division. Gametogenesis Prokaryotic cell division. Cell cycle in eukaryotes: interphase and M phase. The biological significance of mitosis. Mitotic activity of tissues. Control of the cell cycle. Growth factors. Cell specialization and differentiation. Special types of cell division: amitosis and schizogony. Meiosis: stages, behavior of chromosomes and chromatids, bivalents. Differences between meiosis and mitosis. The biological significance of meiosis. Gametogenesis: stages, types of cell division. Differences between oogenesis and spermatogenesis. Structure of gametes. Fertilization.

Topic 4. Chromatin, Chromosomes, and Karyotype. Structure of the nucleus in interphase. Chromatin structure. Chromatin types: euchromatin, heterochromatin, and sex chromatin. Types of chromosomes: mitotic (metaphase), polytene, and lampbrush chromosomes. Structure of the mitotic chromosome. Endomitosis, polyteny. Karyotype. Characteristics and classification of human chromosomes. Karyogram, idiogram. Normal and abnormal chromosomes. Cytogenetic method: material for investigation, cytostatic agents, chromosome analysis. Banding techniques. Usage of karyotyping in medicine. Bacterial chromosome.

Substantial module 2. «Classical Genetics»

Topic 5. Mendel's First and Second Laws. Monohybrid Cross Probability of a random event. Multiplication rule and addition rule. Genetics, its subject, objectives, and a brief history. Main terms used in genetics. Classical objects in genetics. Principles of genetic analysis. Mendel's experiments with one trait. Law of dominance and law of segregation. Rules used for writing of schemes of crosses; steps used for solving genetic problems.

Topic 6. Mendel's Third Law. Types of Crosses. Lethal Genes Dihybrid cross: law of independent assortment. Polyhybrid cross. Chromosome theory of heredity. Cytological bases of Mendel’s laws. Statistical character of Mendel’s laws. Deviations from the expected ratios. Conditions when Mendel’s laws are performed. Deviations form Mendel’s laws. Test cross and its practical usage. Dominant and recessive normal and pathologic human traits. Lethal and semilethal genes (sickle-cell anemia, thalassemia, brachydactyly, achondroplasia).

Topic 7. Interaction of Allelic Genes. Multiple Allelism. Blood Groups Allelic genes. Interaction of allelic genes: complete dominance, incomplete dominance, codominance, overdominance. Multiple alleles, causes of their appearance. Human blood groups. ABO, MN, and Rhesus systems. Rhesus incompatibility. **Interaction of Nonallelic Genes.** Nonallelic genes. Complementation; 9:3:3:1 and 9:7 ratios. Epistasis; 13:3 and 12:3:1 ratios in the case of dominant epistasis; 9:3:4 ratio in the case of recessive epistasis. Qualitative and quantitative characteristics. Polygenic traits, multiple genes. Cumulative effect in the case of polygenic inheritance.

Topic 8. Gene Linkage. Chromosome Mapping Morgan’s experiments with linked genes. Linkage groups. Complete and incomplete linkage. Crossing over, its mechanism, cytological evidence, biological importance. Factors that influence crossing over. Genetic maps, purpose and methods of their construction. Eukaryotic gene mapping, map units. Somatic-cell hybridization.

Topic 9. Genetics of Sex. Sex Linkage. Cytoplasmic Inheritance Sex and sex characteristics. Hermaphroditism. Sex determination in mammals, birds, reptilians, insects, worms, fish, and mollusks. Inheritance of sex in human. Bisexual nature of human. Autosomes, sex chromosomes. Homogametic and heterogametic sex. Biological importance of sex chromosomes. Structure of X and Y chromosomes in human. Sex chromatin. Sex linkage: dominant and recessive X linked inheritance, holandric inheritance. Hemizygous genes. Sex-linked diseases: hemophilia, colour blindness, muscular dystrophy, hypophosphatemia (vitamin D-resistant rickets). Cytoplasmic inheritance.

Topic 10. Genotype and Phenotype. Penetrance. Expressivity (example – phenylketonuria). Pleiotropy (examples – sickle-cell anemia, Marfan syndrome). Sex and heredity. Sex-influenced and sex-limited characteristics. Variation, phenotypic and genotypic variation. Age variation. Phenotype as a result of interaction of genotype with environment. Modifications and norm of reaction. Genocopies and phenocopies.

Substantial module 3. «Molecular Genetics. Mutations»

Topic 11. The Structure of Nucleic Acids. DNA Repair DNA as the genetic material. Central dogma of molecular biology. Nucleotide structure. Purines and pyrimidines. Ribose and deoxyribose. Ribonucleotides and deoxyribonucleotides. Energy-rich bond. Primary, secondary, and tertiary structure of DNA. RNA molecules. Phosphodiester and hydrogen bonds. Chargaff's rules. Changes in DNA structure. DNA repair systems. Xeroderma pigmentosum.

Topic 12. DNA Replication. Transcription DNA replication: mechanism, enzymes. Replication in prokaryotes and eukaryotes. Okazaki fragments. Proofreading mechanisms. Transcription of a prokaryotic gene: mechanism. Structure of a prokaryotic gene: the promoter, the structural part, and the terminator. Structure and transcription of eukaryotic genes. Exons and introns. RNA processing: capping, splicing, polyadenylation, cutting, and base modifications. Influence of antibiotics on transcription. Reverse transcription.

Topic 13. Translation. Gene Regulation Primary, secondary, tertiary, and quaternary structure of a protein. Peptide and disulfide bonds. The genetic code and its properties. Translation, its stages (activation of amino acids, initiation, elongation, and termination). Colinearity. Influence of antibiotics on translation. Regulation of gene activity on the chromatin level. Transcriptional level of gene regulation. An operon in prokaryotes; the lac and trp operons. Translational level of gene regulation. Posttranslational modifications of proteins.

Topic 14. Genes and Genomes. Horizontal Gene Transfer Methods of investigation of genes and genomes. DNA sequencing. The structure of prokaryotic and eukaryotic genes. Structural and regulatory genes, genes for tRNAs and rRNAs. Genomes of viruses, bacteria, and eukaryotes. Transposable genetic elements. Human genome. Gene engineering. Biotechnology. Gene therapy. Horizontal gene transfer: bacterial conjugation, bacterial transformation, and transduction; their importance for science and practice. Conjugation in infusorians. Sex factor in bacteria. Construction of genetic maps of prokaryotes.

Topic 15. Mutations. Classification of mutations. Gene and chromosome mutations. Variation caused by mutations. Molecular mechanisms of mutations. Induced mutagenesis. Physical, chemical, and biological mutagens. Genetic monitoring. Genetic danger of environmental pollution.

Practical skills from the course «Medical Biology».
Preparation for the licensing exam «KROK-1».

Thematic plan of practical lessons

№	Theme	Amount of hours
	Unit 1.	
1.	Introduction to Medical Biology Biology as a Science. Light Microscopy	2
2.	Cell Structure	2
3.	Cell Division. Gametogenesis	2
4.	Chromatin, Chromosomes, and Karyotype	2
	Unit 2.	
5.	Mendel's First and Second Laws. Monohybrid Cross	2
6.	Mendel's Third Law. Types of Crosses. Lethal Genes	2
7.	Interaction of Allelic Genes. Multiple Allelism. Blood Groups. Interaction of Nonallelic Genes.	2
8.	Gene Linkage. Chromosome Mapping	2
9.	Genetics of Sex. Sex Linkage. Cytoplasmic Inheritance	2
10.	Genotype and Phenotype	2
	Unit 3.	
11.	The Structure of Nucleic Acids. DNA Repair	2
12.	DNA Replication. Transcription	2
13.	Translation. Gene Regulation	2
14.	Genes and Genomes. Horizontal Gene Transfer	2
15.	Mutations	2

Types of individual work of students

№	Type, content of self-work	Amount of hours
Unit 1.		
1	Organization of substance and energy flows in the cell. Stages of energy exchange. Energy supply of the cell, ATP. Distribution of energy.	2
2	Life of cells outside the body. Cell cloning. Use of cell clones in medicine.	2
3	Methods of studying the structure and functioning of the cell.	2
4	Cell differentiation and proliferation; concepts of apoptosis and necrosis; tumor growth.	2
5	Preparation of permanent preparations, fixation, staining. Study and description of micropreparations. Creating visibility and a bank of micropreparations.	3
	Total	**11**
Unit 2.		
6	Back crossing; genomic imprinting; uniparental disomy; epigenetics	3
7	Immunogenetics: subject, tasks; tissue and species specificity of proteins, their antigenic properties.	3
8	Genetic maps. Methods of human chromosome mapping. Current status of human genome research.	3
9	The concept of biofields, biological rhythms and their medical significance.	3
10	Congenital malformations. Critical periods of development. Female and male pseudohermaphroditism.	3
11	The law of homologous series of hereditary variability, its practical significance; anticipation; intelligence.	2
	Total	**17**
Unit 3.		
12	Genetic engineering. Biotechnology. The concept of gene therapy. Genomics, proteomics.	**4**
13	Genetic danger of environmental pollution. The concept of antimutagens and commutagens.	**4**
14	Genetic load and its biological essence. Genetic structure of populations and burden of hereditary pathology.	**3**
	Total	**11**

Substantial module 1. «Cytogenetics».

Topic 1. Introduction to Medical Biology.

Optical microscopy

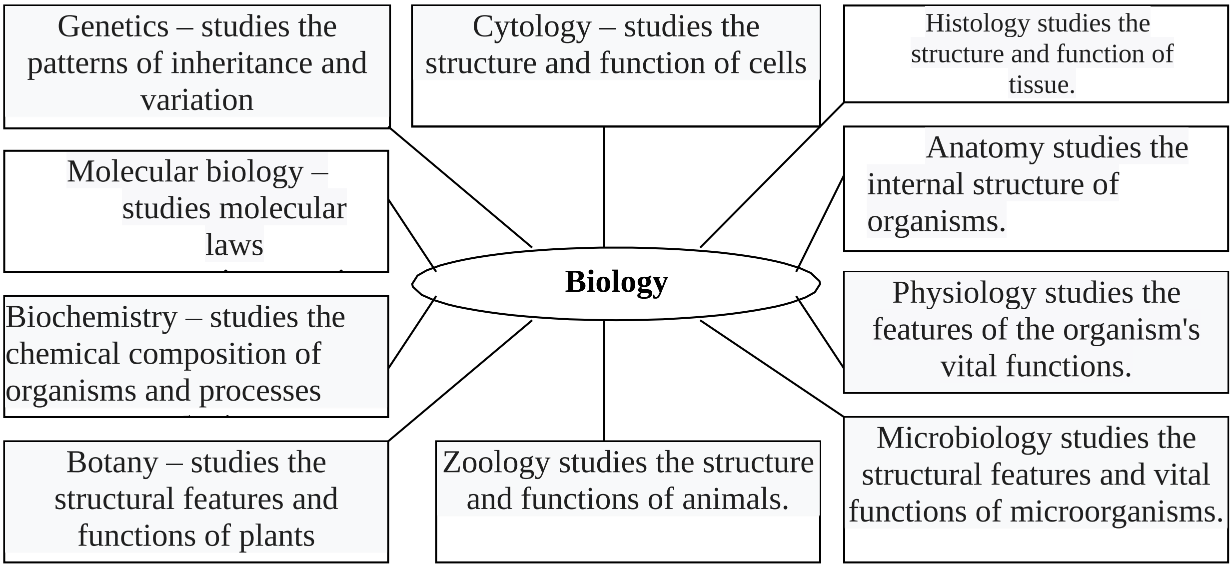
Biology – (Greek: Bios – life + Logos – science) – a complex of sciences about living nature. The subject of study of biology is all manifestations of life: the structure and functions of living beings and their natural groups, their distribution, origin and development, their relationships with each other and with inanimate nature.

The task of biology is to study all biological laws, to reveal the essence of life and its manifestations in order to know and manage them.

The term «biology» was proposed by the German botanist G.R. Treviranus and the French naturalist J. B. Lamarck in 1802.

Modern biology is a complex, highly differentiated complex of fundamental and applied research on living nature. Relying on the latest achievements of physics, chemistry, and technology, it has been possible to solve many medical and biological problems, penetrate the depths of the cell, and obtain fundamentally new information about the processes occurring in the cell under normal and pathological conditions.

Medical biology is a set of biological sciences about humans. These sciences study the macro- and microstructure of the human body, the basics of the functioning of organs and systems, the causes of their disorders and the occurrence of diseases, methods of diagnosing diseases, as well as their prevention. Medical biology studies the laws of heredity and variability in humans, the causes of hereditary diseases. It also pays attention to the impact of the environment on humans, including parasitic diseases.



Genetics – studies the patterns of inheritance and variation

Cytology – studies the structure and function of cells

Histology studies the structure and function of tissue.

Molecular biology – studies molecular laws

Anatomy studies the internal structure of organisms.

Biochemistry – studies the chemical composition of organisms and processes

Physiology studies the features of the organism's vital functions.

Botany – studies the structural features and functions of plants

Zoology studies the structure and functions of animals.

Microbiology studies the structural features and vital functions of microorganisms.

Fig. 1. System of biological sciences.

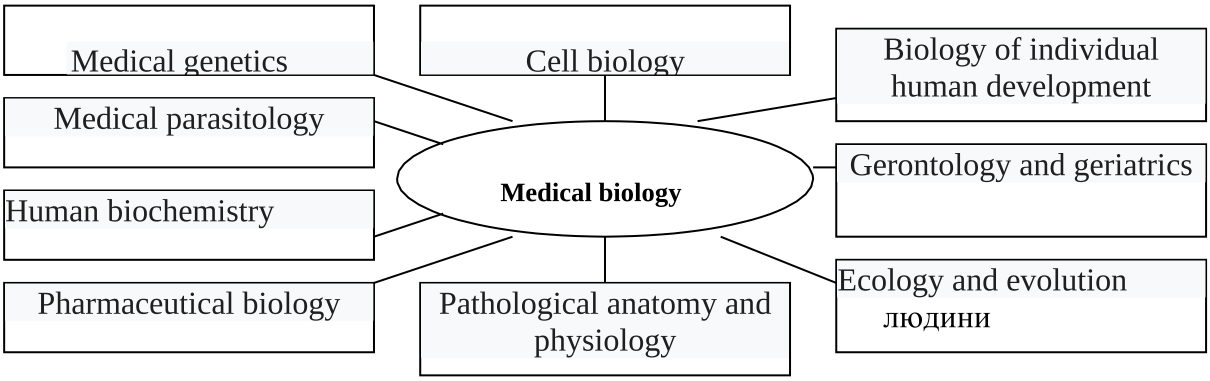


Fig. 2. Main branches of medical biology.

The concept of life encompasses the totality of all living organisms on Earth and the conditions of their existence. The essence of life is that living organisms leave behind offspring. Hereditary information is passed on from generation to generation. Life is a special qualitative, highest form of matter, which, leaving offspring, is capable of self-reproduction.

Based on the latest scientific research in modern biological science, scientists have derived a new definition of life: «Life is open, self-regulating and self-reproducing systems of living organisms, which are built from complex biological polymers - proteins and nucleic acids.» Nucleic acids and proteins are considered the basis of all living things, since they, functioning in the cell, form complex compounds that are part of the structure of all living organisms. The best way to define life is to list the properties of living organisms.

Properties of living things:

1. Self-renewal, which is associated with the constant metabolism of substances and energy, and is based on the ability to store and use biological information in the form of unique information molecules: proteins and nucleic acids.
2. Self-reproduction, which ensures continuity between generations of biological systems.
3. Self-regulation, which is based on the ability of organisms to maintain relative constancy of the chemical composition and the course of physiological processes - homeostasis.
4. The exchange of matter, energy and information is a special way of interaction of living organisms with the environment. A living organism is an open system.
5. Growth and development. Growth is accompanied by an increase in the mass of an organ of the organism, or an increase in the number of individuals in a population, etc. Development - irreversible natural changes in a biological system. The development of the components of the organism - ontogenesis (individual development), the development of living nature with the formation of new species by the progressive complication of life forms - phylogenesis (historical development).
6. The ability to resist the increase in entropy.
7. Irritability, which involves the ability of organisms to respond to certain environmental influences.

8. Heredity.
9. Variability
10. Discreteness and integrity.

Levels of organization of living matter:

The organic world on Earth is a complex biocenological system of life forms, consisting of separate complex formations, biotic groups of different levels. Each level constitutes a continuous in development, internally opposite biotic system. Level - the degree of differentiation of a biological object.

The allocation of levels of organization of biological systems aims to reveal the essence of living nature in its movement, in the historical interaction of elements, in the knowledge of the laws of development. Most often, five main structural levels of life are distinguished: molecular, cellular, organismal, population-species, biosphere-biogeocenotic.

Molecular level of life organization: this is the level of functioning of biological macromolecules - biopolymers: nucleic acids, proteins, polysaccharides, lipids, steroids, which are in a living cell.

1. Elementary structures: molecules of inorganic and organic compounds, molecular complexes (membranes, etc.), codes of hereditary information (sequence of nucleotide triplets in the DNA molecule).
2. Basic processes: combining molecules into complexes, carrying out physicochemical reactions, reproducing codes of hereditary information according to the principle of matrix synthesis (convariant DNA replication)
3. Sciences conducting research at this level: biochemistry, biophysics, molecular biology, molecular genetics.

Cellular level of organization of life: this is the level of unicellular organisms and cells that are part of multicellular organisms.

1. Elementary structures: cells, complexes of molecules of chemical compounds and cell organelles.
2. Basic processes: cell division, regulation of chemical reactions, biosynthesis, photosynthesis.
3. Sciences conducting research at this level: genetic engineering, cytogenetics, cytology, embryology.

Organismal level of life organization: this is the level of unicellular and multicellular organisms of plants, animals, fungi, bacteria. 1. Elementary structures: organisms and organ systems of which they consist. 2. Basic processes: metabolism, irritability, reproduction, ontogenesis, neurohumoral regulation of vital processes, homeostasis. 3. Sciences conducting research at this level: anatomy, developmental biology, genetics, hygiene, morphology, physiology.

Population-species level of life organization: represented by a large variety of species and their populations.

1. Elementary structures: populations.
2. Basic processes: interaction between individuals and populations, speciation, emergence of adaptations to changing environmental conditions.

3. Sciences conducting research at this level: population genetics, evolution, ecology.
Biosphere-biogeocenotic level of life organization: represented by a variety of natural and cultural biogeocenoses and a global form of organization of biosystems - the biosphere.
1. Elementary structures: biogeocenoses, environmental factors, anthropogenic impact.
2. Basic processes: the circulation of substances and the flow of energy, the dynamic equilibrium between living organisms and the environment (homeostasis), the provision of living organisms with living conditions and resources (food, housing), the active biogeochemical participation of man in all processes of the biosphere, his economic and ethnocultural activities. 3. Sciences conducting research at this level: biogeography, biogeocenology, ecology.

Basic methods of biological research:
When performing biological research, both well-known and specific methods are used:
- observation method;
- biological experiment method;
- historical method;
- descriptive method;
- microscopic method;
- X-ray structural analysis;
- step centrifugation;
- electron microscopy;
- scanning electron microscopy;
- electron microscopic histochemistry;
- microspectral analysis;
- statistical methods.

Optical systems in biological research are used during practical classes in medical biology, genetics and parasitology. Various devices and tools are used, primarily a microscope (from the Greek μιχρός - small and σχοπεω - I observe, I examine). In ultraviolet microscopy, observations are made using ultraviolet rays.
Phase-contrast microscopes make it possible to study microscopic objects without prior special staining based on the difference in the refractive indices of light. For the in-depth study of microscopic organisms, electron microscopes, which magnify the object 1,000,000 times or more, are increasingly used. The principle of operation of this microscope is that the image of an object is formed not by light rays, but by a flow of electrons. As a result, with the help of an electron microscope, it is possible to examine ultramicroscopic structures of cells, large molecules, and viruses. To study biological objects, light microscopes of various systems are most often used, in which the object is illuminated by a normal (undissected) light beam. Each light microscope has three main parts: **mechanical, illuminating, and optical.**

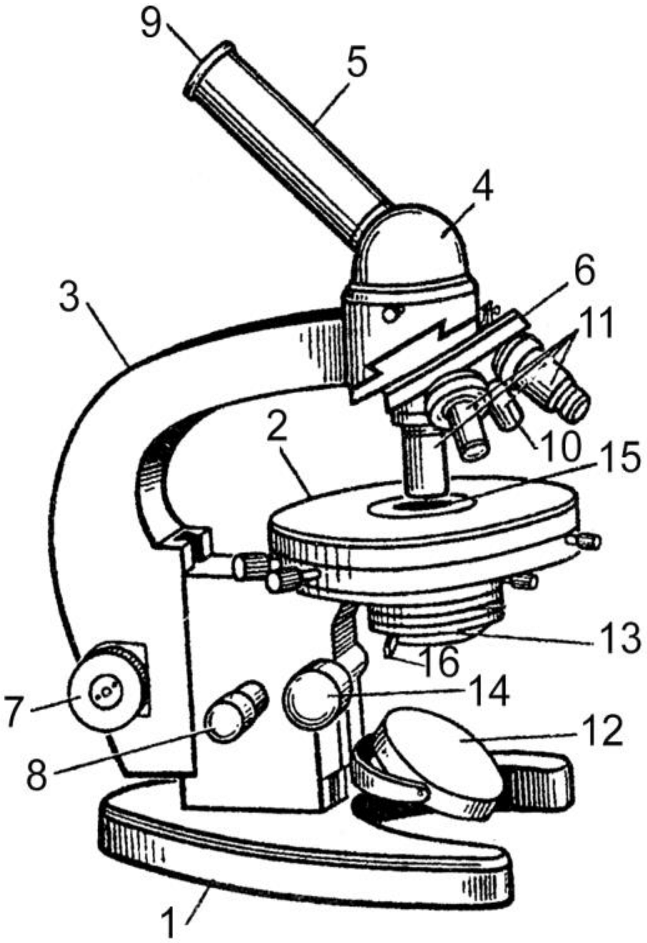
The mechanical part of the microscope consists of a tripod, a tube, a turret, a stage, a macrometric screw (or rack) and a micrometric screw. The tripod consists of a massive leg - the base on which the entire microscope rests, and a tube holder. A tube (spectroscope) is attached to the tube holder, which moves up and down using macrometric and micrometric screws. A stage (round or rectangular) is attached to the tripod. In the center of the stage there is a hole, over which a slide with an object is placed, which is fixed with two clamps or terminals. A revolver - a plate with three or four objectives - is movably attached to the tube from below. By turning the revolver, an objective of a certain magnification can be placed under the lower hole of the tube.

The illuminating part of the microscope consists of a mirror, a condenser, and an iris diaphragm. The mirror is movably mounted under the stage. It is flat on one side and curved on the other; the flat and curved surfaces are used depending on the light source and the nature of the object.

The condenser, located between the stage and the mirror, consists of several lenses. The iris diaphragm is fixed on the lower surface of the condenser. The condenser lenses concentrate the light rays and direct them through the opening of the stage onto the object under study and into the objective. The iris diaphragm regulates the width of the light beam, increasing or decreasing the illumination of the object.

The optical part of the microscope consists of systems of eyepiece lenses and objectives. The eyepiece is inserted into the tube from above, on the eyepiece frame there are numbers that show its magnification (for example, x7, x10, x15). The objective is a system of lenses inserted into the tube - the sleeve. The objectives are fixed in a revolver. They can provide low magnification (numbers on the frame x7, x8, x10) and high (numbers on the frame x40, x90).

To know the total magnification of a microscope, you need to multiply the numbers of the eyepiece and objective. In addition to low and high magnification objectives, the microscope revolver also has a so-called immersion (Latin immersio, from immergo - I immerse) objective, which is denoted by the letters "OI" (immersion objective) and is designed for examining objects and objects at high magnification when a liquid (cedar oil, petroleum jelly, an aqueous solution of glycerin) is introduced between the object and the microscope objective to increase the illumination of the image.



I. Mechanical part
1 – stand, 2 – object stage with a hole,
3 – tube holder, 4 – tube holder head, 5 – tube, 6 – revolver with lens sockets,
7-macrometric coarse adjustment screw,
8-micrometric fine adjustment screw (only for work at high magnification, rotation no more than 360º, preferably 180º).
Observation system:
9– eyepiece, 10 – low magnification objective (m/z), 11 – high magnification objective (v/z).
Illum ination system:
12– movably fixed mirror with flat and concave surfaces (flat surface is used in bright lighting, concave – in low lighting),
13– condenser, which adjusts the image contrast using a screw (14),
15– iris diaphragm, located under the stage (2), adjusts the clarity and brightness of the image using a knob (16).

Fig. 3. Structure of a light microscope.

Topic 2. Structure of a cell.

Cellular life forms.

The bulk of living beings are organisms that have a cellular structure. In the process of evolution of the organic world, the cell acquired the properties of an elementary system in which the manifestation of all the laws that characterize life is possible.

Cellular organisms are divided into two categories: those that do not have a typical nucleus - prokaryotes (Procaryota) and those that have a nucleus - nuclear, or eukaryotes (Eucaryota). Prokaryotes include bacteria and blue-green algae, eukaryotes include most plants, fungi and animals. The difference between unicellular prokaryotes and eukaryotes is more significant than between unicellular eukaryotes and higher plants and animals.

Prokaryotes are prenuclear organisms that do not have a typical nucleus surrounded by a nuclear envelope. The genetic material is represented by a genophore - a DNA strand that forms a ring. This strand has not acquired the complex structure that is characteristic of eukaryotic chromosomes, it is not associated with histone proteins. Prokaryotic cells lack mitochondria, centrioles, and plastids, but a membrane system may be developed.

Bacteria and blue-green algae are grouped into the subkingdom Protozoa. The cell of typical protozoa is covered with a cellulose membrane. Protozoa play an important role in the cycle of substances in nature:
blue-green algae – as synthetics of organic matter, bacteria – as mineralizers of it. Many bacteria have medical and veterinary importance as pathogens.

Eukaryotes – nuclear organisms that have a nucleus surrounded by a nuclear membrane. Genetic material is concentrated mainly in chromosomes, which consist of DNA strands and protein molecules. These cells divide mitotically. There are centrioles, mitochondria, plastids. Among eukaryotes there are both unicellular and multicellular organisms.

A living cell is an ordered system, for which it is characteristic to receive from the outside, transform and partially secrete various chemical compounds. In general, this ensures the fundamental property of life - the historical continuity of biological processes.
The transmission of hereditary information is carried out due to the ability of the cell to divide and is characteristic of all living beings.

What object is considered alive? According to modern ideas, the following features are characteristic of a living organism:

1) reproduction - the ability to reproduce, self-reproduce, multiply;
2) use and transformation of energy (conversion of one type of energy to another);
3) metabolism (metabolism);
4) sensitivity, i.e. perception of external actions (irritations) and irritability - the ability to respond to irritation by changing its state (contraction of organs and individual structures) or by specific activity (in the form of various movements, for example, taxis and tropisms);
5) variability - the ability to change its characteristics.

Each property separately from each other can be characteristic of an inanimate object (for example, if you hit a stone, it will break - characteristic sensitivity). But only together these features characterize the object as living, and the entire set of these features appears already at the cellular level. The smallest unit of living is the cell.

Cell theory

The structure of the cell is studied by the science of cytology. The bodies of all living organisms are composed of cells, which were first observed in 1665 by the English physicist Robert Hooke. Significant contributions to the study of the cell were made by Malpighi, Leeuwenhoek, and Brown.

Based on the works of botanist M. Schleiden, German zoologist T. Schwann in 1838–1839 formulated the hypothesis that the cell is the structural and functional basis of life, that plant and animal cells are similar to each other (homologous), develop according to the same principle - they originate in the depths of cells from a certain «granular mass» (cytoblastema theory), and tissue growth is due to the formation of new cells. However, Schwann believed that a multicellular organism is only the sum of individual cells. Certain shortcomings of these views were in the works of R. Virchow.

In 1858, the German pathologist R. Virchow completed the creation of the cell theory. He was not a supporter of the idea of spontaneous generation of life and formulated the conclusion that cells are formed only as a result of the division of previous (mother) cells – «each cell from a cell».

Schwann's views on the functioning of a multicellular organism were expanded by Virchow and became known as the "cell state" theory, according to which the organism is the sum of cells arranged in a manner similar to a state.

Despite the fact that cells are closely connected to each other in tissues and are dependent, they are quite independent, acting on their own, although they receive stimuli from other (master) cells.

Such views of the organism were erroneous, because it was not perceived as a single whole, in which there is no main organ or main cells. In reality, cells are united into tissues and organs, into functional systems, interconnected with each other within the organ (tissue), and at the same time their activity is regulated by intercellular, humoral and nervous factors. Schleiden, Schwann, and Wichrow are the founders of the cell theory, which was later developed by other researchers.

The main provisions of modern cell theory:

1. A cell is the basic structural, functional, and genetic unit of a living thing. Life does not exist outside a cell. A cell is an open biological system that exchanges substances and energy with the environment.
2. Cells of different organisms are homologous (similar in structure and origin).
3. A cell is formed from a previous cell (mother cell) as a result of division. Spontaneous generation of a cell from non-living matter is impossible.
4. Cell – a structural and functional unit of a multicellular organism that possesses new properties and characteristics not characteristic of cells. An organism is a holistic system of tissues and organs interconnected by complex forms of regulation.

The chemical composition of living organisms is relatively similar. All chemical elements that make up cells are divided into four groups:

- *macroelements* (content of which is from 1% and above): oxygen, carbon, nitrogen, hydrogen, calcium and phosphorus;
- *oligoelements* (content of 0.1-1%): potassium, sodium, chlorine, sulfur, magnesium and iron;
- *microelements* (content of less than 0.01%): zinc, manganese, cobalt, fluorine, bromine, iodine;
- *ultramicroelements* (concentration from 10-4 to 10-6%) - include the remaining elements: boron, lithium, aluminum, silicon, cadmium, selenium, etc.

The similarity of the elemental composition of living and inanimate nature indicates their common origin.

Among the inorganic compounds of living organisms, **water** plays a special role. It is the main medium where all metabolic processes occur. Its content in most living organisms is 60 - 80%, and in some (jellyfish) - up to 98%. Water has unique chemical and physical properties.

It has relatively high boiling, melting, and evaporation temperatures, which is due to the interaction between water molecules. The water molecule (H_2O) is polar. In it, two hydrogen atoms are combined with an oxygen atom by a strong covalent bond, which arises due to the formation of a shared pair of electrons, one from each atom.

A water molecule is electrically neutral, but its poles have positive and negative charges (polarity). That is why water molecules can be attracted to each other due to the forces of electrostatic interaction between the partially negative charge on the oxygen atom of one molecule and the positive charge on the hydrogen atom of the other. This type of bond is called hydrogen, it is 15-20 times weaker than covalent.

Water is a much better solvent than most other liquids. Therefore, all substances are divided into those that are well soluble in water - hydrophilic (many crystalline salts, acids, etc.), insoluble - hydrophobic (lipids, some proteins, etc.) and amphiphilic (combine the properties of both classes).

Most chemical reactions occur only in aqueous solutions. Water determines the physical properties of the cell: volume, intracellular pressure. The regulation of the thermal regime of organisms is associated with it. It has a high heat capacity, that is, the ability to absorb heat with minor changes in its temperature. It is thanks to this that water provides thermoregulation in the cell.

Substances that have skeletons of covalently bonded carbon atoms are called *organic compounds*. Almost all the dry matter of the cell is made up of proteins, carbohydrates, lipids and nucleic acids. These are relatively large structures with high molecular weight - macromolecules (biopolymers).

Among cellular macromolecules, proteins play the leading role in terms of functional significance and quantity. In an animal cell, they make up 40-50%. *Proteins* are high-molecular polymers, the monomers of which are amino acids. The great diversity of proteins is provided by combinations of only 20 amino acids, which are called *basic*.

All amino acids that make up proteins have a common group of atoms consisting of an *amino group* (- NH_2), which is characterized by alkaline properties, and a *carboxyl group* (- COOH) with acidic properties, which are bonded to the same carbon atom.

And they differ from each other in side chains (*radicals*, or R-groups), which in different amino acids are different in chemical structure, electrical charge, and solubility in water. Amino acids are classified according to the possibility of their synthesis in organisms - *essential and non-essential*.

The first are synthesized in the human or animal body, and the second enter them only with food products (they are synthesized by plants, fungi, bacteria). Protein molecules are formed by peptide bonds between the amino group of one amino acid and the carboxyl group of another. Amino acids connected in the process of translation form a polypeptide. The composition of simple proteins includes only amino acids. Complex proteins include lipids (lipoproteins), carbohydrates (glycoproteins).

Proteins differ not only in the number of monomers and the composition of amino acids, but also in the sequence of their arrangement in polypeptide chains - the *primary structure.*

The variety of variants of the primary structures of proteins is very large: even three peptides consisting of three amino acids can have 6 variants. When arranged in space, amino acids are grouped in the middle of the polypeptide molecule, and the occurrence of local hydrogen bonds between peptide groups leads to the formation of α-helices - *the secondary structure.*

Fibrillar proteins have a regular secondary structure - long, elongated, poorly soluble in water (collagen, actin, myosin, etc.). The spatial arrangement of a polypeptide in the form of a globule is called *tertiary structure. Globular proteins* have the appearance of a sphere and are well soluble in water (hemoglobin, most enzymes). If a protein consists of several polypeptides, their mutual arrangement in space is called *quaternary structure.*

The main functions of proteins: 1) structural - all elements of both cells and the organism as a whole are formed from proteins; 2) protective - proteins create protective covers of the organism, form antibodies; 3) regulatory - protein hormones participate in the regulation of many metabolic processes; 4) catalytic - enzyme proteins accelerate chemical reactions in the body and ensure all cell functions; 5) receptor - receptor proteins perceive signals, convert and transmit them to the appropriate area of the cell or organism; 6) transport function - proteins are able to bind and transport inorganic ions and specific organic substances; 7) contractile, or motor - provides the ability of cells, tissues or the body to change shape, move; 8) energetic - when proteins are broken down in the cell, energy is released.

Carbohydrates are organic compounds, the general structure of which corresponds to the formula $Cx(H_2O)y$. In animal cells, carbohydrates are present in small quantities (1-5%), in plant cells they are much more (70-90%). Carbohydrates are divided into three main classes: monosaccharides, oligosaccharides, polysaccharides. Monosaccharides (simple sugars) have the general formula CnH2nOn. In nature, the most common hexoses are fructose and glucose. Of the pentoses, ribose and deoxyribose are better known, which are part of RNA and DNA.

Oligosaccharides are polymeric carbohydrates in which monosaccharide units are connected by a covalent (glycosidic) bond. Among oligosaccharides, the most common are disaccharides: sucrose, lactose, maltose, etc. Most carbohydrates are polysaccharides - biomolecules with a high degree of polymerization (starch, cellulose, glycogen, etc.).

In living organisms, oligosaccharides are found in complexes with proteins (glycoproteins) and lipids (glycolipids).

In living organisms, carbohydrates perform two main functions - energy and structural.

Polysaccharides and oligosaccharides are broken down to monosaccharides with subsequent oxidation to CO_2 and H_2O. With the complete decomposition of one gram of these substances, 17.6 kJ of energy is released. The structural function of carbohydrates is that they are part of the supporting elements.

Lipids are water-insoluble (hydrophobic) organic compounds that can be extracted from the cell using nonpolar solvents. Almost all lipids are esters of fatty acids and alcohol. Fats are the main substance of fatty inclusions in the cell. Their content is from 5% to 15% of the dry mass, and in adipose tissue - up to 90%.

The main functions of lipids: 1) energy - when 1 g of fats is completely broken down into CO_2 and H_2O, 38.9 kJ of energy is released; 2) structural - lipids form the basis of biological membranes and are part of nerve fibers; 3) protective - protecting organs from mechanical damage; 4) thermal insulation - fats accumulate in subcutaneous adipose tissue.

Abbreviations of amino acids, their replaceability (r) or irreplaceability (i) for humans.

N n/n	Amino acid name	Abbreviation
1	Alanine (r)	Ala
2	Arginine (r), (essential for children)	Arg
3	Asparagine (r)	Asn
4	Aspartic acid (r)	Asp
5	Valine (i)	Val
6	Histidine (r), (essential for children)	His
7	Glycine (r)	Gly
8	Glutamine (r)	Gln
9	Glutamic acid (r)	Glu
10	Isoleucine (i)	Ile
11	Leucine (i)	Ley
12	Lysine (i)	Liz
13	Methionine (i)	Met
14	Proline (r)	Pro
15	Serine (r)	Ser
16	Tyrosine (r)	Tyr
17	Threonine (i)	Tre
18	Tryptophan (i)	Try
19	Phenylalanine (i)	Fen
20	Cysteine (r)	Cys

Content of chemical compounds in the cell (in % of fresh weight)

Substances			
Inorganic		Organic	
Water	70–80 %	Proteins	10–20 %
Other inorganic substances: cations	1,0–1,5 %	Fats	1–5 %
		Nucleic acids (DNA, RNA)	1–2 %
		Carbohydrates	0,2–2,0 %

– K^+, Na^+, Ca^{++}, Mg^{++}, anions – Cl^-, HCO_3^-, $H_2PO_4^-$		Low molecular weight organic substances	0,1–0,5 %

CELL SURFACE APPARATUS

The main components of the cell surface apparatus are the biomembrane and the glycocalyx. Cell membranes, which are the most important component of a living cell, are built according to a single principle. According to the fluid mosaic model proposed in 1972 by D. Nicholson and S. Singer, the membranes include a bimolecular layer of lipids, to which protein molecules are associated.

Lipids are water-insoluble substances whose molecules are divided into two parts: a hydrophilic «head» and a hydrophobic «tail». In a biomembrane, lipid molecules of both layers are turned towards each other with their hydrophobic tails, and their hydrophilic heads remain outside, forming hydrophilic surfaces. Membranes are composed of three groups of lipids: phospholipids, glycolipids and cholesterol.

Membrane proteins can be divided into two groups: peripheral (those that lie on one of the membrane surfaces) and integral (those that are to some extent embedded in the membrane). The position of embedded proteins in the membrane is stabilized by peripheral proteins.

Functions of biological membranes

1. Limiting. The membrane limits the cytoplasm from the intercellular space, and most of the cell organelles from the cytoplasm, protects the cell from the penetration of unnecessary substances, maintains its homeostasis.
2. Formation of a hydrophobic zone. The hydrophobic zone is the main barrier that protects the cell from the penetration of most substances. A number of the most important metabolic processes occur only in a non-polar environment.
3. Barrier. Not all substances that are in the cell and outside it pass through the membrane, that is, the membrane is semipermeable.
4. Transport. This transfer of substances through the membrane, which ensures the movement of certain molecules and ions, creates a transmembrane difference in electrical potential.
5. Cell compartmentalization. The system of internal membranes divides the contents of the cell into compartments. They contain certain substances necessary for performing specific functions. All membrane organelles are intracellular compartments.
6. Formation of organelles. Membrane organelles ensure the simultaneous occurrence of many diverse metabolic processes.
7. Receptor. The presence of various receptors in the membrane that perceive chemical signals in the form of hormones, mediators and other biologically active substances determines the ability of the cell to change metabolic activity.
8. Formation of intercellular contacts. Biomembranes can form the following types of contacts:

- *simple contact* (approach of cell membranes to a distance of 15-20 nm);

- *tight closing contact*, impermeable to macromolecules and ions (fusion of sections of the plasma membrane of neighboring cells);
- *desmosomes* (sections of sealing between cells that form mechanical bonds);
- *gap contact*;
- *synaptic contact* (neurons).

The above types of contacts are important for cell interaction and tissue formation.

9. Energy-transforming. Creation of a charge gradient on the inner membrane of the mitochondria. Use of this potential for the formation of ATP. Integral proteins provide information transmission in two directions: through the membrane towards the cell and back. Integral proteins are of two types: carriers and channel-forming. The latter line the channels filled with water.

Through it, a number of dissolved inorganic substances pass from one side of the membrane to the other. Most membrane proteins are enzymes. Semi-integral proteins form a biochemical "conveyor" on the membrane, on which the transformation of substances is carried out in a certain sequence.

On the outer surface of the plasma membrane in an animal cell, protein and lipid molecules are linked to carbohydrate chains and form a glycocalyx. Carbohydrate chains act as receptors. Thanks to them, intercellular recognition is carried out, and the cell acquires the ability to respond specifically to external influences.

Under the biomembrane on the cytoplasmic side there is a cortical layer and intracellular fibrillar structures that provide its mechanical stability. In plant cells, outside the membrane is a dense structure - the cell membrane, or cell wall, consisting of polysaccharides (mainly cellulose).

It performs a protective function, forms the outer skeleton of the cell, gives it shape, and participates in the formation of osmotic properties.

TRANSPORT OF SUBSTANCES THROUGH THE BIOMEMBRANE

One of the most important properties of a biomembrane is its ability to pass various substances into or out of the cell. This is necessary to maintain the constancy of its composition (homeostasis). The mechanism of transport of substances through the membrane depends on the size of the particles being transported. Small molecules and ions pass through membranes by *passive and active* transport.

The transfer of macromolecules and large particles is carried out by the formation of membrane-bound vesicles and is called *endocytosis or exocytosis*. Passive transport occurs without the expenditure of ATP energy along a concentration gradient. The main types of passive transport are *diffusion and osmosis.*

Diffusion - the transport of molecules and ions across a membrane from an area of high concentration to an area of lower concentration, i.e. substances cross the membrane along a concentration gradient. Diffusion can be simple and facilitated. For example, if substances are well soluble in fats, they enter the cell by *simple diffusion.* Oxygen, used by cells in respiration, and carbon dioxide, produced in this process, diffuse rapidly across membranes. Substances that are insoluble in fats and do not pass through membrane pores are transported through ion channels and by carrier proteins. These are complex globular proteins that have a high affinity for certain molecules.

Diffusion is the transport of glucose, amino acids, and some ions. This is *facilitated diffusion*. For example, glucose enters red blood cells by facilitated diffusion.

Osmosis is the transport of a solvent across a semipermeable membrane. In living systems, such a solvent is water, which is able to pass through special water channels formed by aquaporin proteins and transport molecules and ions of substances dissolved in it.

Active transport is the transport of molecules across the membrane using special proteins against the concentration gradient with the expenditure of ATP energy. These proteins are enzymes and are called ATPases or *ion pumps*.

Sodium - potassium ATPase (Na+, K+-ATPase or Na+, K+-pump). The Na+, K+-pump pumps 3 Na+ ions out of the cell in exchange for 2 K+ ions. The enzyme regulates the concentration of Na+ and K+ inside the cell, H_2O flows, maintains a constant cell volume, and provides Na+-coupled transport of many molecules that participate in the creation of membrane potential and action potentials.

Calcium ATPase (Ca2+-ATPase or Ca2+-pump). The Ca2+-pump pumps calcium ions out of the cell, regulating the concentration of Ca2+ in the cytoplasm, which is necessary for the process of muscle contraction. There are also receptor proteins in the membranes. They specifically bind physiologically active substances, in particular hormones and neurotransmitters, ensuring a certain response of the cells. Macromolecules and larger particles enter the cell through the membrane by endocytosis and are released from it by exocytosis.

In endocytosis, the plasma membrane forms indentations or protrusions that then unlace and become intracellular vesicles containing the material captured by the cell. Thus, the absorbed substances enter the cell in a membrane package.

These processes occur with the expenditure of ATP energy. Types of endocytosis are pinocytosis, phagocytosis and receptor-mediated endocytosis.

Pinocytosis is the process of absorbing fluid and substances dissolved in it with the formation of specific membrane vesicles.

Phagocytosis is the process of capturing and absorbing large particles (sometimes whole cells and their parts) by a cell.

Special cells that perform phagocytosis are called phagocytes. The result is the formation of large vesicles called *phagosomes*.

Receptor-mediated endocytosis is characterized by the uptake of certain macromolecules from the extracellular fluid with the participation of membrane receptors. The receptors bind the molecule and initiate a response.

They are represented by transmembrane proteins that have a special site for binding physiologically active molecules: hormones and neurotransmitters. Many receptor proteins, in response to the binding of certain molecules, change the transport properties of membranes. As a result, membrane polarity can change, a nerve impulse can be generated, or metabolism can change.

The plasma membrane also participates in the removal of substances from the cell, which occurs during the process of *exocytosis*. In this way, hormones, proteins, fat droplets, and other products of the cell's vital activity are removed from the cell. Some proteins secreted by the cell are packaged into transport vesicles, which are continuously transported to the plasma membrane, fuse with it, releasing their contents into the extracellular space. This process is characteristic of all eukaryotic cells.

CYTOPLASM

The cytoplasm makes up the bulk of the cell. It is all of its internal contents, except for the nucleus. It contains 75-85% water, 10-20% proteins, and many other substances, but in smaller quantities. When examining a cell with a light microscope, the cytoplasm appears as a homogeneous, colorless, transparent, viscous liquid. However, the electron microscope has allowed us to see the complex multicomponent, multifunctional, highly ordered structure of the cytoplasm. The cytoplasm consists of cytosol (cytoplasmic matrix), intracellular organelles, and inclusions.

Cytosol. The cytosol makes up a significant part of the cytoplasm (~55% of the total cell volume) excluding organelles. The cytosol is a structured colloid consisting of a complex mixture of organic macromolecules dissolved in water - proteins, fats, carbohydrates, small organic molecules (amino acids, monosaccharides, nucleotides, fatty acids, etc.), as well as inorganic substances. It contains up to 10,000 different types of proteins, mostly enzymes.

Physical properties of the cytosol:

1. A colloid can transition from a more liquid state - a sol, to a more solid state - a gel.
2. The constant Brownian motion of molecules and the constant collision of molecules initiates metabolic reactions.
3. The transition of sections of the cytoplasm from the gel state to the sol state and vice versa causes cyclosis - the movement of the cytoplasm.
4. With the help of chemical buffers, the pH is maintained constant.
5. A certain size and shape of the cell is maintained.

Chemical composition and properties of the cytosol:

1. Inorganic substances: water, salts, gases. Properties of water:
    - a solvent for all substances of the cell;
    - many substances are ionized by water;
    - a medium for reactions and a participant in many of them;
    - water promotes the movement of substances in the cell, from the cell and into the cell;
    - water is a good thermoregulator.
2. Organic substances: proteins, carbohydrates, lipids, nucleotides.

- organic substances provide the specificity of the structure and functions of cells;
- reserve substances - glycogen, lipids;

Biological properties of the cytosol:

1. Ensuring metabolism;
2. Ability to move;
3. Ensuring cell growth and differentiation;
4. Maintaining cell homeostasis;

5. Contains organelles, helps them perform specific functions.

ORGANELLES

Organelles are permanent components of a cell that have a specific structure and perform specific functions. They can be divided into two groups: membranous and non-membranous. Membranous organelles have one or two membranes.

Single-membrane organelles include the endoplasmic reticulum (ER), the Golgi complex (GC), lysosomes, peroxisomes, etc. ***Double-membrane organelles*** include mitochondria and plastids, and ***non-membrane organelles*** include ribosomes, the cellular center inherent in animal cells.

SINGLE-MEMBRANE ORGANELLES

The endoplasmic reticulum (ER) is found in all eukaryotic cells, but is absent in prokaryotic cells, the egg, and mature erythrocytes. The ER is formed by a network of membranous tubules, cisternae, and oval vesicles. The ER is structurally associated with the nuclear envelope. There are two types of ER: smooth and rough, although they are structurally related.

Granular EPS carries ribosomes on its surface, which are not present on the surface of smooth EPS.

Functions of granular EPS:

1. Participation in the process of protein synthesis;
2. Accumulation and modification of synthesized proteins;
3. Packaging of proteins into vesicles, which are synthesized and transported to the site of use;
4. Formation of the membrane system of smooth EPS.

Functions of the smooth EPS:

1. Synthesis of phospholipids and carbohydrates;
2. Accumulation and modification of synthesized substances;
3. Packaging them into vesicles and transporting them to the place of use;
4. Participation in detoxification processes by biochemical enzymatic conversion of toxins into non-toxic substances that are more convenient for excretion.

The Golgi complex (GC), or Golgi apparatus (GA), is an organelle discovered in a cell by the Italian researcher Camillo Golgi in 1898.

It is formed by a complex of dozens of compacted disc-shaped membrane cisterns, sacs, and tubules. Secretory cells have this organelle highly developed. The interior of the GC is filled with a matrix containing special enzymes. The CG has two zones: the formation zone, where material from the EPS enters via transport vesicles, and the maturation zone, where the secretion and mature secretory sacs are formed.

Functions of the Golgi complex:
1. Accumulation and modification of macromolecules synthesized in the EPS;
2. Formation of complex secretions and secretory vesicles;
3. Synthesis and modification of carbohydrates, formation of glycoproteins;
4. The CG plays an important role in the renewal of the cytoplasmic membrane by the formation of membrane vesicles and their subsequent fusion with the cell membrane;
5. Formation of lysosomes and peroxisomes.

Special functions of the Golgi complex:
1. Formation of the sperm acrosome during spermatogenesis;
2. Vittelogenesis - the process of synthesis and formation of yolk in the egg cell.

Lysosomes (from the Greek. lisis - destruction, splitting, soma - body) - vesicles of larger or smaller sizes, filled with hydrolytic enzymes (proteases, nucleases, lipases and others).

Lysosomes in cells are not independent structures. They are formed due to the activity of EPS and KG. The main function of lysosomes is intracellular cleavage and digestion of substances that have entered the cell or are in it.

There are primary and secondary lysosomes (digestive vacuoles, phagosomes, autolysosomes), residual bodies, autophagic vacuoles.

1. Primary lysosomes - small bodies with uniform loose contents. Enzymes are in an inactive state.

2. Secondary lysosomes - larger bodies with uneven contents. They actively digest macromolecules and cellular structures. They are formed by the fusion of primary lysosomes with substances that are absorbed by the cell.

3. *Residual bodies.* Undigested material in lysosomes remains in them, decreases in size, forming residual bodies in the cytoplasm. - Autophagic vacuoles. Primary lysosomes can fuse with external and internal structures of the cell and destroy them. In this case, large vesicles are formed, covered with a common membrane, of various shapes and densities.

Such bodies are called *autophagosomes*, and the process of digestion of the entire cell is called autophagy.

Functions of lysosomes:
1. Digestion of substances that enter the cell from the outside during phagocytosis.
2. Digestion of damaged intracellular macromolecules and organelles and those that have fulfilled their function (autophagy).Participation in the digestion of dead cells.
3. Recycling of organic molecules, breaking down proteins, carbohydrates and nucleic acids into monomers for their reuse in synthesis processes.

Disruption of the functioning of lysosomes leads to the development of severe pathological conditions of the body. These are hereditary diseases, which are called storage diseases, because they are associated with the abnormal accumulation of «undigested» substances in the cell, which interfere with the normal functioning of the cell.

Peroxisomes are small membrane vesicles that contain the enzymes catalase and peroxidase. These organelles get their name from hydrogen peroxide (H_2O_2), which is formed in the cell in biochemical reactions. Peroxisome enzymes, primarily catalase, neutralize this toxic compound, causing it to break down with the release of water and oxygen.

$$2H_2O_2 \rightarrow 2H_2O + O_2\uparrow$$

Peroxisomes are also involved in the metabolism of lipids, cholesterol, etc. In case of genetic disorders, when peroxisomes are absent in the liver and kidney cells of a newborn (Zellweger's disease), the child lives only a few months.

The cytoplasm of plant cells contains vacuoles. They are separated from the cytoplasm by a single membrane - the tonoplast. The vacuole cavity is filled with cell sap, which is an aqueous solution of inorganic salts, glucose, organic acids and other substances. They perform storage, excretory, osmotic and lysosomal functions.

The endoplasmic reticulum, Golgi complex, lysosomes, and vacuoles form the vacuolar system of the cell, individual elements of which can pass into each other during the reorganization and change in the function of the membranes.

DOUBLE-MEMBRANE ORGANELLES

Mitochondria are organelles that convert the energy of chemical bonds of organic substances into the energy of phosphate bonds of ATP molecules, which the cell can conveniently use for all its activities. Mitochondria are fairly large organelles (0.2 - 2.0 microns) covered by two membranes.

They are found in almost all eukaryotic cells, except anaerobic protozoa and erythrocytes. Mitochondria are randomly distributed throughout the cytoplasm, although they are more often found near the nucleus or in places with high energy needs.

The outer membrane of mitochondria is easily permeable to many small molecules. It contains enzymes that convert substances into reactive substrates.

The inner membrane forms protrusions into the matrix - *cristae*. These membranes contain enzymes that determine the processes of ATP formation, for example, redox enzymes, ATP synthases and specific transport proteins.

The intermembrane space is used in particular to create a hydrogen ion gradient across the inner membrane.

The matrix is the content of the mitochondria, where a significant number of biochemical reactions take place. Ribosomes and mitochondrial DNA molecules are found in the matrix, which provide the synthesis of some of the proteins necessary for the functioning of the mitochondria. The main integral function of mitochondria is the formation of ATP molecules, which contain macroergic bonds between phosphate residues. Before cell division, the number of mitochondria in the cytoplasm increases, and then they are more or less evenly distributed between the daughter cells.

Plastids are double-membrane organelles of plant cells and some animal cells (flagellates). In the cells of higher plants, three types of plastids are distinguished: chloroplasts, chromoplasts and leucoplasts.

Chloroplasts – are colored green due to the chlorophyll pigment. They perform the function of photosynthesis. Leucoplasts – colorless plastids that differ from chloroplasts in the lack of a developed lamellar system. They store nutrients. Chromoplasts – plastids that give color (yellow, red, etc.) to petals, fruits, and leaves.

NON-MEMBRANE ORGANELLES

Ribosomes are small non-membrane organelles. They are found in the cytoplasm, mitochondria, and plastids. Each ribosome consists of two parts: a small and a large subunit. The first part consists of protein molecules and one molecule of ribosomal RNA (rRNA), the second part consists of proteins and three molecules of rRNA. The ribosomal subunits assemble in the nucleolus.

Ribosomes can be freely located in the cytoplasm or be associated with the EPS, forming part of the granular EPS.

The main function of ribosomes is protein synthesis. Proteins formed on ribosomes connected to the EPS membrane enter its cisternae, while proteins synthesized on free ribosomes remain in the hyaloplasm. For example, in erythrocytes, hemoglobin is synthesized on free ribosomes.

The cytoskeleton is a network of protein fibrils and microtubules that cover the cytoplasmic membrane from the inside and permeate the interior of the cell. It is inherent in all eukaryotic cells, underlies the cilia and flagella of protozoa, the tails of spermatozoa, and the spindle of cell division.

The cytoskeleton consists of three types of structures: *microtubules* (the thickest elements), formed by several protein fibrils of the globular protein tubulin; *microfilaments* (the thinnest elements), formed by the globular protein actin; they are characterized by contractility; *intermediate filaments* (a combination of several microfilaments). The elements of the cytoskeleton have the ability to assemble from monomers when necessary and disassemble after performing a certain function.

Functions of the cytoskeleton:

1. Maintaining the volume and shape of cells;
2. Changing the shape of cells;
3. Movement of organelles and transport vesicles;
4. Formation of multienzyme complexes;
5. Structuring the cytosol and integrating the cytoplasm;
6. Formation of the division spindle during mitosis;
7. Formation of cilia and flagella in protozoa;
8. Formation of intercellular contacts (desmosomes);
9. Ensuring the contractile function of muscle fibers;
10. Changing the phase state of the cytosol: sol - gel transition by regulated disassembly or assembly of cytoskeleton elements.

The cell center (centrosome) is a non-membrane organelle located near the nucleus. It consists of two mutually perpendicular centrioles. Each centriole is a cylinder, the walls of which are formed by triplets of radially arranged microtubules. The cell center has its own nucleic acid, due to which the number of centrioles in the cell doubles before the division of its genetic material.

The main functions of the cell center are the formation of the spindle in dividing cells and the formation of the microtubules of the cytoskeleton. **Basal bodies** lie in the cytoplasm at the base of cilia and flagella. Each basal body is a cylinder formed by nine triplets of microtubules. Basal bodies are able to regenerate cilia and flagella after they are lost.

Cilia and flagella can be classified as special-purpose organelles, since they are found in a few cells, in particular the ciliated epithelium, spermatozoa, protozoa, zoospores of algae, mosses, ferns, etc. Special-purpose organelles also include *myofibrils* of muscle fibers, *neurofibrils* of neurons.

INCLUSIONS

In the cytoplasm of cells there are also inclusions - non-permanent components that perform the function of storing nutrients (fat droplets, glycogen granules), various secrets prepared for excretion from the cell. Inclusions also include some pigments (bilirubin, lipofuscin), etc. Inclusions are synthesized in the cell during its vital activity and are metabolized.

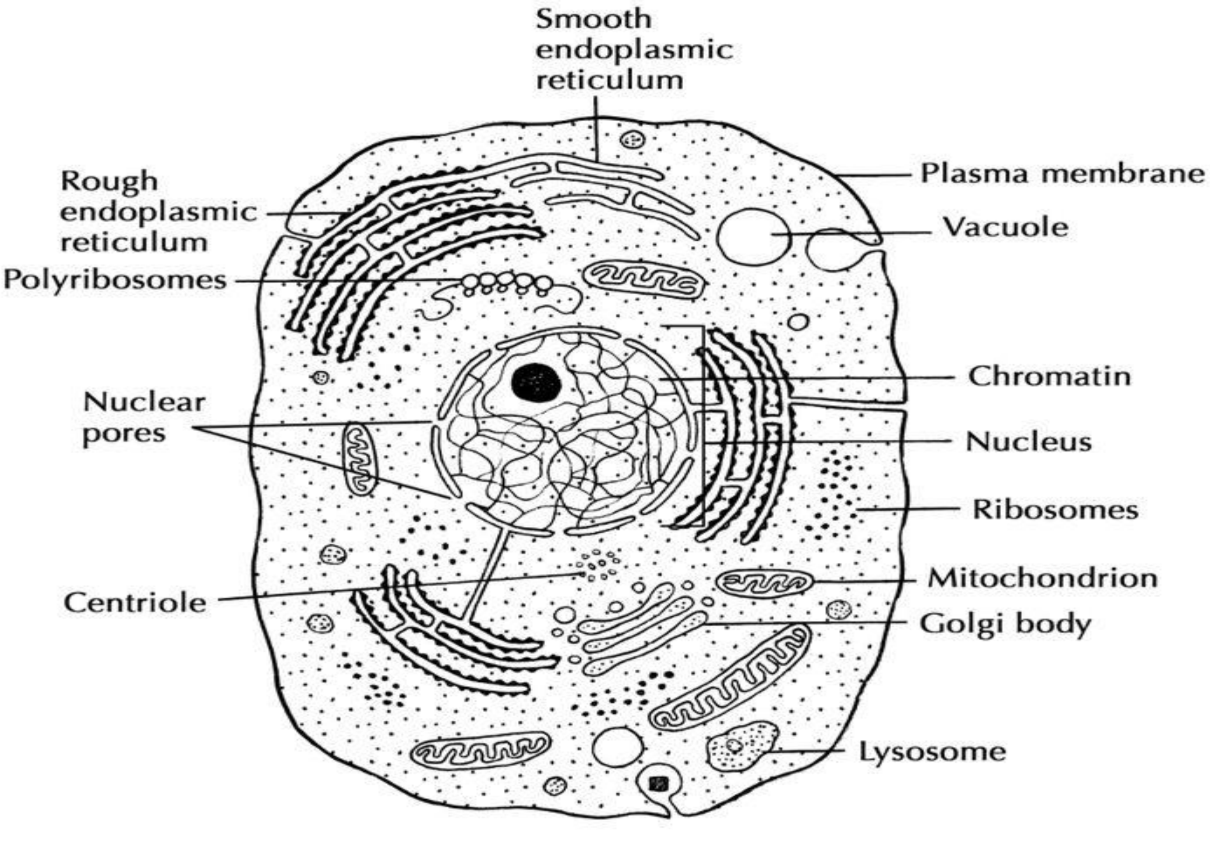


Fig. 4. Cell structure.

The nucleus is the largest and most important double-membrane organelle of eukaryotic cells (the average size of the nucleus is about 10 microns). All eukaryotic cells contain the nucleus at least at one stage of differentiation. It is located in the cytoplasm, and always occupies a central position.

The shape of the nucleus is most often round or spherical, but elongated, lobed and branched nuclei are also found. Their shape may depend on the shape of the cell or its functional state. For example, in leukocytes, the nucleus may acquire a segmented shape during its vital activity.

The nucleus performs genetic and morphophysiological functions. The genetic function of the nucleus is to store and transmit hereditary information, which is passed on to daughter cells during division. The morphophysiological function of the nucleus is to constantly control the vital activity of the cell. This control is carried out with the help of mRNAs, which are synthesized in the nucleus during the implementation of certain genetic programs during cell differentiation or in response to environmental factors.

The role of the nucleus in the cell was proven in experiments on the unicellular alga Acetabularia, which has a very high ability to regenerate. Dividing the cell into two parts by cutting the stem, in which the nucleus remained in one of the parts, led to the completion of part of the alga with the nucleus of the other part, while the nuclear-free part died.

And the exchange of sections of the stem with the core of the white and green acetabularium caused, after some time, a change in the color of the remaining part of the plant that was transplanted.

In connection with the performance of a particular function, the core may be in a state of division or in a metabolically active state. The structure of the core and its structural components is usually considered during the period of its metabolic activity. The main mass of the nucleus is proteins - up to 96%. 80% of them are nucleoproteins: about 70% - deoxyribonucleoproteins (DNP) and about 10% - ribonucleoproteins (RNP). Almost all of the cell's DNA (99%) and much less RNA are concentrated in the nucleus. Simple proteins (histones, globulins) are also present in the nucleus.

It contains many protein enzymes, for example, enzymes that catalyze the synthesis of nucleotides, nucleic acids, proteins, etc. It also contains amino acids, nucleotides, lipids and a small amount of minerals, in particular ions of calcium, manganese, iron, copper, etc. The main structural components of the nucleus are the nuclear envelope, nuclear matrix, chromatin and nucleoli.

The nuclear envelope (karyotheca) is formed by two membranes, between which there is a cavity - the perinuclear space. The outer membrane is continuously connected to the membranes of the granular endoplasmic reticulum, and the perinuclear space communicates with the cavities of its tubules and cisterns. The outer membrane may be rough from ribosomes attached to it.

In places, the inner and outer membranes of the shell merge and form pores. Around the pore between the edges of the membranes are protein globules, and in the center of the pore opening there is also a large globule. The pore opening is covered by a thin diaphragm. Due to the complexity of the structure, nuclear pores are called pore complexes. The transport of substances is carried out through pore complexes. RNA and ribosomal subunits leave the nucleus and enter the cytoplasm, while mononucleotides and proteins, including enzymes, as well as ATP and ions, enter the nucleus from the cytoplasm. Pore complexes occupy from 10 to 50% of the surface of the nuclear envelope, depending on the type of cell and its activity. In the nuclei of young and metabolically active cells, there are usually more pore complexes.

The function of the nuclear envelope is to regulate the exchange of substances between the nucleus and the cytoplasm. On the inner side of the nuclear envelope are the proteins of the nuclear lamina, which give shape and volume to the organelle itself, participate in the assembly of the nuclear envelope after the division of genetic material. Parts of chromosomes are also attached to them.

The main substance of the nucleus – the nuclear matrix – is called *nucleoplasm*, or *karyoplasm*. Nucleoplasm is a structureless mass in which granules are visible. It is connected to the cytoplasmic matrix through nuclear pores. The nucleoplasm contains many protein enzymes that catalyze the exchange of amino acids, nucleotides, proteins, etc.

The functions of the nucleoplasm, as well as the cytoplasmic matrix, are to interconnect all the structural components of the nucleus and to carry out a number of enzymatic reactions.

Nucleoli are unstable structures: they disappear at the beginning of cell division and reappear at the end. Their formation is associated with chromosomes that have a section with a nucleolar organizer. Nucleoli contain proteins and RNA.

The main functions of the nucleolus: 1) synthesis of ribosomal RNA; 2) formation of ribosomal subunits; 3) synthesis of nuclear proteins (histones).

Metabolism is a set of chemical and physical transformations of substances and energy that occur in a living organism and ensure its vital activity. The energy released in the process of metabolism is necessary for the work, growth, development and maintenance of the structure and functions of all cellular elements. Metabolism is a single place. Metabolism and energy are one place. Metabolism consists of the processes of *assimilation and dissimilation.*

Assimilation (anabolism) is the process of assimilation of substances by the body, in which energy is spent.

Dissimilation (catabolism) is the process of decomposition of complex organic compounds, which occurs with the release of energy. The only source of energy for the human body is the oxidation of organic substances that come with food. When food products are broken down into their final elements - carbon dioxide and water - energy is released.

Topic 3. Cell division. Mitosis. Meiosis. Gametogenesis. Fertilization.

Prokaryotes. These organisms divide via binary fission, a type of asexual reproduction (more on this shortly). Because prokaryotes have no organelles, the single DNA molecule attaches itself to the cell membrane and duplicates itself while the cell itself grows in size. The cell membrane then invaginates, or pinches inward, to create two identical daughter cells.

Eukaryotic cell division is a bit more complex.Since there are multiple chromosomes per cell, organisms must properly segregate these chromosomes during duplication. Moreover, we must also make new cytoplasm and organelles. Eukaryotic autosomal cells contain the diploid (2n) number of chromosomes. Haploid, or germ cells contain the n number of chromosomes. For humans, these numbers are 46 and 23, respectively; we inherit 23 of these chromosomes from each parent.
Eukaryotic autosomal cells reproduce by a process known as the **cell cycle.**

THE CELL CYCLE

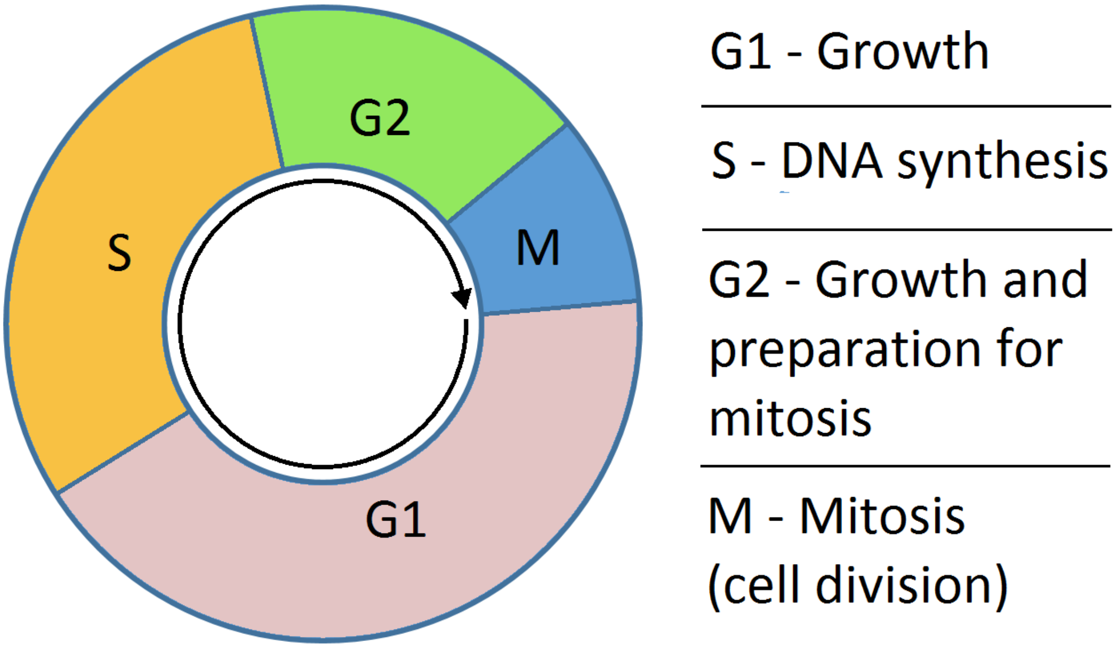


Fig. 5. The Cell cycle.

Mitosis is the stage in which the cells actually divide. The other three phases are collectively known as interphase.

Interphase

This is the longest part of the cell cycle. Cells that divide may spend as much as 90 percent of their time in this phase. On the other hand, cells that enter terminal differentiation (e.g., muscle and nerve cells) spend all of their time in an offshoot of G1 called G0.

G1 Stage (Pre Synthetic Gap)

During this phase, cells create organelles for energy and protein production (mitochondria,ribosomes, and endoplasmic reticulum) while also doubling in size. In addition, the passage into **S (synthesis)** phase is governed by a restriction point. Certain criteria must be met for the cell to pass the restriction point and enter the synthesis phase.

S Stage (Synthesis)

During this phase, the cell replicates, or synthesizes, its genetic material so that each daughter cell will have identical copies. After replication, each chromosome consists of two identical chromatids, which are bound together at a specialized region known as the centromere . Note that the ploidy of the cell does not change, even though the number of chromatids has doubled (in humans, 46 chromosomes and 92 chromatids).Cells entering G2 contain twice as much DNA as cells in G1.

G2 Stage (Postsynthetic Gap)

This is the final stage before actual cell division; think of it as quality control. We have already duplicated the DNA, and now we are just making sure that we have enough organelles and cytoplasm to make two daughter cells.

M Stage (Mitosis)

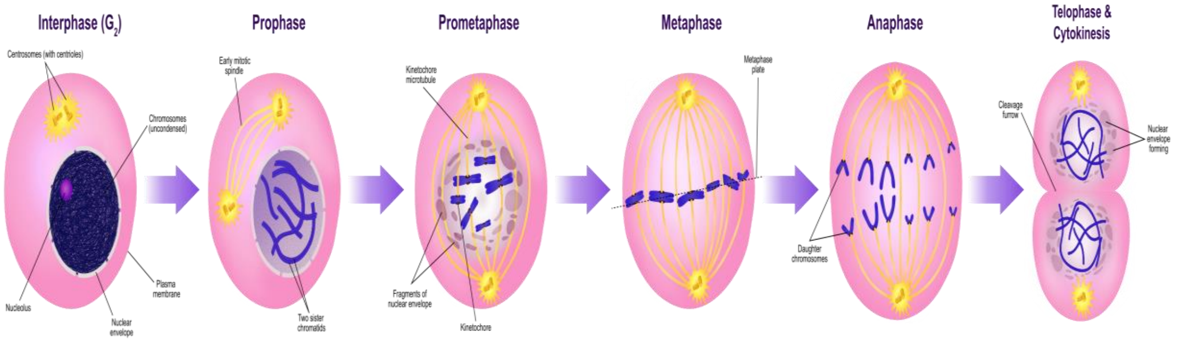


Fig. 6. Stages of mitosis.

The mitotic stage consists of mitosis itself along with cytokinesis. **Mitosis** is divided into four phases: prophase, metaphase, anaphase, and telophase . **Cytokinesis** is the splitting of the cytoplasm and organelles into the daughter cells.

During **interphase**, individual chromosomes are not visible with light microscopy. They are in a less condensed form known as chromatin. Why would this be? During interphase, the DNA must be open so that we can transcribe genes from it and replicate it prior to cell division. During mitosis, however, it’s preferable for the

DNA to be tightly bound into chromosomes so that we don't lose any material during division.

The proper movement of our chromosomes depends on specialized subcellular organelles known as centrioles. These paired cylindrical organelles, located outside the nucleus in a region known as the centrosome, are responsible for the correct division of the DNA. During **prophase**, the centrioles migrate to opposite poles of the cell and begin to form the spindle fibers, which are made from microtubules. Each of the fibers radiates outward from the centrioles, giving the chromosomes an attachment point for later separation during anaphase.

These attachment points are known as asters. The asters extend toward the center of the cell to form a spindle apparatus. Subsequent shortening of this apparatus results in separation of sister chromatids.

Mitosis can be studied in four discrete phases, although the process itself is continuous. Indeed, we can watch certain types of quickly dividing cells undergo the entire mitotic process in about 20 minutes using nothing more than a light microscope.

An autosomal cell never has more or fewer than the 2n (46 in human) number of chromosomes, except in disease conditions. It will have 92 chromatids, however, right before mitosis.

Prophase

The chromosomes condense, the centriole pairs separate and move toward opposite poles of the cell, and the spindle apparatus forms between them. The nuclear membrane dissolves, allowing spindle fibers to enter the nucleus, while the nucleoli become less distinct or disappear. Kinetochores, with attached kinetochore fibers, appear at the chromosome centromere.

Metaphase

The centriole pairs are now at opposite poles of the cell. The kinetochore fibers interact with the fibers of the spindle apparatus to align the chromosomes at the metaphase plate (equatorial plate), which is equidistant to the two poles of the spindle fibers.

Anaphase

The centromeres split so that each chromatid has its own distinct centromere, thus allowing the sister chromatids to separate. The telomeres are the last part of the chromatids to separate. The sister chromatids are pulled toward the opposite poles of the cell by the shortening of the kinetochore fibers.

Telophase and Cytokinesis

The spindle apparatus disappears. A nuclear membrane re-forms around each set of chromosomes, and the nucleoli reappear. The chromosomes uncoil, resuming their interphase form. Each of the two new nuclei has received a complete copy of the genome identical to the original genome and to each other. Cytokinesis occurs.

Cytokinesis

At the end of telophase, cytokinesis allows us to separate the cytoplasm and organelles so that each daughter cell has what it needs to survive on its own. Each cell undergoes a finite number of divisions before programmed death; for human somatic cells, this is usually between 20 and 50. After that, the cell can no longer divide without incorporating errors and will probably die without being replaced.

Some cells never undergo division (muscle and nerve), whereas others, such as cancer cells, escape this cycle and divide continuously. Indeed, unregulated cell division is one of the hallmarks of cancer.

Asexual Reproduction

Asexual reproduction is the production of offspring from the genetic material of a single parent. It is similar to mitosis in eukaryotic cells in that the daughter cells will be genetically identical to their parents (other than random mutations that may arise during the process). We will briefly examine four different forms of asexual reproduction : binary fission, budding, regeneration, and parthenogenesis.

BINARY FISSION

This is a simple form of reproduction seen in prokaryotes (think bacteria). The circular chromosome attaches to the cell wall and replicates while the cell continues to grow in size. Eventually the plasma membrane and cell wall will begin to grow inward along the midline of the cell to produce two equal daughter cells. This process also occurs in some simple eukaryotic cells. This process is simple, so it can proceed rapidly; indeed, some strains of Escherichia coli can replicate every 20 minutes under ideal growth conditions. Some bacteria have plasmids of additional DNA that contribute to genetic diversity; however, this is an evolved adaptation and not the basis of binary fission.

BUDDING

Budding is equal replication followed by unequal cytokinesis. In other words, the daughter cell receives DNA identical to her parent's but far less cytoplasm . The daughter cell may immediately break off or stay attached to the parent until it grows to full size. Budding takes place in several organisms, including hydra and yeast (both eukaryotes).

Binary fission results in two cells of equal size, whereas budding results in cells of unequal size. Both methods however, give rise to genetically identical cells.

REGENERATION

One of the most fascinating topics in the entire animal kingdom is regeneration, in which an entire body part can be regrown. Lizards that lose their tails when threatened may regrow them, and annelid worms can regenerate anterior head segments. Regeneration primarily occurs in lower organisms and is accomplished by mitosis. Some animals have extensive capabilities; in fact, sea stars may reproduce their bodies from just an arm, as long as an area known as the central disk is intact. Higher organisms have more difficulty with this process, primarily due to nerve damage, as central nervous system nerves do not regenerate. There are always exceptions; in humans for example, the liver exhibits extensive regenerative properties.

In fact, it is now possible to perform liver transplants in which a piece of a living donor's liver is transplanted into a recipient. Both livers (or liver pieces) will grow back to the appropriate size, no worse for the wear!

PARTHENOGENESIS

Parthenogenesis is the process whereby an adult organism develops from an unfertilized egg. Many social insects (bees and ants) produce males via parthenogenesis. This process does not occur naturally in higher organisms, although it has been induced in the laboratory in rabbits. What does this mean in terms of the number of chromosomes that will be found in each cell? They will be haploid in number because only one parent contributed genetic material.

Sexual Reproduction

Each parent contributes one-half of the offspring's genetic material.
The specialized sex cells that contribute to this process are known as gametes, and they are produced through a process known as meiosis. Meiosis shares some similarities with mitosis. In both processes, for instance, genetic material must be duplicated. Mitosis results in two identical diploid (2n) daughter cells, whereas meiosis yields four different haploid (n) gametes; somatic cells undergo mitosis, whereas gametocytes undergo meiosis.

MEIOSIS

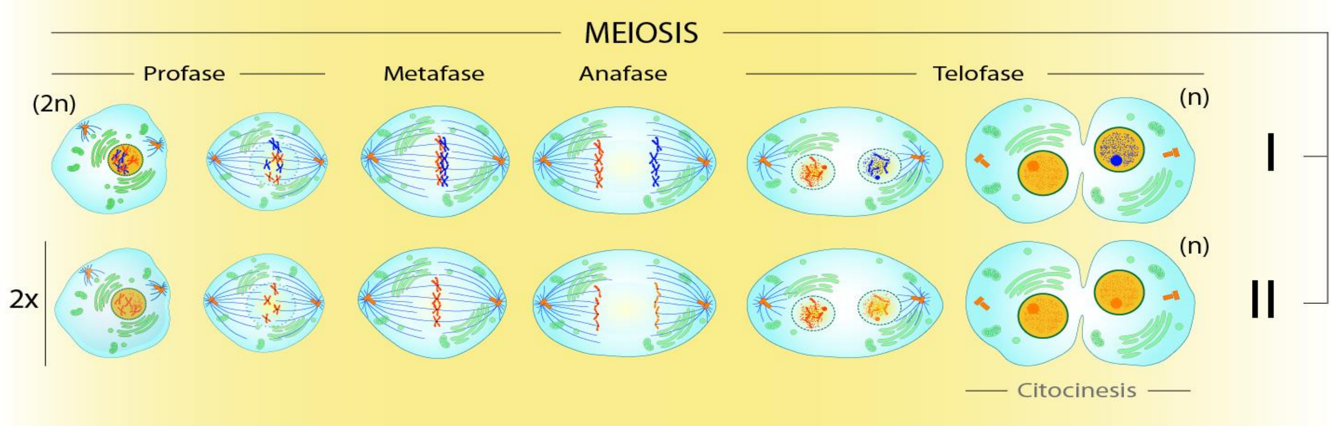


Fig. 7. Meiosis.

Whereas mitosis consists of one round of replication and division each, meiosis is composed of one round of replication followed by two rounds of division. Meiosis I (the first division) results in homologous chromosomes being separated, generating haploid daughter cells; this is known as the reductional division. Meiosis II (the second division) is similar to mitosis in that it results in the separation of sister chromatids, and is also known as the equational division. The result is four genetically unique haploid cells.

MEIOSIS I

Prophase I

Although we begin the discussion with prophase, it's important for us to know that an interphase similar to that of mitosis duplicates homologous chromosomes in preparation for division. Homologous chromosomes code for the same genes; one is inherited from each parent. During prophase, the chromatin condenses into chromosomes, the spindle apparatus forms, and the nucleoli and nuclear membrane disappear. The first major difference between meiosis and mitosis occurs at this point. Homologous chromosomes come together and intertwine in a process called synapsis.

At this stage, each chromosome consists of two sister chromatids, so each synaptic pair of homologous chromosomes contains four chromatids and is, therefore, referred to as a tetrad. Chromatids of homologous chromosomes may break at the point of synapsis (chiasma; pl: chiasmata) and exchange equivalent pieces of DNA; this process is called crossing over . Note that crossing over occurs between homologous chromosomes and not between sister chromatids of the same chromosome. (The latter are identical, so crossing over would not produce any change.)

Those chromatids involved are left with an altered but structurally complete set of genes. Sister chromatids are no longer identical. Such genetic recombination can unlink linked genes, thereby increasing the variety of genetic combinations that can be produced via gametogenesis. Recombination among chromosomes results in increased genetic diversity within a species.

The rate of gene unlinking is used to map distances between two genes on the same chromosome. The farther apart two genes are, the more likely they are to become unlinked during crossing over. This distance can then be used to follow genetic disease within families.

Metaphase I

Homologous pairs (tetrads) align at the metaphase plate, and each pair attaches to a separate spindle fiber by its kinetochore. Metaphase is the easiest to identify pictorially because the chromosomes are all neatly lined up on the metaphase plate.

Anaphase I

Homologous pairs separate and are pulled to opposite poles of the cell. This process is called disjunction, and it accounts for a fundamental Mendelian law. During disjunction, each chromosome of paternal origin separates (or disjoins) from its homologue of maternal origin, and either chromosome can end up in either daughter cell. Thus, the distribution of homologous chromosomes to the two intermediate daughter cells is random with respect to parental origin. Each daughter cell will have a unique pool of alleles (genes coding for alternative forms of a given trait; e.g., yellow flowers versus purple flowers) from a random mixture of maternal and paternal origin.

It is critical to understand how meiosis I is different from mitosis. The chromosome number is halved (reductional division) in meiosis I. The daughter cells have the haploid number of chromosomes (23 in humans). Meiosis II is similar to mitosis in that sister chromatids are separated from one another; therefore, no change in ploidy is observed.

Telophase I

A nuclear membrane forms around each new nucleus. At this point, each chromosome still consists of sister chromatids joined at the centromere. Are the cells haploid or diploid at this point? They are haploid; once homologous chromosomes separate, only the n number of chromosomes is left (23 in humans). There are still 46 chromatids: 2 per chromosome. Each chromatid within a pair, however, has the same origin (save for genetic recombination). The cell divides (by cytokinesis) into 2 daughter cells. Between cell divisions, there may be a short rest period, or interkinesis, during which the chromosomes partially uncoil.

Meiosis II

This second division is very similar to mitosis. Thus, we only need to learn the few salient differences between the two, and we’ll have a good grasp on both. We shouldn’t do more work than is necessary for Test Day; instead, we should study efficiently, and this is a perfect example of how to do just that. First of all, meiosis II is not preceded by chromosomal replication. Let’s go through the steps of meiosis II as a quick review. We’ll see a couple more differences along the way.

Mitosis	**Meiosis**
2n →2n	2n →n
Occurs in all dividing cells.	Occurs in sex cells only.
Homologous chromosomes don’t pair.	Homologous chromosomes pair up at metaphase plate, forming tetrads.
No crossing over.	Crossing over can occur.

Prophase II

The centrioles migrate to opposite poles, and the spindle apparatus forms.

Metaphase II

The chromosomes line up along the metaphase plate. The centromeres divide, separating the chromosomes into pairs of sister chromatids.

Anaphase II

Sister chromatids are pulled to opposite poles by the spindle fibers.

Telophase II

A nuclear membrane forms around each new (haploid) nucleus. Cytokinesis follows, and two daughter cells are formed. Thus, by the completion of meiosis II, four haploid daughter cells are produced per gametocyte. (In females, only one of these becomes a functional gamete.)

The random distribution of chromosomes in meiosis, coupled with crossing over in prophase I, enables an individual to produce gametes with many different genetic combinations. Thus, as opposed to asexual reproduction, which produces identical offspring, sexual reproduction provides the advantage of great genetic variability, which is believed to increase the capability of a species to evolve and adapt to a changing environment.

HUMAN SEXUAL REPRODUCTION

The haploid sperm and ovum fuse during fertilization to form a single-celled zygote in the fallopian tubes. These cells are produced by the gonads, which in both males and females are derived from the same embryological structure.

Spermatogenesis

Spermatogenesis, the formation of haploid sperm through meiosis, occurs in the seminiferous tubules. The diploid stem cells in males are known as spermatogonia (sing: spermatogonium). In the process of differentiation, they replicate their genetic material and develop into diploid primary spermatocytes.

spermatogonia (2n)

↓
1 spermatocytes (2n)
↓ meiosis l
2 spermatocytes (n)
↓ meiosis ll
spermatids (n)
↓
spermatozoa (n)

The first meiotic division will result in haploid secondary spermatocytes, which then undergo meiosis II to generate haploid spermatids. The spermatids undergo maturation, to become spermatozoa. Spermatogenesis creates four functional sperm for each spermatogonium. A mature sperm is very compact. It consists of a head (containing the genetic material), a midpiece (to generate energy from fructose for motility), and a tail (for motility) . What sort of organelles would we expect an abundance of in the midpiece? Since we're looking to create ATP, mitochondria would be our best bet. Each sperm head is covered by a cap known as an acrosome. This structure is derived from the Golgi apparatus and is necessary to penetrate the ovum. Once a male reaches sexual maturity (puberty), approximately 3 million sperm are produced per day.

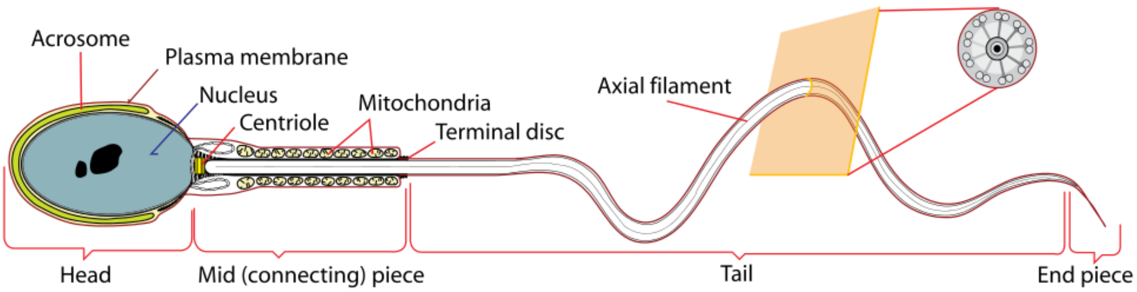


Fig. 8. Spermatogenesis.

Oogenesis

The production of female gametes is known as oogenesis. Although gametocytes undergo the same meiotic process in both females and males, there are some test-worthy differences to keep track of. First, there is no unending supply of stem cells analogous to spermatogonia in females. All the oogonia a woman will ever have are formed during fetal development. At birth, females have predifferentiated cells known as primary oocytes. These cells are 2n (like primary spermatocytes) and are actually frozen in prophase I. Once a woman reaches menarche, one primary oocyte per month will complete meiosis I, producing a secondary oocyte and a polar body. The division is characterized by unequal cytokinesis, which doles ample cytoplasm to one daughter (the secondary oocyte) and nearly none to the other (polar body). The polar body does not divide any further and never produces functional gametes. The secondary oocyte remains frozen in metaphase II and does not complete the remainder of meiosis II, unless fertilization occurs.

Remember that spermatogenesis in males is a 1:4 division, whereas in females, oogenesis is 1:1.

Two cell layers surround oocytes: the zona pellucida and the corona radiata. Meiosis II is triggered when a sperm penetrates these layers with the help of acrosomal enzymes. The secondary oocyte undergoes the second division to split into a mature ovum and another polar body, which will eventually die. With respect to the scheme of meiosis we learned earlier, are four haploid daughter cells formed through oogenesis? Sort of. If the first polar body underwent equational division, we’d have three polar bodies and one ovum as our final products. Although the ovum is the only functional gamete, all four would carry the haploid genetic material prescribed by theoretical meiosis. But, simply put, because it's daughters would not be functional anyway, there is no productive reason for the first polar body to divide again. A mature ovum is a very large cell consisting of large amounts of cytoplasm and organelles.

1 oocyte (2n)
↓meiosis l
2 oocyte (n)
↓ fertilization
↓ meiosis ll
ovum (n)

Until menopause (usually between ages 45 and 55), women ovulate one secondary oocyte approximately every 28 days. After menopause, the ovaries become less sensitive to their stimulating hormones (follicle-stimulating hormone [FSH] and luteinizing hormone [LH]) and eventually atrophy. So, if the ovaries contribute to a negative feedback loop and are not responding to FSH and LH, what do we think will happen to the levels of these hormones? They will shoot sky-high because they have no estrogen and progesterone feedback (both of which are secreted by the ovaries). Profound physical and physiological changes usually accompany this process.

Fertilization

Secondary oocytes are capable of being fertilized within 24 hours of ovulation. Sperm will usually survive for one to two days after ejaculation if the environment (uterine, in this case) is suitable. The fusion of these haploid cells, usually in the widest part of the fallopian tube, results in restoration of the diploid chromosome number and a cell known as a zygote.

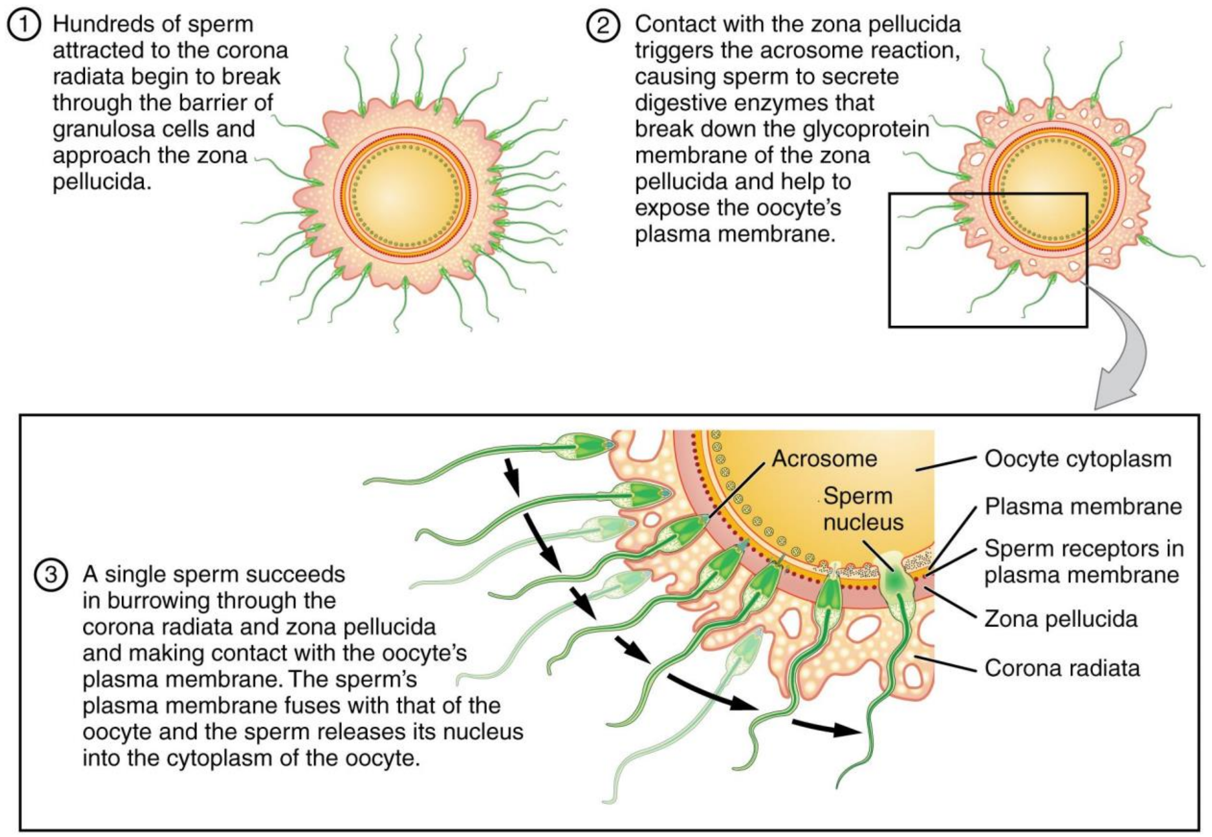


Fig. 9. Fertilisation.

How does fusion occur? Sperm cells secrete acrosomal enzymes to digest the corona radiata and penetrate the zona pellucida . Once the first sperm comes into direct contact with the secondary oocyte's cell membrane, it forms a tubelike structure known as the acrosomal apparatus, which extends to and penetrates the cell membrane. Its nucleus may then freely enter the ovum (no longer a secondary oocyte). After this process, the ovum undergoes a cortical reaction. Ca^{2+} ions are released into the cytoplasm, which in turn leads to the formation of the fertilization membrane. This membrane is impenetrable to other sperm – can we figure out why? To prevent multiple fertilizations. The release of Ca^{2+} also greatly increases the metabolic rate of the ovum and soon-to-be zygote.

CONCEPTS TO REMEMBER

- Reproduction is necessary for propagation of a species.
- Mitosis involves one round of DNA replication and one round of cellular division. Daughter cells are genetically identical.
- Asexual reproduction results in organisms that are genetically identical, thus severely limiting diversity in the species.
- Asexual reproduction is primarily used by lower organisms, such as prokaryotes, yeasts, and hydra, and in certain circumstances by some animals.

- Sexual reproduction provides for the combination of two genomes, resulting in genetically unique offspring.
- The generation of specialized sex cells for sexual reproduction is known as gametogenesis.
- Meiosis is a process similar to mitosis but consists of one round of replication followed by two rounds of division. Thus, the daughter cells are unique and haploid.
- The male reproductive and excretory tracts share some common structures.
- Females are born with all their gametes already existing as primary oocytes.

Topic 4. Chromatin. Chromosomes. Karyotype.

The cell nucleus (Latin nucleus, Greek karion - nucleus) is the central information apparatus of eukaryotic cells, which performs genetic functions and regulates all processes of the cell's vital activity (metabolic functions). The components of the nucleus are the nuclear envelope, karyoplasm (nuclear juice), nucleoli (one or two), chromatin, and nuclear protein matrix. The nucleus was first discovered in 1831 by the English botanist R. Brown in the cells of plants from the orchid family.

Functions of the nucleus:

1) preservation of hereditary information in DNA molecules;
2) implementation of hereditary information by regulating protein synthesis. This maintains the structural order of cells, regulates their metabolism, functions and division processes;
3) transmission of hereditary information to subsequent generations as a result of DNA replication through the formation of chromosomes and their division.

Nuclear envelope — consists of two membranes, which are separated by a perinuclear space 20-50 nm wide. At the base of each membrane lies a lipid bilayer, with proteins embedded in it. The outer nuclear envelope directly passes into the membranes of the endoplasmic reticulum. From the cytoplasm side it is covered with ribosomes. The nuclear envelope has holes - pores with a diameter of 80-90 nm to ensure the transport of macromolecules.

In the pore zone, the inner and outer membranes merge. The pore opening contains a complex that has a specific structure (diameter about 120 nm). A thin diaphragm closes the pore opening. Along the periphery of the pore, on both sides of the diaphragm, there are protein granules and another granule in the center, which is connected by fibrils to the peripheral ones. Thus, a structure resembling a bicycle wheel is formed.

Temporary cylindrical channels can form in the diaphragm itself, through which substances are transported. The number of pores depends on the functional state of the cell: the more intensively synthetic processes occur in the cell, the more pores there are.

For example, in erythroblasts, where hemoglobin intensively accumulates, there are up to 30 pores per 1 μm^2 of the nuclear envelope, and in mature animal erythrocytes, which retain the nucleus, there are up to 5 pores.

In the area of the pore complex, a protein layer begins that covers the inner nuclear envelope — a dense thin plate (nuclear lamina), which performs a supporting function and also contributes to the ordered arrangement of chromosomes in the interphase nucleus. Chromatin threads are attached to the lamina by telomeric sections. It is formed by intermediate filaments (d = 10 nm) and is part of the nuclear matrix. The matrix also includes an intranuclear fibrillar network and protein complexes with enzymatic and regulatory functions.

The main functions of the nuclear membrane: 1) barrier function - separates the contents of the nucleus from the cytoplasm; 2) regulates the transport of macromolecules between the nucleus and the cytoplasm. Thus, proteins (histone and non-histone) after synthesis in the cytoplasm are transported to the nucleus, and RNA and ribosomal subunits synthesized in the nucleus - to the cytoplasm. In the prophase of mitosis, the nuclear envelope disintegrates into membrane vesicles, and in telophase it is formed again.

Karyoplasm (nuclear juice) is the internal environment of the nucleus, which plays an important role in ensuring the normal functioning of genetic material. Nuclear juice contains enzymes that are necessary for the synthesis of nucleic acids.

Nucleus - a structure where the formation and maturation of ribosomal RNAs (rRNAs) occurs. Nuclei are not independent structures of the nucleus, but derivatives of chromosomes. rRNA genes occupy certain loci of one or more chromosomes, for example, in humans, 13-15, 21-22 pairs - these are nucleolar organizers, which form the nucleolus.

Such areas of metaphase chromosomes are narrowed, they are called secondary constrictions. Filamentous (fibrillar) and granular components are also found in the nucleolus. The fibrillar component is a complex of protein and precursor RNA molecules (pro-RNA), from which mature rRNAs are formed during processing. The granular component determines the size of the nucleolus. Nucleoli are not permanent structures of the nucleus: at the beginning of cell division they disappear, and at the end of division they reappear.

The most important structure of the nucleus is chromatin, located in the karyoplasm. This is a thread-like complex of DNA and proteins that is highlighted in the interphase nucleus by dyes specific for DNA. During cell division, chromatin decreases in size due to spiralization, forming chromosomes that are clearly visible during mitosis.

1) Functions of chromatin:

2) 1) preservation of genetic hereditary information in the form of a clear sequence of DNA nucleotides, stabilized by proteins and special packaging;

3) 2) transmission of hereditary information from parents to offspring through the formation of chromosomes;

4) 3) ensuring cell growth, maintaining their structure and functions by controlling the synthesis of structural proteins;

5) control of metabolism by regulating the formation of necessary enzymes;
6) formation of nucleoli, where ribosomes are formed.

Types of chromatin.

Depending on the degree of condensation (coiling), chromatin is divided into heterochromatin and euchromatin.

Euchromatin - functionally active, practically uncondensed (despiralized) and therefore light areas of chromatin, which are transcribed (genetically active) and are located between the depths of heterochromatin. With the onset of mitosis, all euchromatin condenses into chromosomes and becomes visible.

Heterochromatin is highly condensed and therefore functionally inactive regions of chromatin (genetically inert). A distinction is made between constitutive (structural) and facultative heterochromatin.

Constitutive heterochromatin is found in the pericentromeric and telomeric regions of all chromosomes, as well as in some internal regions of individual chromosomes. It supports the overall structure of the nucleus, attaches to the nuclear envelope, determines the interaction between homologous chromosomes during meiosis, and participates in the regulation of gene activity.

Facultative heterochromatin is formed by whole chromosomes. For example, in homogametic sex, one of the gonosomes forms a sex chromatin body (Barr body).

Sex chromatin: distinguish between X- (1949 M. Barr and C. Bertram) and Y- sex chromatin.

X-sex chromatin (Barr body) - one of the two X chromosomes of female individuals (mammals, humans), which heterochromatizes (tightly condenses) in the early stages of embryogenesis and passes into a genetically inactive state. In this case, in one part of the cells the maternal X chromosome is inactive, in the other - the paternal one.

Inactivation of one of the X chromosomes is a mechanism that equalizes the balance of sex chromosome genes in the cells of male (XY) and female (XX) organisms.

Determination of X-sex chromatin is used for express diagnostics of the number of X chromosomes in the karyotype, which is necessary for determining the genetic sex of a person at the Olympic Games, in forensic medicine, clinic, as well as for the diagnosis of hereditary diseases associated with a violation of the number of sex chromosomes.

Y-chromatin (F-body) is the Y chromosome in the nuclei of male somatic cells. The determination of X- and Y-sex chromatin is part of the cytogenetic method.

The following levels of chromatin compaction (packaging) are distinguished:

1. Molecular - double helix of DNA.
2. Nucleosomal - nucleosomal thread with a diameter of 10-12 nm.
3. Fibrillary - elementary chromatin helix with a diameter of 25-30 nm.

4. Chromoneme - interphase chromoneme with a diameter of up to 200 nm.
5. Chromatid-chromosomal - metaphase chromosome (with 2 or 1 chromatid). Chromatid has a diameter of up to 600 nm.

Chromosomes (from the Greek χρώμά – color, σώμά – body) are threadlike dense bodies visible in a light microscope only during cell division. They are formed as a result of condensation and spiralization of chromatin. The length of chromosomes depends on the amount of DNA and proteins, as well as on the degree of chromatin coiling.

Properties of chromosomes:

1. Specificity of the chromosome set for each species. Plants and animals have a fixed set of chromosomes in each somatic cell.
2. Pairing of chromosomes. Each pair of chromosomes that has the same size, shape, and composition of genes that control alternative traits is called homologous.
3. Individuality of individual pairs of chromosomes. Each pair of homologous chromosomes of an individual differs from the other pair in size, shape, and genetic composition.
4. Continuity of chromosomes. Each daughter chromosome is derived from a maternal chromosome.

In successive generations of cells, a constant number of chromosomes and their individuality are maintained due to the ability of chromosomes to reproduce precisely during cell division. Thus, not only «each cell from a cell», but also «each chromosome from a chromosome».

The smallest structural components of chromosomes are nucleoprotein fibrils. Chromosomal nucleoproteins include DNA and proteins, mainly histones. Piston molecules form *nucleosomes*, on which DNA is packaged. Each nucleosome is a globule consisting of 8 protein molecules (octamer): it includes two molecules of four types of histones (H2A, H2B, H3, H4). The size of the nucleosome is 11 nm. Around each such globule, the DNA molecule makes approximately two turns. Such a DNA segment has a length of 140 nm and is called cor-DNA (nDNA). Each nucleosome is separated from the other by a segment of linker DNA (iDNA), 60 np long. 1 molecule of another histone protein - H1 - is bound to each linker segment. The period of nucleosome organization is 200 np. DNA fibrils are twisted in pairs, forming chromonemes, which are part of half-chromatids. A pair of half-chromatids makes up a chromatid, and a pair of chromatids makes up a chromosome.

Human Karyotype. Chromosomal Analysis

The set of chromosomes in a cell, characterized by their specific number, size, and shape, is called a ***karyotype.*** Each species of living organisms has a specific and constant number of chromosomes, that is, the number of chromosomes and the characteristic features of their structure are a species characteristic.

Karyotype is a relatively stable system of nuclear chromosomes of independent cells, which is characterized by a certain diploid number, characteristic sizes, shapes and groups of linked genes. This term was introduced into science in 1924 by the Ukrainian cytologist G.A. Levitsky (1878-1942). Karyotype is a species characteristic of organisms.

The human karyotype was established in 1956 by Swedish scientists D. Tijjo and A. Levan on human cell culture. The human karyotype includes 46 chromosomes, or 23 pairs of chromosomes: 22 pairs of autosomes and one pair of sex chromosomes (heterochromosomes).

The nuclei of somatic cells contain a complete double set of chromosomes - *diploid* (2n). In the nuclei of germ cells, only one of each pair of homologous chromosomes is present, all of them are non-homologous - *haploid* set of chromosomes (n). During fertilization, the germ cells fuse, each with a haploid set of chromosomes, and the diploid set is restored in the zygote (n+n=2n).

In female and male individuals of the same species, there is a difference in one pair of chromosomes - sex chromosomes or heterochromosomes: in women - XX, in men - XY. All other chromosomes - autosomes are the same in both sexes. The normal karyotype of a woman is recorded as 46, XX, in men - 46, XY. A normal karyotype is an important condition for the formation of a healthy person. Changes in the number and structure of chromosomes (mutations) cause chromosomal diseases.

The study of the human karyotype is carried out on a culture of bone marrow cells, fibroblasts or peripheral blood leukocytes. Chromosomes are studied during mitotic division (metaphase), when they are maximally coiled. Cell division is stimulated with phytohemagglutinin.

Treatment with colchicine (or colchamine) stops the process of cell mitosis at the metaphase stage, as the achromatin threads of the division apparatus (division spindle) are destroyed and the chromosomes remain maximally spiraled in the center of the cells.

The use of a hypertonic solution causes swelling and destruction of the cells and the chromosomes become free and separated from each other (metaphase plate), which makes it possible to count the chromosomes and perform chromosome analysis and identification. Almost every chromosome has the following parts:

a) *centromere* (primary membrane);

b) *arms* - parts of the chromosome on the sides of the centromere;

c) *telomeres* - the end sections of the arms. Telomeric ends of chromosomes prevent chromosomes from sticking together.

Some chromosomes have a secondary constriction. It is located closer to the end of the chromosome and separates a small area called a satellite. The thin threads that connect the satellites to the chromosome arms are involved in the formation of nucleoli. These areas in human chromosomes are the nucleoli organizers.

Secondary constrictions are usually found in acrocentric chromosomes. In humans, secondary constrictions are found on the long arms of chromosome pairs 1, 9, and 16 and on the terminal portions of the short arms of chromosomes 13-15 and 21-22.

The location of the centromere determines the **shape of the chromosomes:**

a) metacentric chromosomes - the centromere is located in the middle of the chromosome and divides its body into two equal arms; b) submetacentric chromosomes - the centromere is slightly offset from the center and divides the chromosome into arms of different lengths; c) acrocentric chromosomes have a centromere that is offset to one of the ends of the chromosome and divides its body into a short and long arm; d) telocentric chromosomes - the centromere is at the end of the chromosome. Such chromosomes are not found in a normal human karyotype.

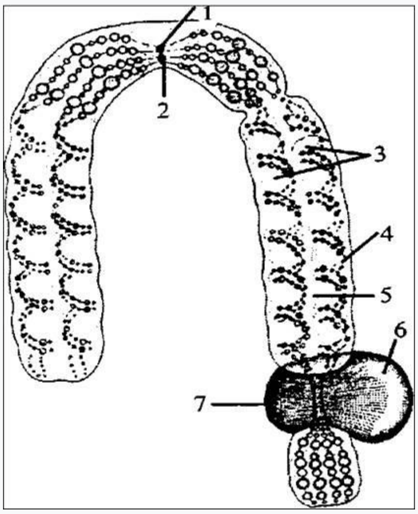


Fig. 10. Metaphase chromosome: 1 - centromere; 2 - kinetochore; 3 - chromatid; 4 - chromomere; 5 - matrix; 6 - nucleolus; 7 - secondary constriction.

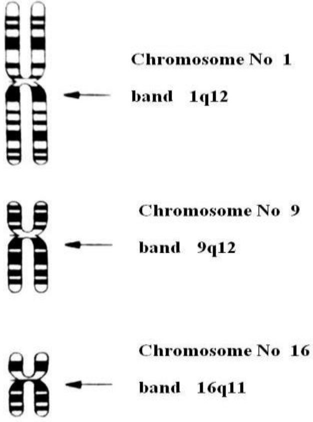


Fig. 11. Types of human chromosomes depending on the position of the centromere (metaphase stage): 1 – metacentric; 2 - submetacentric; 3 – acrocentric.

In the centromere area there is a **kinetochore** - the place of attachment of the spindle fibers. Morphometric analysis is used to study and identify chromosomes: the length of chromosomes is measured (in microns) and the centromeric index is determined (the ratio of the length of the short arm of the chromosome p to the length of the entire chromosome p+q, where q is the length of the long arm of the chromosome). In metacentric chromosomes, the centromeric index is about 50%, in submetacentric - less than 50%. The size of metaphase chromosomes ranges from 11 to 2.3 microns.

Chromosome rules:

1. The rule of constancy of the number of chromosomes: it is established that each species of plants and animals has a certain constant number of chromosomes and characteristic features of their structure - this is a species characteristic. The number of chromosomes does not depend on the degree of organization of organisms and phylogenetic relationship. Examples: chimpanzee (Anthropopithecus) - 48 chromosomes, crayfish (Astacus fluviatilis) - 116 chromosomes, fruit fly (Drosophila melanogaster) - 8 chromosomes.
2. The rule of chromosome parity: the number of chromosomes in a karyotype is even. Chromosomes that belong to the same pair are called homologous: they are the same in size, shape - the location of centromeres, chromomeres, interchromomeric filaments and other structural details and genetic composition coincide.
3. Chromosome individuality rule: non-homologous chromosomes have differences. Each pair of chromosomes differs from the others in shape, size, and genetic composition.
4. Chromosome continuity rule: each chromosome originates from a maternal chromosome (autoreproduction).

An idiogram is a systematized karyotype in which chromosomes are arranged in a sequence of decreasing length. The construction of an ideogram and the term itself were proposed by the Soviet cytologist S.G. Navashin.

Intensive study of human chromosomes in laboratories of different countries was accompanied by the creation by cytologists of systems of classification and nomenclature of chromosomes. There was a need to unify the nomenclature of human chromosomes. Work on creating a common system for designating human chromosomes was carried out in 1960 by a special commission assembled in the American city of Denver.

The «Standard System of Nomenclature of Human Mitotic Chromosomes» (Denver Chromosome Classification System) was created: according to shape and size, metaphase chromosomes are divided into 7 groups, which are designated by Latin letters: A, B, C, D, E, F, G, sex chromosomes are separately distinguished. Each pair of chromosomes has its own number from 1 to 22. Only sex chromosomes do not have numbers. They are designated X and Y chromosomes.

Many scientists have noted some heterogeneity in the density of staining in chromosomes stained by conventional methods. Casperson and co-workers (1968) found that after treatment of chromosomes with acrylonitrile-mustard, the fluorescence is not uniform, but is distributed in segments. The same segmental pattern can be obtained using Giemsa dye.

At the Paris Conference on Standardization and Nomenclature of Human Chromosomes in 1971, the following designations were adopted for the staining of **chromosome segments**:

a) *Q - segments* (quinacrine) - sections of chromosomes that are stained with quinacrine mustard.

b) *G - segments* (Giemsa) - segments that are stained with Giemsa stain during certain additional chromosome processing techniques.

Q and G segments are identical. The Q method allows you to detect the Y chromosome in the interphase nucleus by bright fluorescence.

c) *R segments* (reverse) are stained after heat treatment. They are located between the Q (or G) segments.

d) *C segments* (constitutive heterochromatin) are located around the centromeric regions of both chromosome arms.

Differential staining is associated with the chemical features of chromosomes (DNA nucleotides and proteins). Acrychin-mustard binds to areas rich in A=T pairs, R - segments correspond to areas rich in G=C pairs.

Differential staining allows you to clearly select homologous pairs and detect chromosomal aberrations. Each pair of chromosomes has its own transverse banding, its own order of placement, and its own number of transverse bands. Such analysis, combined with genetic observations, allowed us to begin compiling human chromosome maps, that is, to find the locations of genes on certain sections of chromosomes.

CHARACTERISTICS OF CHROMOSOME GROUPS AND NUMBERS

Group	Number	Size, µm	Centrometric index, %	Characteristic
A	1,2,3	11,0; 10,8; 8,3	chr. 1: 48-49 chr. 2: 38-40 chr. 3: 45-46	Often the long shoulder of Chr.1 has a «secondary constriction». Chr.2 is the largest submetacentric. Chr.3 is almost 20% shorter than Chr.1.
B	4-5	7,7	ch. 4,5: 24-30	Large submetacentric chromosomes.
C	6,7,8,9,10-11,12	7,2; 6,8; 5,7; 5,8; 5,8-5,8; 5,8	chr. 6,7,8,11,12: 27-35	Medium size, submetacentric. Chr.9 often has a secondary constriction in the q arm. The X chromosome resembles the longest ones from group C with a high centromeric index.
D	13-15	4,2	15	Acrocentric, have a satellite.
E	16,17,18	3,6; 3,5; 3,2	chr. 16-40 chr. 17-31 chr. 18-26	Short submetacentric chromosomes.
F	19-20	2,9	chr. 36-46	The smallest are metacentric. They are very different in differential coloration.
G	21,22	2,8; 2,3	chr. 13-33 16	Small acrocentric chromosomes. Y chromosome is larger than group G chromosomes. Satellites are absent. When stained with acrychin, the distal part of the long arm fluoresces.

The material basis of heredity and variability are nucleic acids. Nucleic acids (NA) are high-molecular organic compounds, biopolymers, the monomers of which are nucleotides. They were first discovered by F. Miescher in the nuclei of dead leukocytes (1869). The term nucleic acids (NA) was introduced by biochemist R. Altman in 1889. Evidence that DNA is directly involved in the transmission of hereditary information was obtained when studying microorganisms and viruses in the phenomena of transformation and transduction.

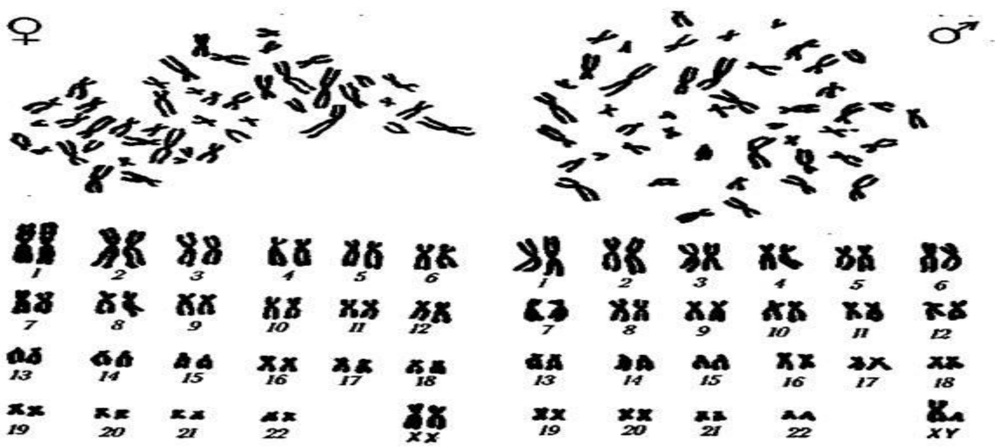


Fig. 12. Human karyotype: left - female, right - male. Top - metaphase plates, bottom - idiograms. In idiograms, chromosomes are arranged in pairs in decreasing order of length. Sex chromosomes are highlighted separately: in women - XX, in men - XY.

Questions for preparation

1. Definition of biology as a science.
2. The place and tasks of biology in the training of a doctor.
3. Definition of the concept of life at the current level of development of biological science.
4. Cell - an elementary structural and functional unit of living things.
5. Proto- and eukaryotes.
6. Cell theory, its current state and significance for medicine.
7. Morphophysiology of the cell. Cytoplasm and organoids.
8. Cell membranes. Chemical composition. Spatial organization and significance.
9. Active and passive types of transport of substances through the plasma membrane.
10. Structure and functions of the nucleus.
11. Chromatin: levels of organization (packaging) of hereditary material (euchromatin, heterochromatin).
12. Chemical composition of chromosomes.
13. Structure of metaphase chromosome.
14. Forms of chromosomes.
15. Human karyotype.
16. Morphofunctional characteristics and classification of human chromosomes.
17. The importance of studying the karyotype in medicine.
18. Cell cycle, its periodization.
19. Mitosis. Violations of mitosis.
20. Meiosis. Mechanisms that determine the genetic diversity of gametes.

Substantial module 2 «Classical Genetics».

Topic 5,6. Mendel's laws. Monohybrid and dihybrid crosses. Types of crosses. Lethal genes.

Genetics explores heredity, patterns and mechanisms of inheritance, variability at all levels of organization of living matter.

Heredity - it is the ability of organisms to preserve and transmit to future generations a certain form of life, i.e. a set of morphological and physiological features. Every organism develops according to its own genetic program inherited from its parents, i.e. it has a set of genes that act in a unique way during ontogenesis, have complex interactions with each other and with the environment and form a certain genotype and phenotype.

The following research methods are used in genetics.

Hybridological - method of planned crossing and analysis of offspring from this crossing. This is the oldest informative classical method of genetics, widely used for all organisms, but for humans (at the organismal level) it is not used. Recently, the hybridological method in human genetics is gaining relevance at the cellular level (the method of hybridization of somatic cells).

A ***genealogical method*** is used to study human heredity- method of compiling and analyzing pedigrees. Using this method, find out whether the trait is inherited, the nature of its inheritance and make a prognosis for offspring. To compile pedigrees use certain symbols and form of record.

Twin Method - a method of research and observation of twins. The most valuable are monozygotic (identical) twins, as their heredity is almost identical and embryogenesis takes place under the same conditions. This method allows us to identify the role of genotype and environment in the formation of the organism and personality.

Medical and genetic consultations use the ***dermatoglyphic method,*** ie the study of the individual pattern of the skin of the palms (palmoscopy), toes (dactyloscopy) or feet (plantoscopy) and the establishment of correlations between morphological features of the skin and hereditary pathologies.

Cytogenetic the method is used to study the karyotype: morphology, number and characteristics of human chromosomes and other creatures. It allows you to detect chromosomal abnormalities, which is important for the diagnosis of hereditary pathologies.

Biochemical method widely used for molecular genetics, genetics of ontogenesis, elucidation of features or pathologies of metabolism, detection of enzymopathies, etc.

Molecular genetic methods are various methods used to detect variations in the structure of the studied DNA regions and to decipher the primary nucleotide sequence.

In modern science it is impossible to do without a statistical method that can prove the reliability of research results. In general, modern genetics can use almost the entire arsenal of biology methods.

Population-statistical methods allow to determine the genetic composition of the population and to give a forecast of its dynamics, genetic load, frequencies of individual genes and genotypes and to outline the prospects for its development.

Gene- is a structural and functional unit of heredity. In terms of structure, a gene is a region of a DNA molecule, for eukaryotes it is a region of a chromosome, for prokaryotes it is a region of a plasmid (or circular DNA molecule), i.e. it is a specific sequence of nucleotides.

By the nature of the action there are the following *types of genes:*

constitutive- maintain a constant level of activity of the body, regulate the synthesis of proteins needed by the cell, support cell metabolism;

modifiers - change the manifestations of other genes;

mutators - can dramatically change some features of the body;

inducible - show activity in response to a special signal from the cell or organism;

pleiotropic - affect the manifestation of several symptoms;

lethal- cause the death of the organism in the embryonic period, if they are in a homozygous state;

sublethal- genes that significantly reduce the viability of the organism, lead to its death before puberty;

epistatic- genes that inhibit the action of other, non-allelic genes (hypostatic);

complimentary **-** complementary genes, which when combined form a different phenotype in comparison with the action of each gene separately.

Genes located in the same regions (loci) of homologous chromosomes have the same nucleotide sequences and are responsible for the formation of a single trait, called ***allelic.***

In most cases, there are two variants of allelic genes: *dominant* and *recessive*. The ***dominant gene*** is a gene whose expression is completely predominant in the first generation, suppressing the manifestation of an alternative, recessive gene. Manifestation of ***recessive genes*** is possible only when allelic genes are the same. In this case, the organism is called *homozygous* (homo - similar). If an individual has both variants of allelic genes, it is called *heterozygous* (hetero - different).

The totality of all genes in an organism is called a ***genotype.*** If we study the inheritance of not all, but one or more genes, then the genotype means a combination of them.

A ***genome*** is a collection of all genes in a haploid (n) set of chromosomes in an organism. The female gamete is an egg that contains the mother's genome, and the male gamete is the sperm that contains the father's genome. During fertilization, these genes merge, there is a recombination of genes, traits, as a result of which the new organism acquires individuality. ***Gene pool*** - the totality of all genes of a given species or population.

Phenotype- is a set of all external and internal features and properties of the organism, which are formed under the influence of genotype and its interaction with the environment.

Types of interaction of allelic genes:

Complete dominance. In this case, the dominant gene completely suppresses the manifestation of the recessive gene and in the phenotype is only the dominant gene (A> a).

For example: in a marriage between a homozygous woman with normal skin pigmentation (dominant trait) and an albino man (recessive trait), the children will be normal. A> a.

***Incomplete dominance*.** In this case, the dominant gene does not completely suppress the manifestation of another, which is denoted as Ā; both allelic genes are almost equal in strength and equally affect each other A = Ā. At such interaction the intermediate phenotype is formed.

For example, when crossing night beauty plants with red flowers (dominant trait) with plants with white flowers (recessive trait) hybrids will be with pink flowers.

Codominance. In this case, none of the allelic genes suppresses the other. Each allelic gene forms its own manifestation of the trait in the homozygote, and in the heterozygote they form a new, not an intermediate manifestation of the trait.*For example*, the blood group according to the MN system is inherited by the type of codominance: if a person has both allelic genes in the M state - blood group M; if both genes are in state N - blood group N; if one allelic gene in state M and the other in state N is a blood group MN, qualitatively different from M and N. dominance.

Types of crosses:

1. ***monohybrid*** is a type of crossing in which we observe the inheritance of only one trait. It is incorrect to say that monohybrid crossing is a crossing in which the parental organisms differ in one feature, because even identical twins have more differences;
2. ***dihybrid*** is a type of crossing in which the inheritance of two traits is analyzed simultaneously;
3. ***polyhybrid*** is a type of crossing, which analyzes the inheritance of several traits simultaneously;
4. ***analyzing*** is a type of crossing in which an organism with an unknown genotype is crossed with a recessive homozygote on this basis to show its homo- or heterozygosity.

Mendelian Genetics

A monk named Gregor Mendel developed several of the tenets of genetics in the 1860s based on his work with pea plants. By crossing only true-breeding plants (those whose offspring only ever have the same traits as the parents) with different traits, he was able to determine the laws of inheritance

The successes achieved by Mendel are partly due to the successful selection of the object for experiments - *garden peas* (Pisum sativum).

This object has certain advantages:

1) many varieties that clearly differ in a number of features;
2) plants are easy to grow;
3) plants are self-pollinating;
4) traits from generation to generation remain unchanged ("clean lines");
5) artificial crossing of varieties is possible, as a result of which fertile hybrids appear.

Mendel's first law: *law of homogeneity of first-generation hybrids***.**
Mendel's second law: *law of splitting.* **Monohybrid Cross.**

A cross in which only one trait is being studied is said to be monohybrid (mono– means «one»).Gregor Mendel used pea plants with either purple or white flowers. The parent or P generation refers to the individuals being crossed; the offspring are the filial or F generation. The F distinction can be applied to multiple generations by using numeric subscripts. If we think of our grandparents as the P generation, then our parents are F_1, and we are F_2. In Mendel's experiments, the purple flowers were determined to be homozygous dominant. This genotype can be designated as PP. The white flowers were homozygous recessive; their genotype would be written pp. When crossed, the genotype of the F1 generation will be 100 percent Pp; we will show this graphically in a moment. What does this mean in terms of the color (phenotype) of our F1 flowers? They will all be purple, because purple is dominant to white.

The discovered pattern was called the ***law of homogeneity of first-generation hybrids*****.** The manifestation of the trait in the first generation was called *dominant*, and the manifestation that was suppressed, i.e. did not manifest, was called *recessive*. Mendel proposed to denote by letters of the Latin alphabet. Alleles of one gene are usually denoted by one letter, but dominant - capital (A), and recessive lower (a). An individual homozygous for the dominant allele is recorded as ***AA***, for recessive - ***aa***, heterozygotic - ***Aa***. Experiments have shown that the *recessiv*e allele is manifested only in the homozygous state, and the *dominant* - in both homozygous and heterozygous.

It is suggested to record experiments on crossing in the form of schemes. It was agreed to denote parents by the letter *P* (Latin parents - father), individuals of the first generation - *F1* (Latin filii children), individuals of the second generation - *F2,* etc. Crossings are denoted by the sign of multiplication (x), the genotypic formula of the maternal individual is written first, and the paternal - the second. In the first line the genotypic formulas of the parents are written, in the second - the types of their gametes, in the third - the genotype of the first generation hybrids.

R: ♀ AA x ♂ aa
Gametes: A a
F1: Aa
100%

Since the first parent has only one type of gametes (A) and the second parent also has one type of gametes (a), only one combination is possible - Aa. All first-generation hybrids turned out to be monotonous; heterozygous by genotype and dominant (yellow seed) by phenotype.

Thus, *Mendel's first law, or the homogeneity of first-generation hybrids,* can be formulated as follows: when crossing homozygous individuals that differ in one pair of alternative traits, all offspring in the first generation are homogeneous in both phenotype and genotype.

Punnett Square

We will want to be able to draw and analyze a Punnett square, which is a diagram that predicts the relative genotypic and phenotypic frequencies that will result from a crossing of two individuals. The alleles of the two parents are arranged on the top and side of the square, with the genotypes of the progeny being represented at the intersection of these alleles . The genotypes of the progeny will be the sum of the parental alleles.

If the F_1 generation crosses with itself (self-cross), the resulting offspring (F_2 generation) will be more phenotypically and genotypically diverse than their parents. First, note that the F1 generation is 100 percent Pp; all the flowers are purple heterozygotes. Now, if we take two of these individuals and cross them, we will get the Punnett square shown on the right side. The genotypic percentages will be 25 percent PP, 50 percent Pp, and 25 percent pp. Phenotypically, we get a 3:1 distribution, because both the homozygous dominant and heterozygous dominant will result in a purple-flowering plant. We should clearly notice that, unlike the F_1 generation in which the phenotype and genotype had the same percentages (100 percent) in the F_2 generation, there is a 1:2:1 distribution (homozygous dominant:heterozygous dominant:homozygous recessive) genotypically and a 3:1 distribution (purple:white) phenotypically. These ratios are, of course, theoretical and will not always hold true. They represent the probabilities of certain outcomes but not complete certainty. Usually, the more offspring a couple has, the closer their phenotypes will be to the expected ratios.

The law of splitting. When crossing homogeneous hybrids of the first generation with each other (self-pollination or related crossing) in the second generation there are individuals with both dominant and recessive manifestations of the trait, i.e. splitting is observed.

R: ♀ Aa x ♂ Aa
Gametes: A a A a
F1: AA: 2Aa: aa
25% 50% 25%

Summarizing the factual material, Mendel concluded that in the second generation there is a splitting of the manifestations of the trait in certain frequency ratios, namely: 75% of individuals have dominant manifestations of the trait, and 25% - recessive (phenotype ratio 3: 1). However, the genotype ratio is 1AA: 2Aa: 1aa. This pattern is called ***Mendel's second law, or splitting law.***

From Mendel's second law we can conclude:

1) gene alleles, being in a heterozygous state, do not change each other;
2) during maturation of gametes in hybrids approximately the same number of gametes with dominant and recessive alleles is formed;
3) When fertilized, male and female gametes carrying dominant and recessive alleles are freely combined.

Thus, ***Mendel's second law*** is formulated as follows: when crossing two heterozygous individuals, ie hybrids, which are analyzed for one pair of alternative manifestations of the trait, in the offspring there is a split by phenotype in the ratio 3: 1 and genotype 1: 2: 1.

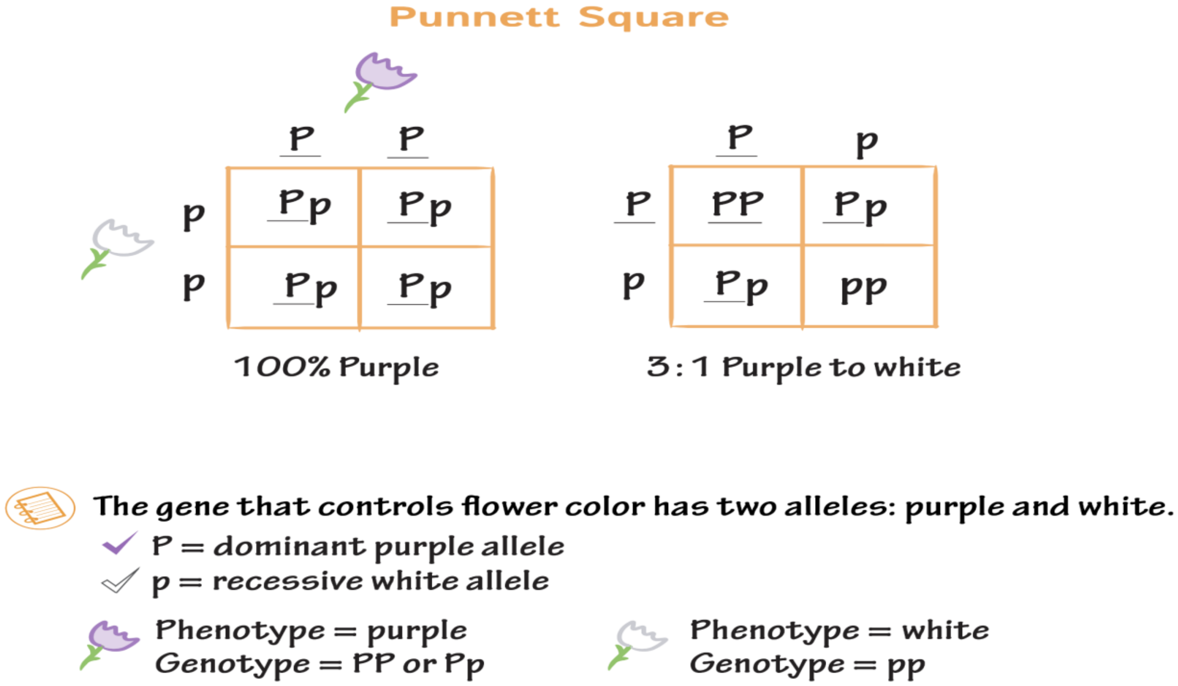


Fig. 13. Mendel's second law.

Mendel's III law (law of independent inheritance and combination of traits)

The third law of heredity was established in ***dihybrid crossing.*** The inheritance of two pairs of alternative traits was analyzed: yellow and green color of seeds and smooth and wrinkled shape of pea seeds.

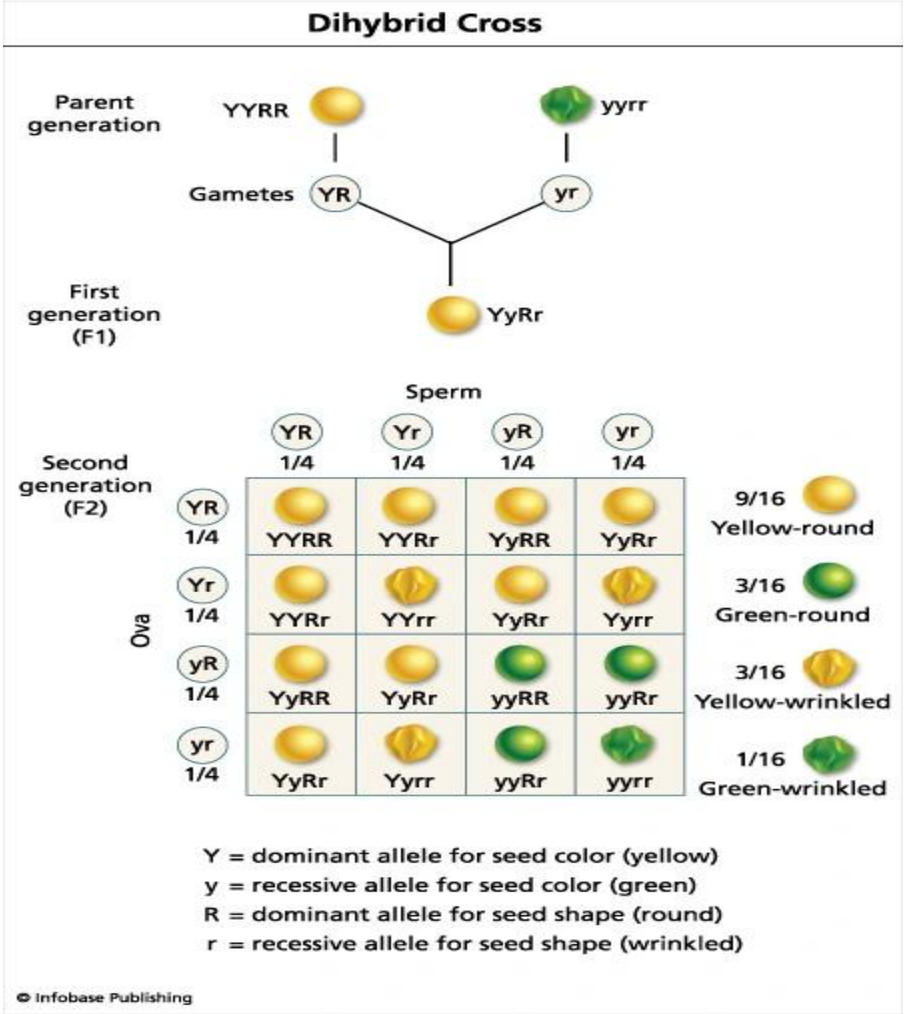


Fig.14. Mendel's III law.

Given:

Y- gene for yellow color of pea seeds;
y- gene for green color of pea seeds;
R- gene of smooth shape of pea seeds;
r- the gene of a wrinkled form of pea seeds.
YYRR- genotype of homozygous yellow and smooth peas,
yyrr- genotype of homozygous green and wrinkled peas.

Solution:

P:♀YYRR *X* ♂yyrr
Gametes (G): YR ; yr

F1: YyRr- diheterozygous yellow smooth peas (uniformity of first generation hybrids).

P: ♀YyRr *X* ♂YyRr
Gametes (G):
YR YR
Yr Yr
yR yR
yr yr

Punnett square

Gametes	YR	Yr	yR	yr
YR	YYRR	YYRr	YyRR	YyRr
	yellow, smooth	yellow, smooth	yellow, smooth	yellow, smooth
Yr	YYRr	YYrr	YyRr	Yyrr
	yellow, smooth	yellow, wrinkled	yellow, smooth	yellow, wrinkled
yR	YyRR	YyRr	yyRR	yyRr
	yellow, smooth	yellow, smooth	green, smooth	green, smooth
yr	YyRr	Yyrr	yyRr	yyrr
	yellow, smooth	yellow, wrinkled	green, smooth	green, wrinkled

The results of ***dihybrid crossing*** and the ***3rd law of heredity*** are determined by the fact that:

a) the genes we analyzed are located on different non-homologous chromosomes, only in this case there will be an independent inheritance and random combination of traits;

b) during meiosis in anaphase I there is an independent difference of homologous chromosomes;

c) in anaphase II there is an independent divergence of chromatids (allelic genes). Due to the independent separation of chromosomes and chromatids, gametes with different combinations of genes are formed;

d) During fertilization there is a random combination of gametes with different combinations of allelic and non-allelic genes, as a result of which zygotes (organisms) with different genotypes and combinations of traits are formed. A certain proportion of offspring (6/16 or 37.5%) have phenotypes with new combinations of traits.

Gamete purity law

Allelic genes, being in a heterozygous state, do not merge, do not change each other and, without losing their individuality, are transferred to gametes. Gametes are «***pure***»: they carry only one of the two alleles of a particular gene.

The fact that the recessive trait (green color of seeds), which was absent in the first generation F_1 hybrids, reappeared in 1/4 of the second generation F_2 hybrids, G. Mendel explained that it is not the traits themselves that are inherited, but hereditary factors (genes).), which determine their development and that these factors are discrete. In hybrids F (Aa) there are two hereditary factors, one of them A is responsible for the yellow color of the seeds, the other a - for green.

This pattern is called the law of «***purity of gametes***» and received a cytological justification:

a) for each trait in the body are responsible for two allelic genes located (hair dryer) in homologous chromosomes;

b) a haploid set of chromosomes (one of the homologous chromosomes, and hence one of the allelic genes) enters the gamete during meiosis. Gametes remain "pure" because they have (normally) one allele of the gene, which determines one of the alternative features;

c) during fertilization, during the fusion of gametes, the diploid set of chromosomes is restored, and hence the parity of allelic genes.

Lethal genes

Deviation from the expected results of cleavage is often associated with the phenotypic manifestation of lethal alleles, when cleavage among second-generation hybrids may differ from that expected, because homozygotes and heterozygotes for some alleles have different viability. An allelic gene that, when manifested in a phenotype, leads to the death of an individual is called ***lethal.***

For example, the platinum color of fox fur is highly valued for the manufacture of fur products. It arose at the beginning of the XX century as a result of mutation and is caused by a dominant allele (P): when crossing platinum foxes among themselves there are individuals with both platinum and silver color of fur.

Attempts to breed homozygous platinum foxes were unsuccessful, although in theory it seemed possible. Analytical crosses revealed that all platinum foxes are heterozygous because the offspring are as follows: in 58 broods - 127 platinum and 58 silver puppies (ie the ratio was close to 2: 1, not 3: 1, as might be expected). according to the law of splitting). In addition, when silver foxes mated with each other or with platinum, in the broods mostly had 4-5 puppies, and when crossing platinum foxes with each other only 3-4. It turned out that individuals homozygous for the platinum color allele do not exist at all, because embryos with this genotype (PP) die in the early stages of development. A similar phenomenon is known for gray doodle sheep, in which lambs, homozygous for the dominant allele of gray wool, die due to underdevelopment of the digestive system. Mice are known to have a lethal short-tailed allele.

Thus, the quantitative ratios of different phenotypic groups of offspring are influenced by *lethal alleles*, which, manifesting themselves in the phenotype, destroy the organism before the full completion of its development. In the case of platinum foxes, the dominant allele was lethal, but its negative effect was manifested only in the homozygous state. Most lethal alleles are recessive and therefore cause the death of individuals homozygous for them (for example, the allele that causes hydrocephalus in Ayrshire calves).

Mendelian signs in humans, monogenic diseases, monogenic inheritance

Traits that are inherited according to the laws established by G. Mendel are called mendelian. Some mendelian signs of the person are listed in the tab. The total number is over 2300.

Mendelian signs in humans

Dominant	*Recessive*
Normal signs	
Brown eyes Dark hair Oblique incision of the eyes Nose with a hump Wide gap between the incisors Teeth large, protruding	Blue eyes Blonde hair Straight incision of the eyes Straight nose Narrow gap between the incisors or lack thereof The usual shape and position of the teeth
Dimples on cheeks White curl of hair The presence of freckles The lobe of the ear is free Lips are full Better possession of the right hand Blood rhesus-positive The ability to curl the tongue with a tube Ability to feel the bitter taste of FTC (phenylthiourea)	No dimples Even hair pigmentation No freckles The lobe of the ear grew Lips thin Better possession of the left hand Rhesus-negative blood Inability to curl the tongue with a tube Inability to feel the bitter taste of FTC
Pathological signs	
Dwarf chondrodystrophy	Normal skeletal development
Polydactyly (6 or more fingers)	Normal number of fingers
Brachydactyly (short-sightedness)	Normal structure of the fingers
Syndactyly (finger fusion)	Normal structure of the fingers
Normal blood clotting	Hemophilia (blood clotting disorder)
Polyposis of the colon	No polyposis
Normal color perception	Color blindness (color perception disorder)
The presence of pigments in the skin, hair	Albinism (lack of pigments)
Normal absorption of phenylalanine	Phenylketonuria (inability to digest
Normal absorption of lactose	galactosemia (inability to absorb lactose)
Normal absorption of fructose	Fructosuria
Normal hemoglobin molecule structure	Sickle cell anemia

All mendelian traits are discrete and are controlled monogenically, i.e. by one gene (monogenic inheritance). Mendelian traits include monogenic diseases, which are also controlled by a single gene. There are the following types of monogenic inheritance: autosomal dominant, autosomal recessive, X-linked (dominant and recessive), Y-linked. Traits of these types of inheritance are identified using a genealogical method by compiling and analyzing pedigrees.

Topic 7. Interaction of allelic genes. Multiple allelism. Blood groups. Interaction of non-allelic genes.

The development of any traits in organisms is the result of a complex interaction of genes, or rather, between the products of their activity - protein enzymes. This interaction can be depicted in the form of a diagram:

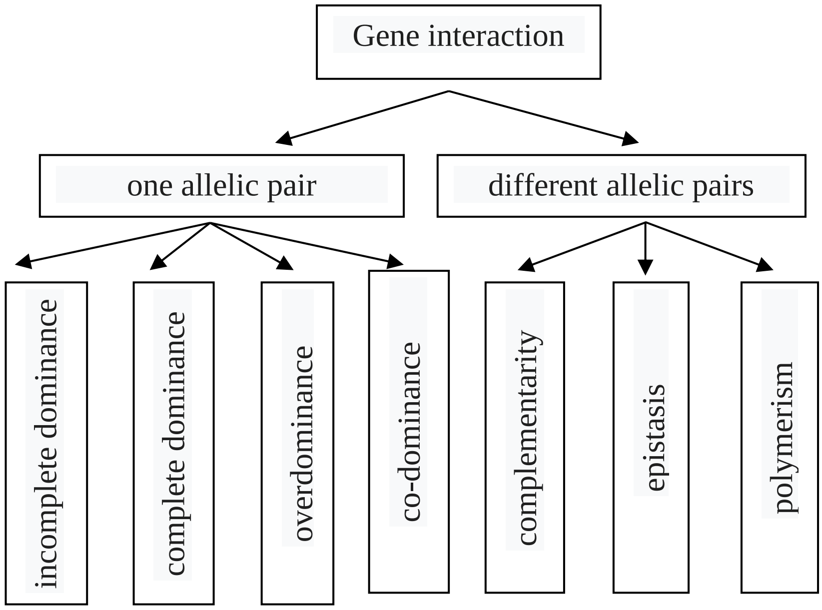


Fig. 15. Interaction of genes.

Allelic genes are genes located in the same areas (loci) of homologous chromosomes and cause the formation of alternative traits.

The following types of interaction of allelic genes are distinguished:

complete dominance, incomplete dominance, overdominance, codominance.

Complete dominance is suppression, the manifestation in hybrid cells of a gene from one parental genome (the totality of the organism's hereditary material), while the homologous gene from the other parental genome is present but not manifested, its action is suppressed.

A – yellow P: ♀AA X ♂aa
a – green F_1: Aa (yellow)

Incomplete dominance is a form of interaction when, in a heterozygous organism (Aa), the dominant gene (A) does not completely suppress the recessive gene (a), resulting in a trait intermediate between the parental traits:

A – red flowers   P: ♀*AA* X ♂*aa*
a – white flowers F_1: *Aa* (pink)

Overdominance – when a gene in the heterozygous state is stronger than in the homozygous state.
AA – normal lifespan;
Aa – prolonged lifespan;
aa – lethal (in Drosophila).

Heterosis in plants and animals – «hybrid strength» - is used in breeding (viability, rapid growth, weight, fertility).

Codominance is the simultaneous manifestation of alleles in a heterozygote in the absence of any tendency for one to dominate over the other. A classic example is the AB0 blood group system, when the red blood cells of a person with blood group IV carry antigens on their surface that are controlled by both alleles.

Inheritance of ABO and MN blood groups; genetics of blood groups The discovery of the ABO blood group system belongs to K. Landsteiner (1901). The ABO blood group system in humans is inherited according to the type of multiple alleles of one autosomal gene located on chromosome 9, the locus of which is designated by the letter I (from the word isohemagglutinogen). The study of the nature of inheritance of different blood groups of the ABO system has established that they are determined by different combinations of three alleles of one allelomorphic group of genes, which are designated IA, Ib and I0. They determine four phenotypes: with the first group I (0), the second II (A), the third III (B), the fourth IV (AB) (table).

ABO blood groups

Blood groups (phenotype)	Genotypes	Red blood cell antigens	Blood plasma antibodies (agglutinins)
I (0)	I^0I^0	there is no	α i β
II (A)	I^AI^A, I^AI^0	A	β
III (B)	I^BI^B, I^BI^0	B	α
IV (AB)	I^AI^B	A, B	there is no

Each phenotype is distinguished by specific antigen proteins contained in erythrocytes and antibodies concentrated in the blood serum. Phenotype I (0) is due to the absence of antigens A and B in erythrocytes and the presence of antibodies α and β in the blood serum. Phenotype II (A) is characterized by the presence of antigen A in erythrocytes and antibodies β in the blood serum.

Phenotype III (B) is associated with the presence of antigen B in erythrocytes and α antibodies in the blood serum. Phenotype GU (AB) depends on the presence of antigens A and B in erythrocytes and the absence of α and β antibodies in the blood serum.

Antigen A and antibody a are never found together, as is antigen B with antibody p. When antigens interact with antibodies of the same name, erythrocytes stick together (agglutination), which indicates incompatibility of the blood of the donor and recipient. When blood is transfused, it is necessary that the donor's antigens do not meet with the recipient's antibodies of the same name.

Since the first group has no antigens, people with such blood are called *universal donors*, and people with the fourth group are called *universal recipients*.

The inheritance of two alleles out of three possible obeys Mendelian laws. Blood groups II (A) and III (B) are inherited in an autosomal dominant manner, group I (0) in an autosomal recessive manner. Genes Ia and IB behave dominantly in relation to gene I0. If parents have blood group II (A), then their children can have II (A) and I (0), but not III (B) and not IV (AB). The fourth blood group (AB) is not inherited according to the rules of G. Mendel, but according to the type of codominance. Since blood groups are genetically determined and do not change throughout life, their determination can help in the case of disputed paternity. It must be remembered that it is not possible to establish by the blood group that this particular man is the father of the child. We can only say that he could have been the father of the child or that paternity is excluded.

In people with IV (AB) blood group, in 0.1-0.2% of cases, a special position of genes is observed - *cis-position*, when both genes Ia and Ib are located on the same chromosome. Then, in the marriage of such a person with a person with I (0) blood group, the birth of children with I (0) blood group is possible, which must be taken into account during medical and genetic counseling and forensic medical examination.

People with the IaIa genotype are phenotypically no different from people with the IaI0 genotype, but their children have their own characteristics. In children from a marriage in which one parent has the IaI0 genotype and the other has the I0I0 genotype, half of the children have the A phenotype (with the IaI0 genotype), and half have the 0 phenotype. If one parent has the IaIa genotype and the other has the I0I0 genotype, then all children have the A phenotype (with the IaI0 genotype). The same difference is observed in people with the IBIB and IBIB0 genotypes.

Offspring expected from marriage, according to parents' blood types

Types of combinations	Blood groups of parents	Blood groups in children
1	00x00	00
2	00xA0	A0, 00
	00xAA	A0

3	00xB0	B0, 00
	00xBB	B0
4	A0xA0	AA, A0, 00
	AAxA0	AA, A0
	AAxAA	AA
5	A0xB0	AB, A0, B0, 00
	AAxB0	AB, A0
	A0xBB	AB, B0
	AAxBB	AB
6	B0xB0	BB, B0, 00
	B0XBB	BB, B0
	BBxBB	BB
7	00xAB	A0, B0
8	A0xAB	AA, AB, A0, B0
	AAxAB	AA, AB
9	B0xAB	AB, BB, A0, B0
	BBxAB	AB, BB
10	ABxAB	AA, AB, BB

Note: Within each of the ten types of combinations, the genotype of the blood group can be distinguished only on the basis of studying the descendants.

Phenotypic manifestations of the AB0 blood group system are among the most stable signs and never change during a person's life.

More than 20 different blood systems are distinguished by the presence of antigens, including the Rh factor and the MN system.

Codominance also occurs in the inheritance of blood type according to the MN system, discovered in 1927. This system is determined by two alleles: I^M and I^N. Both alleles are codominant, so there are people with the genotype I^MI^M (in the phenotype they have the M factor), I^NI^N (in the phenotype they have the N factor), I^MI^N (in the phenotype they have both M and N factors). In the blood serum of people with a particular phenotype according to this blood group system, there are no antibodies to the corresponding antigens, as is the case in the AB0 system. Therefore, this system may not be taken into account when blood transfusions are performed. Among Europeans, the I^MI^M genotype occurs in approximately 36%, I^NI^N - in 16%, I^MI^N - in 48%.

Inheritance of Rh factor

Rh factor is a protein (antigen), so named because it was first isolated (1940) from the erythrocytes of the rhesus monkey (Macacus resus), and then from humans. About 85% of Europeans are able to synthesize it and are Rh-positive (Rh), 15% are unable and are called Rh-negative (Rh-). Rh factor is caused by three dominant closely linked genes (C, D, E), located on the first chromosome. They are inherited as in monohybrid crossing. The main role belongs to the D antigen, if it is determined, then the blood belongs to Rh-positive (DD or Dd), if not determined - to Rh-negative (dd).

The Rh factor must be taken into account during blood transfusion and transplantation, because antibodies are produced in the body against it. Rh factor can be the cause of Rh conflict between mother and fetus. When a woman with Rh negative blood marries a man who is Rh positive homozygous, all children will be Rh positive, and if he is heterozygous, 50% will be Rh positive and 50% will be Rh negative.

1) P: dd x DD
G: d D
F: Dd
Rh-positive –100%

2) P: dd x Dd
G: d D,d
F: Dd dd
Rh-positive – 50%
Rh-negative – 50%

The conflict occurs when the mother has Rh-negative blood, and the child has received the dominant D allele from the father and is Rh-positive. The blood of the mother and the fetus does not mix. Therefore, the first pregnancy ends normally. But during the birth of the first child, when the placenta separates, the child's red blood cells enter the mother's body, where antibodies are formed against the Rh antigen.

During subsequent pregnancies, these antibodies penetrate the placental barrier into the fetal blood, combine with the Rh antigen, causing erythrocytes to stick together and lyse (*erythroblastosis, or hemolytic disease of the newborn*). Moreover, with each subsequent birth, the disease in children manifests itself in a more severe form. If a Rh-negative girl receives a Rh-positive blood transfusion before marriage, the first child (if she is Rh-positive) will be non-viable. Therefore, even a single transfusion of Rh-positive blood to girls with Rh-negative blood is absolutely unacceptable.

In Japan, Korea, China, India, hemolytic disease of newborns is very rare. This is explained by the fact that the frequency of Rh(-) among them is very low (from 0 to 1.5%). Rh(-) blood group is rarely found in Eskimos, Evenks. In Australian aborigines, Rhesus conflict in pregnant women does not exist, since the frequency of the Rh(+) gene in them is 100%.

Hemolytic disease of the newborn was described over 400 years ago. It occurs in case of incompatibility not only according to the Rh system, but also according to the AB0 system: most often, when the mother has group I (0), and the child has group II (A) or III (B).

Interaction of non-allelic genes

The main forms of interaction of non-allelic genes are complementarity, epistasis and polymer. They mainly modify the classical formula of splitting by phenotype, established by G. Mendel for dihybrid crosses (9:3:3:1).

Complementarity (Latin complementum - addition) - a form of interaction of non-allelic genes, in which one gene complements the action of another, non-allelic gene. When simultaneously present in the genotype, complementary genes determine the development of a new trait (neoplasia).

In humans, normal hearing is due to the complementary interaction of two dominant non-allelic genes D and E, one of which determines the development of the cochlea, the other - the auditory nerve. People with genotypes D-E- have normal hearing, with genotypes D-ee and ddE - deaf. In a marriage where parents are deaf (DDee x ddEE), all children will have normal hearing (DdEe).

The gray color of the coat in mice is controlled by two genes. Gene A determines the synthesis of pigment, gene B ensures the accumulation of pigment mainly at the base and tips of the hair. Crossing diheterozygotes (AaBbxAaBb) leads to the splitting of hybrids in the ratio 9:3:4 (9 – «agouti» color: 3 - black coat: 4 - white coat). The numerical ratios can be as 9:7; 9:6:1 (a variation of Mendelian splitting).

To protect against viruses, immunocompetent human cells produce a specific protein called interferon. Its production in the body is associated with the complementary interaction of two non-allelic genes located on different chromosomes. Adult hemoglobin contains four polypeptide chains, each encoded by a separate, independent gene. Therefore, four complementary genes are required for the synthesis of the hemoglobin molecule.

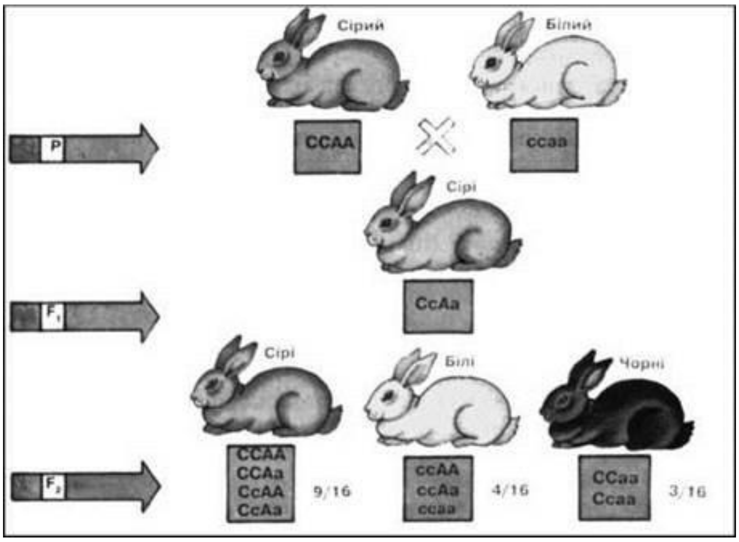


Fig. 16. Complementary interaction of non-allelic genes in rabbits.

In animals (mice, rats, rabbits), the formation of dark fur color requires the presence of two dominant non-allelic genes (C and A), one of which determines the presence of pigment, and the other - its distribution throughout the hair. If one of the genes is in the homozygous recessive state (cc), then the pigment is not formed and white individuals (albinos) are born.

Epistasis is the interaction of non-allelic genes, in which one gene suppresses the action of another, non-allelic, gene. The first gene is called *epistatic*, or suppressor (inhibitor), the other, *non-allelic*, gene is *hypostatic*. If the epistatic gene is dominant, epistasis is called dominant (A>B). And, conversely, if the epistatic gene is recessive, epistasis is recessive (aa>B or aa>bb). The interaction of genes in epistasis is the opposite of complementarity.

In chickens, the dominant allele C of one gene determines the development of feather color, but the dominant allele I of another gene is its suppressor. Therefore, chickens with the genotype I-C- are white, and with the genotypes iiCC and iiCC -

colored. In the crossing of white chickens (IICC x iiCC), the hybrids of the first generation F_1(IiCc) will be white, but when F_1 is crossed with each other in the second generation F_2, a split in phenotype will occur in the ratio 13:3. Of the 16 individuals, 3 will be colored (iiSS, iiSS) because they lack the dominant suppressor gene and have the dominant color gene. The other 13 individuals will be white. This example illustrates the phenomenon of dominant epistasis.

An example of recessive epistasis is the *Bombay phenomenon* - an unusual inheritance of blood groups of the ABO system, first discovered in one Indian family. In a family where the father had blood group I (0) and the mother - III (B), a girl with group I (0) was born, she married a man with blood group II (A) and they had two girls: one with blood group IV (AB), the other with I (0).

The birth of a girl with IV (AB) blood group in a family where the father had II (A) and the mother - I (0) was unusual. Geneticists explained this phenomenon as follows: the girl with group IV (AB) inherited the I^a allele from the father and the I^b allele from the mother, but the I^b allele was not phenotypically manifested in the mother, because in her genotype there was a rare recessive epistatic gene s in the homozygous state, which suppressed the phenotypic manifestation of the I^b allele. In the case of epistatic gene interaction, the split in phenotype in F2 is 13:3; 12:3:1 or 9:3:4, etc.

Hypostasis is the interaction of non-allelic genes, in which the dominant gene of one allelic pair is suppressed by the epistatic gene from another allelic pair. If gene A suppresses gene B (A>B), then in relation to gene B the interaction of non-allelic genes is called hypostasis, and in relation to gene A - epistasis.

Polymerism - the interaction of non-allelic genes, in which the same trait is determined by several dominant non-allelic genes, which act on this trait uniquely, to the same extent, enhancing its manifestation. Such genes are called polymeric (plural, polygenes) and are denoted by one letter of the Latin alphabet, but with different numerical indices.

For example, dominant polymeric genes are A1, A2, A3, etc., recessive ones are a1, a2, a3, etc. Accordingly, genotypes are designated as A1A2A3; a1a2a3a.,. Traits that are controlled by several genes (polygenes) are called polygenic, and the inheritance of these traits is polygenic, in contrast to monogenic, where the trait is controlled by one gene. The phenomenon of polymerization was first described in 1908 by the Swedish geneticist G. Nilsson-Ele while studying the inheritance of grain color in wheat.

The color of seeds of wheat, oats, etc. can range from red to white. The intensity of the color depends on the number of dominant genes in the genotype.

The content of all four dominant alleles (A1A1A2A2) determines a dark red color, the absence of dominant genes (a1a1a2a2) - white, and genotypes with three, two or one dominant genes cause a transitional color from light red to pink and white (A1A1A2a2 or A1a1A2A2 - light red color, A1A1a2a2 or a1a1A2A2 - pink color, a1a1b2b2 - white color). Splitting by phenotype 15:1.

Polymerization can be cumulative and non-cumulative. In cumulative polymerization, each gene individually has a weak effect (weak dose), but the number of doses of all genes in the final result is summed up, so that the degree of expression of the trait depends on the number of dominant alleles. The summation of doses of polymeric genes (additivity) ensures the existence of continuous series of quantitative changes.

By the type of polymer, a person inherits height, body weight, skin color, mental abilities, blood pressure, and in nature, productivity, egg production, milk production, etc. Thus, skin pigmentation in a person is determined by 4-6 pairs of polymer genes. The genotype of the indigenous people of Africa contains predominantly dominant alleles (P1P1P2P2P3P3P4P4), while in representatives of the Caucasian race there are recessive alleles (p1p1p2p2p3p3p4p4). From the marriage of a Negro and a white woman, children with an intermediate skin color are born - mulattoes (P1p1P2p2P3p3P4p4). If the spouses are mulattoes, then the birth of children with skin pigmentation from the lightest to the darkest is possible.

In typical cases, quantitative traits are inherited polygenically. However, in nature there are examples of polygenic inheritance of qualitative traits, when the final result does not depend on the number of dominant alleles in the genotype - the trait either manifests itself or does not manifest itself (non-cumulative polymorphism).

Pleiotropy (from the Greek πλείων - more numerous and τροπή - direction, turn) - the dependence of several traits on one gene, or the multiple modifying action of one gene. There is no unambiguous relationship between genotype and phenotype. The same gene can act on different traits of the organism. Thus, in higher plants, the gene that determines the color of flowers controls the color of the stems.

In humans, a dominant gene that causes arachnodactyly («spider fingers») simultaneously causes a disorder of connective tissue development, an anomaly of the lens of the eye, and a heart defect - aortic aneurysm (Marfan syndrome). Another example, a person can be a carrier of a gene that causes the absence of sweat glands. At the same time, this gene leads to the absence of some teeth, etc.

The manifestation of pleiotropy depends on the stage of ontogenesis at which it acts - the earlier, the greater the effect.

Pleiotropic action can be primary and secondary. In primary pleiotropy, the gene simultaneously manifests its multiple effects.

For example, in Hartnapp's disease, a gene mutation leads to impaired absorption of the amino acid tryptophan in the intestines and its reabsorption in the renal tubules. This simultaneously affects the membranes of intestinal epithelial cells and renal tubules, with disorders of the digestive and excretory systems.

In secondary pleiotropy, there is one primary phenotypic manifestation of the gene, followed by a stepwise process of secondary changes that lead to multiple effects. Thus, in sickle cell anemia, homozygotes have several pathological signs: anemia, enlarged spleen, skin, heart, kidney, and brain lesions. Therefore, homozygotes for the sickle cell anemia gene usually die in childhood. All these phenotypic manifestations constitute a hierarchy of secondary manifestations. The primary cause, the direct phenotypic manifestation of the defective gene, is abnormal hemoglobin and sickle-shaped erythrocytes. As a result, other pathological processes occur sequentially:

clumping and destruction of erythrocytes, anemia, defects in the heart, kidneys, and brain. These pathological signs are secondary. Secondary pleiotropy is more common.

Multiple allelism

In the experiments of G. Mendel, genes existed in only two forms - dominant and recessive. But most genes are represented not by two, but by a larger number of alleles. In addition to the main alleles (dominant and recessive), there are also intermediate alleles. A series of alleles (three or more) of one gene is called multiple alleles, and the phenomenon itself is called multiple allelism.

Multiple alleles arise as a result of multiple mutations of the same chromosome locus. In the genotype of a diploid organism, only two alleles of one gene are represented, and in the population their number is practically unlimited.

A feature of interactions between multiple alleles is that they can be placed in one consecutive row, in which each member will be dominant to all subsequent ones and recessive to the previous ones. For example, in rabbits, solid dark color is due to the dominant allele A, homozygous recessive animals (aa) are white.

But there are several more alleles of this gene that have their own phenotype in the homozygous state - chinchilla ($a^{ch}a^{ch}$) and Himalayan (a^ha^h). Chinchilla rabbits are gray, Himalayans are white, but the tips of the ears, tail, legs and nose are colored. The entire series of alleles can be written as the sequential series $A>a^{ch}>a^h>a$.

Dark color will be rabbits with genotypes AA, Aa^{ch}, Aa^h, Aa, chinchilla - with genotypes $a^{ch}a^{ch}$, $a^{ch}a^h$, $a^{ch}a$, Himalayan - with genotypes a^ha^h, a^ha. Significance: multiple allelism increases the gene pool of the population, its genotypic and phenotypic polymorphism, which is important for evolution.

The inheritance of ABO blood types in humans is associated with a series of multiple alleles.

Topic 8. Gene linkage. Chromosome mapping

Independent combination of genes can only occur under the condition that the genes are located in different pairs of chromosomes. In each organism, the number of genes that independently combine during meiosis is limited by the number of chromosome pairs. But the number of traits of the organism that are controlled by genes is very large, and the number of chromosome pairs is small.

If we assume that each chromosome contains more than one gene, then how are genes located on one chromosome inherited? T. Morgan obtained the answer to these questions in experiments on the fruit fly Drosophila. Genes are the components of chromosomes. Since there are more genes than chromosomes, it can be predicted that there will be not one gene in one chromosome, but several that are inherited together. This phenomenon was called gene linkage by T. Morgan. The inheritance of genes that are on one chromosome, which limits their free combination, is called *gene linkage.*

Genes located on the same chromosome are called linked and are inherited mostly together (linked inheritance). All genes on one chromosome form one linkage group. Homologous chromosomes have the same linkage groups, so each organism will have as many linkage groups as there are pairs of homologous chromosomes.

Traits whose genes belong to the same linkage group do not obey the principle of independent assortment in dihybrid crosses (AaBb x AaBb) in the ratio 9:3:3:1 and in dihybrid analytical crosses (AaBb x aabb) in the ratio 1:1:1:1. Genes linked together are not always transmitted.

The phenomenon of linkage of traits was discovered in 1906 by W. Bateson and R. Pennett in experiments with sweet pea when crossing two of its races, which differed in two pairs of traits - pollen shape and flower color. Instead of the expected splitting in the second generation F2 (9:3:3:1), splitting was observed in a ratio close to 3:1. The traits, therefore, did not show independent inheritance.

The phenomenon of gene linkage was analyzed by T. Morgan. In Drosophila, the allele for gray body color (B) dominates over the allele for black body color (b), and the allele for normal wing length (V) dominates over the allele for rudimentary wings (v). Crossing a homozygous gray fly with normal wings (BBVV) and a black fly with rudimentary wings (bbvv) produced in the first generation F1 hybrids with a gray body and normal wings (BbVv), which confirmed the law of uniformity of first-generation hybrids established by G. Mendel.

The results of the experiment did not depend on the sex of the recessive homozygote. Two analytical dihybrid crosses were then carried out. In the first of these, the male was an F dihybrid (gray body and normal wings), and the female was homozygous for the recessive alleles (black body and rudimentary wings). This cross produced two phenotypic classes, similar to the original parental forms, in equal proportions: 50% gray with normal wings (BbVv) and 50% black with rudimentary wings (bbvv). In the second dihybrid screening cross, the female was an F1 dihybrid (gray with normal wings) and the male was a recessive homozygous (black with rudimentary wings).

This cross resulted in four phenotypic classes in the following proportions:

1) gray with long wings (BbVv) 41.5%;
2) gray with rudimentary wings (Bbvv) 8.5%;
3) black with long wings (bbVv) 8.5%;
4) black with rudimentary wings (bbvv) 41.5% (Fig.)

The results of both analyzed dihybrid crosses did not match the expected ratio of phenotypes - 25% gray with normal wings, 25% gray with rudimentary wings, 25% black with normal wings and 25% black with rudimentary wings, as occurs with independent inheritance (G. Mendel).

Morgan explained the deviation from the expected splitting (1:1:1:1) by the fact that the genes for the studied traits (B and V) are located on the same chromosome and are inherited together (linked). The strength of linkage between genes is inversely proportional to the distance between them on the chromosome (Morgan's rule or law).

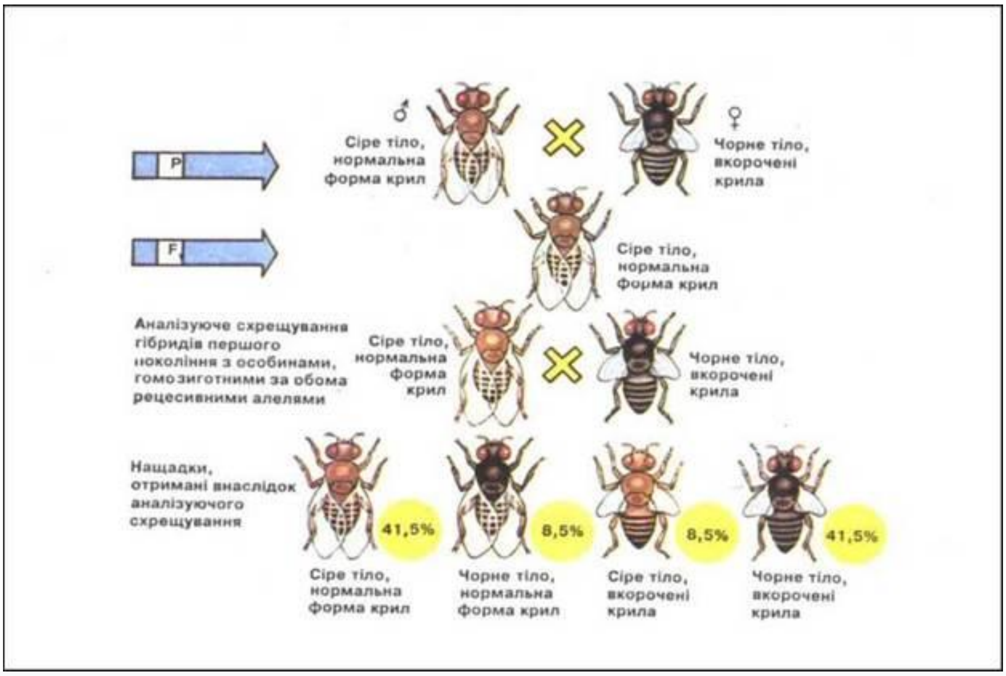


Fig.17. Linked inheritance in Drosophila.

Gene linkage can be complete or incomplete. In the first analytical cross, there was complete gene linkage. In the second analytical cross, the number of individuals with phenotypes that repeat the phenotypes of the parents prevailed (83%) and also indicated a close linkage of the B and V alleles.

The appearance of a smaller number (17%) of offspring with phenotypes that combined the traits of both parents, T. Morgan, relying on the discovery of chiasmata in meiosis by F. Jansen (1909), explained by a violation of coupling as a result of chromosome crossing over at the point between genes B and V. Morgan called the process of crossing over crossover.

The differences in the results of the 1st analytical cross, when the dihybrid was a male, and the 2nd analytical cross, when the dihybrid was a female, are explained by the peculiarity of Drosophila biology, which consists in the absence of crossover in male gametogenesis.

Therefore, a dihybrid male (BbVv) forms only non-crossover gametes (BV and bv) of two varieties, 50% of each variety, and a dihybrid female (BbVv) - 83% of non-crossover gametes of two varieties (41.5% BV and 41.5% bv) and 17% of crossover gametes of two varieties (8.5% Bv and 8.5% bV).

Crossover gametes are called gametes, in the process of their formation, crossover occurred, non-crossover gametes were formed without crossover. Accordingly, individuals that arose with the participation of crossover gametes are called crossovers, and those formed without them are called *non-crossovers*. So, in T. Morgan's experiment, crossovers in the offspring were 17%, non-crossovers - 83%.

Crossing over (chromosome crossover) is the mutual exchange of parts of homologous chromosomes. It normally occurs in the prophase of the first meiotic division at the pachyneme stage during gametogenesis (spermatogenesis and oogenesis). Homologous chromosomes (maternal and paternal) of prophase I are most closely adjacent to each other (conjugate).

Each of them is represented by two chromatids. Before they diverge, the chromatids form X-shaped figures (chiasmata), at the points of intersection the chromatids break off, and then connect, but not the maternal one with the maternal one, but the maternal one with the paternal one. The exchange of genetic material occurs, as a rule, between non-sister chromatids of homologous chromosomes, but can also occur between sister chromatids.

Crossing over breaks the linkage of genes. As a result, *recombinant* chromosomes with new combinations of genes, new linkage groups, arise, which leads to the appearance of offspring with new combinations of parental genes. Crossing over is important for evolution as one of the mechanisms for the emergence of combinatorial variability.

In addition to meiotic crossover, which naturally occurs in meiosis during the formation of gametes, there is sometimes an exchange of genetic material between chromatids of homologous chromosomes in somatic cells (mitotic crossover). Thus, the human autosomal recessive mutation known as *Bloom syndrome* is accompanied by a cytological picture that resembles the conjugation of homologous chromosomes and even the formation of chiasmata.

Crossover frequency is measured as the ratio of the number of crossovers to the total number of individuals in the offspring from the analyzed cross and is expressed as a percentage. The frequency of crossover between genes is directly proportional to the distance between them. The closer the genes are located, the fewer possible crossover points between them and, conversely, the further the genes are located, the more possible crossover points between them. Crossover between two genes can occur not only at one, but also at two (double crossover) or even a larger number of points.

The crossover frequency reflects the degree of linkage of genes and for given two genes, under the same conditions, is always constant. For other genes on the same chromosome, the crossover frequency is necessarily different, but also constant: from fractions of a percent to almost 50%. The constancy of the crossover percentage between genes is used as an indicator of the relative distance between them. *One morganide* is taken as the unit of distance between genes. It corresponds to the distance at which the crossover frequency is 1%. In Morgan's experiment, the crossover frequency in the offspring was 17%. Hence, the crossover frequency between genes B and V is 17%, the distance between genes is 17 morganids. Based on these data, T. Morgan and his colleagues developed a proposition about the linear arrangement of genes in chromosomes and proposed the principle of constructing chromosome maps.

The main provisions of the chromosome theory of heredity

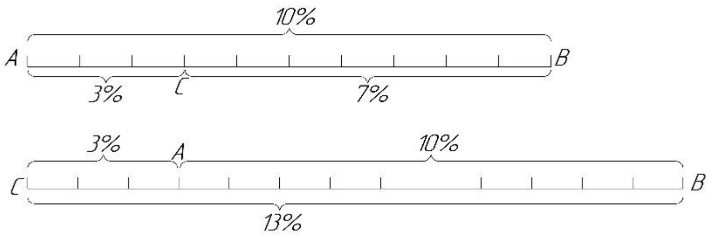
The chromosome theory of heredity was formulated and experimentally substantiated in experiments on the fruit fly Drosophila melanogaster, conducted in 1910-1925 by the American geneticist T. Morgan and his school - A. Sturtevant, G. Meller, K. Bridges. The main provisions of the chromosome theory of heredity:

1. Genes are arranged in chromosomes along their length in a linear order; different chromosomes contain different numbers of genes; the set of genes of each non-homologous chromosome is unique.
2. Allelic genes occupy specific and identical loci (places) of homologous chromosomes.
3. Genes located on one chromosome form a linkage group, due to which some traits are linked, which are transmitted together (linked) to offspring. The number of linkage groups is equal to the haploid set of chromosomes. Linkage is not absolute.
4. During meiosis, which occurs only during the formation of gametes, the diploid number of chromosomes is halved (the haploid number). This corresponds to the law of splitting, according to which the genetic material of both parents must split and enter different gametes.
5. According to the law of independent assortment, the paternal and maternal sets of unlinked genes segregate independently of each other. If the unlinked genes are located on different chromosomes, then during meiosis the maternal and paternal chromosomes should distribute themselves randomly between the gametes.
6. Reciprocal recombination can occur between genes of homologous paternal and maternal linkage groups due to crossing over. This corresponds to the formation of chiasmata during the conjugation of homologous chromosomes in meiosis (genetic crossing over).
7. The strength of linkage between genes is inversely proportional to the distance between them. The closer the genes are located on one chromosome, the stronger their linkage, the less recombination will occur between them, and vice versa. The distance between genes is measured in percentages of crossover. One percentage of crossover corresponds to one morganid.
8. Each biological species is characterized by a specific set of chromosomes - karyotype. The study of the chromosomal mechanism of determining and inheriting sex-linked traits, the linkage of genes, genetic maps with cytological chromosome maps - all this is the basis of the chromosome theory of heredity, on which the entire development of genetics is based.

Linear arrangement of genes.

Genetic maps of eukaryotes The existence of crossover allowed Morgan's school to develop in 1911-1914 the principle of constructing genetic maps of chromosomes. This principle is based on the idea of the arrangement of genes along the chromosome linearly. It was agreed to take 1% of the crossover between two genes as a unit of distance. This value is called a centimorganide, in honor of the geneticist T. G. Morgan. Suppose that genes A and B belong to the same linkage group. A 10% crossover has been found between them. Therefore, these genes are 10 units (centimorganids) apart. Suppose also that gene C belongs to the same linkage group. To find its place in the chromosome, we need to find out what percentage of crossover it gives with each of the two already known genes.

For example, if it gives 3% crossover with A, then we can assume that gene C is located either between A and B, or at the opposite end, that is, A is located between C and B. If there is a 7% crossover between B and C, then they must be arranged on the chromosome in the order shown in the diagram.



If the crossover between B and C is 13%, then the arrangement of genes in the chromosome should be as in the diagram below. In general, this pattern can be expressed by the following formula: if genes A, B, C belong to the same linkage group and the distance between genes A and B is k units, and the distance between B and C is m units, then the distance between A and C can be either k + m or k - m.

The most detailed chromosome maps have been compiled for Drosophila, which has long been a classic genetic object. Among plant objects, corn and tomatoes have been relatively well studied in this regard, and among animals, chickens and mice. Human chromosome maps have been compiled for all 24 linkage groups.

Genetic chromosome maps are constructed on the basis of hybridological analysis. However, for Drosophila, a significantly different method of constructing genetic chromosome maps is used. The fact is that in the salivary gland cells of fly larvae there are giant (polytene) chromosomes, which exceed the size of chromosomes from other cells by 100-200 times and contain 8000 times more chromonemes.

It turned out that in those cases where the hybridological method revealed any hereditary disorders, the corresponding changes also occurred in the giant chromosomes. As a result of the comparison of genetic and cytological data, it became possible to construct cytological chromosome maps. This discovery confirms the correctness of the principles that were laid down as the basis for the construction of genetic chromosome maps.

Prokaryotic chromosome maps

Two methods have been developed for compiling prokaryotic chromosome maps. They are based on the existence of conjugation in bacteria. The first method is based on the possibility of partial transfer of a chromosome from a donor bacterium to a recipient bacterium, which lasts about 2 hours. Bacteria are very weakly connected during conjugation, and their rupture most often occurs before the chromosome is completely transferred.

This feature is used to determine the order of placement of genes in a chromosome. It is understood that the sequence of genes and the distance between them is proportional to the time during which conjugation took place. By artificially stopping conjugation after certain periods of time and finding out which genes have passed into the recipient cell during this time, it is possible to establish the order of their location.

The second method is that as a result of conjugation, a part of the chromosome in the recipient bacterium is doubled. Over several generations of bacteria, this section remains doubled (diploid). Such individuals are used to find out which of the genes is dominant and which is recessive. As a rule, after several divisions, a number of genes localized in a region of the chromosome from the donor bacterium are included in the homologous loci of the chromosome of the recipient bacterium by crossing over and replace the allelic genes, while other genes of the donor are eliminated (disappear). The resulting recombinant chromosome can be used to study the localization of genes according to the principle that was developed for eukaryotes.

Topic 9. Genetics of sex. Coupling with the article. Cytoplasmic inheritance.

Sex chromosomes

At the end of the XIX century. Scientists have noticed a difference in one of the pairs of homologous chromosomes in the chromosome set of men and women.

In humans, 46 chromosomes: 44 - autosomes and 2 - heterosomes (sex chromosomes). There are 4 main types of sex regulation by sex chromosomes:

XY-type: XX - female, XY - male (characteristic of mammals, insects and angiosperms);

X0-type: XX - female, X - male (occurs among insects and mammals);

ZW-type: the female has one sex chromosome W and the second sex chromosome Z differs from it in shape and size, the female is heterogametic, and the male is ZZ (this type is characteristic of some fish, butterflies, birds);

Z0-type: the female has only one Z-chromosome and heterogametic, and male - two Z-chromosomes and homogametic. This type is known only in one of the species of lizards.

The origin of gender differences, sex determination, maintaining the ratio of heterosexual individuals in the population is a very important biological problem, which also affects the social, cultural and other aspects of human life

The occurrence of sexual differences is associated with sexual reproduction, which is inherent in all organic forms, starting with microorganisms. We call sexual reproduction the change of generations and the development of organisms on the basis of the fusion of germ cells and the formation of a zygote. Gender differences determine the most significant phenotypic features between individuals in the population. Due to sexual reproduction, the combinatorial hereditary variability it provides in the process of crossover and fertilization, any gene can become the property of the population. Due to sexual reproduction under the control of natural selection, the species accumulates the most successful combinations of genes (gene pool).

Sex - is a set of features and properties of the organism that ensure the transmission of hereditary information and its recombination in the reproduction of offspring through the formation of gametes. It is necessary to distinguish between the processes of sex determination and its development. Gender determination can occur at different stages of the reproductive cycle. In humans, as in all mammals, sex is determined at the time of gamete fusion during fertilization (syngamous).

In most species, the most noticeable phenotypic difference between individuals is sex. Gender is an extremely important and interesting set of characteristics. Sex differences determine the most significant features of the body, because sex affects many organs and traits that are not directly related to sexual reproduction. In most organisms known to us, sex is determined genetically. Sexual reproduction is known even in microorganisms, and from the cellular level of the organization of living matter, sex division exists for all living things that live on Earth. Signs that distinguish individuals of different sexes are divided into primary and secondary.

Primary and secondary sexual characteristics.In the process of zygote development there is a formation (differentiation) of sex. Gender differentiation is understood as development, which leads to differences between male and female organisms during ontogenesis. In humans, sexual differentiation causes changes throughout the organization: anatomical, physiological, biochemical. Sex differences affect the structure of internal and external reproductive organs, the phenotype of the individual, complex acts of behavior, metabolism, hormonal activity, resistance to damaging agents, and so on.

There are usually primary and secondary sexual characteristics. Primary sexual characteristics include morphological and physiological features, in particular the internal genitals, which ensure the formation of gametes and the process of fertilization, as well as differences in the structure of internal and external reproductive organs. Secondary include signs and properties of the organism that do not directly ensure gametogenesis, mating or fertilization, but are important for sexual reproduction. Male secondary sexual characteristics are a type of figure with broad shoulders and a narrow pelvis, developed muscle tissue, mastery of the face, cadix and tone of voice. Female secondary sexual characteristics include the type of figure with narrow shoulders and wider thighs, developed adipose tissue, the presence of mammary glands, the tone of voice. This division is quite conditional, because the secondary sexual characteristics are controlled by hormonal activity and are directly related to the normal functioning of the primary sexual organs - the gonads. Disease or underdevelopment of the gonads in women will weaken the activity of androgens, which can lead to the appearance of secondary sexual characteristics in men and vice versa.

It is known that in the vast majority of populations of heterosexual organisms, the ratio of males to females is approximately 1: 1 (50%: 50%). There are many theories of sex determination, but the most acceptable are chromosomal, hormonal and balance, which not only do not contradict each other, but, on the contrary, complement each other.

THEORIES OF GENDER DETERMINATION

Chromosomal theory of sex determination. The best sex ratio in populations is explained by the chromosomal theory of sex determination, formulated by T.G. Morgan and his colleagues - K. Bridges, G. Stertevant and G. J. Meller.

In humans, mammals, birds, and most other organisms, one sex is heterozygous and the other is homozygous for one pair of chromosomes, called sex. Sex chromosomes are denoted by the letters X and Y, because under a microscope they resemble these letters.

Chromosomal theory explained the approximately equal probability of giving birth to females and males:
P: ♀ XX × ♂ XY G: X X X Y½ ♀ XX: ½ ♂ XY

This sex ratio is reached before the beginning of the reproductive period, while fertilization per 100 zygotes of XX produces approximately 125 zygotes of XY. At birth, there are about 106 boys per 100 girls, in childhood the sex ratio is 103 boys per 100 girls, in adolescence there are already 100 girls per 94 boys. At the age of 50, there are 85 men per 100 women, and at the age of 85, there are only 50.

Changes in the sex ratio are due to various factors of ontogenesis. The predominance of females can be explained by their greater viability, which is associated with the function of procreation. This may be due to the greater stability and viability of the XX chromosome combination compared to XY, and many other factors. In many species, including humans, males have a higher level of metabolism and less resistance to adverse environmental factors, which causes a decrease in its number. Of course, this relationship is explained not only by biological but also social factors.

If the cells of an individual have the same sex chromosomes - such sex - homogametic (XX), if different (or one) - heterogametic (XY, XO).

The following types of sex determination are known in nature:

Type	Gametes		Become heterogametic	Representatives
X Y	X Y	X X	Men's	Man, mammal, Drosophila
X 0	X 0	X X	Men's	Some species of bedbugs, grasshoppers
X Y	X X	X Y	Women's	Birds, amphibians, butterflies
X 0	X X	X 0	Women's	Some types of moths

Inheritance of traits linked to sex. Traits whose genes are contained in the sex chromosomes are called sex-linked traits.

In females, sex-linked genes behave like a pair of allelic genes, affecting each other by type of complete or incomplete dominance. The genes of sex-linked traits are mainly located on the X chromosome and are therefore passed from mother to son and from father to daughter. This type of inheritance is called cross-cross (cross to cross).
Y - chromosome differs in activity from X - chromosome, it carries almost no active genes, i.e. genetically inert. Those few genes contained in the Y chromosome are called golandric and they are inherited from father to son. Therefore, in individuals with the Y chromosome, the genes located on the X chromosome do not have an allelic gene. This condition is called hemizygous.

Thus, the inheritance of traits linked to sex is different from the inheritance of autosomal traits and is not always subject to Mendel's laws.

Studying the nature of inheritance of sex-linked genes is very important, because hereditary diseases are often determined by recessive genes and they are suppressed by the action of dominant alleles. Phenotypic expression of such genes is possible either in a recessive homozygous state (XaXa) or in a hemizygous state (XaY).

More than 100 genes located on the X chromosome have been identified in humans. For example, color blindness (color blindness), the ability to smell hydrocyanic acid (18% of men and 4-5% of women do not feel this smell), several types of chicken blindness, hemophilia (blood clotting), Duchenne muscular dystrophy; Eye albinism and erythrocyte glucose-6-phosphate dehydrogenase deficiency are inherited as recessive traits, while rickets associated with inability to absorb vitamin D and tooth enamel defect (dark teeth) are dominant traits. The latter disease is observed in almost 10% of American Negroes. When they are in contact with pollen of horse beans (Vicia faba), sulfanilamide drugs, naphthalene destruction of a large number of erythrocytes begins, anemia develops.

The role of genes in determining sex.

Sex is determined in the first stages of embryogenesis, when the rudimentary reproductive organs are formed, which are neither female nor male. Which of them will be formed depends on the presence of the Y chromosome.

In humans, the Y chromosome has a TDF gene responsible for testicular development. Under the control of this gene, a protein is formed that is localized on the surface of Leydig cells, which begin to secrete androgens, and a special protein that inhibits the development of the female genitals. In the presence of this protein in the embryo from the sixth week of embryogenesis will begin to form testicles. If there are two X chromosomes in the karyotype of the embryo, then the ovaries will begin to form from the rudimentary gonads in the seventh week. Thus, the sex of the organism depends on the Y chromosome. But in the future, the normal development of sex is influenced by many genes; most of which are in autosomes.

Indirect evidence in favor of the chromosomal theory of sex determination is the fact that in the presence of a single X chromosome in the karyotype (45, X0) develops an organism with a female phenotype, and one Y chromosome for any number of X chromosomes (47, XXY, 48, XXXU, etc.) contributes to the formation of the male phenotype. Such pathology by quantity sex chromosomes occur because of violation of chromosome behavior in meiosis during gametogenesis.

♀	X	Y

For example, if the mother did not diverge sex chromosomes, and the father had meiosis occurred normally, the following karyotypes are formed:

♂		
XX	XXX	XXY
-	X–	Y–

P ♀ XX ′ ♂ X Y

Inheritance of sex-restricted and sex-dependent traits.

Among the secondary sexual traits are sex-restricted traits, ie genetic information about them is carried by all individuals and passed on to their offspring, but they are manifested only in one sex. For example, genes that control lactation.

There are also sex-dependent genes. The nature of the dominance of these genes varies depending on gender. For example, the alopecia gene dominates in men and is recessive in women. Thus, a man heterozygous for this gene will be bald and a woman will not. The dominance of such genes is determined by the amount and ratio of sex hormones - androgens and estrogens.

Balance theory of sex determination.

The author of this theory, T. Morgan's student K. Bridges, believed that the development of male or female sex depends on the ratio of autosomes and sex chromosomes. For example, the Drosophila fly - a classic object of genetics - normally has 6 autosomes and 2 sex chromosomes, ie 6A + XX - female, and 6A + XY - male, but sometimes they have individuals - aneuploids with an increased number of chromosomes and then the sex changes: if 8A + XX it will be a male, 8A + XY - a female. This phenomenon may to some extent explain the change in normal sexual characteristics in humans with non-divergence of sex chromosomes. Indeed, in Kleinfelter, Shereshevsky-Turner and Down syndromes, the ratio of sex chromosomes and autosomes changes, respectively, 44A + XXY, 44A + X0 and 45A + 2XX, or 45A + 2XY, and normal sex development is disrupted.

Sex chromatin.By the stage of gastrula, both X chromosomes function in the female body. Later, in all cells, except those from which the ovaries and ova are formed, one X chromosome is inactivated and remains in a condensed form in the nuclei in the form of a ball. Under the microscope, it is visible as deep chromatin, which is called Barr's body, or sex chromatin. The localization, shape and structure of sex chromatin are not affected by sex hormones, so it is not a secondary sexual sign.

If a woman has several X chromosomes in the cell nuclei, then several Barr bodies are formed. Only one X chromosome remains active. Not all chromosomes are inactivated during the formation of Barr bodies; the short shoulder area remains active.

In 1961, the English researcher M. Lyon hypothesized the nature of Barr's body:

- one of the two X chromosomes of a woman's cells is inactive;
- the inactive chromosome may be from the paternal or maternal organism
-inactivation occurs in early embryogenesis and persists throughout the subsequent reproduction of this cell line (cells have inactivated this particular chromosome).

Barr's body is used to diagnose some hereditary diseases (Kleinfelter's-syndrome, Shereshevsky-Turner syndrome, etc.).

Hormonal theory.

Its essence is that sex is regulated by the hormonal system of the ratio of male and female hormones in the body. This obvious conclusion is confirmed by many experiments of famous geneticists - AI Zavadovsky, Yamamoto and others. The content of sex hormones must be balanced during ontogenesis. In humans, during the menopausal period, along with the attenuation of the activity of the hormonal system, there may be a disorder of other body systems: cardiovascular, nervous, and others. In medicine, the facts of the birth of dizygotic (dizygotic) twins of male and female sex are known, but in girls there is a possibility of suppression of the normal formation of sexual functions. This is probably due to the fact that male embryos develop slightly earlier than females and begin to synthesize androgens, which, in turn, can affect the normal development of the female. Therefore, geneticists believe that the birth of heterosexual twins should be carefully considered for the hormonal development of the girl.

There are known facts of mismatch of human karyotype and its morphophysiological sexual characteristics, which is a consequence of various deviations.

Therefore, man as a biosocial being has four levels of gender determination:

1) genotypic (by karyotype);
2) gonadal (gonads);
3) phenotypic (by a set of external sexual characteristics);
4) psychological.

Psychological sex is determined by special methods show the ratio of purely male and female traits and tendencies.

Cytoplasmic inheritance

In eukaryotic cells, in addition to hereditary material located in the nucleus, cytoplasmic heredity, or extranuclear, is also detected. It consists in the ability of certain structures of the cytoplasm to store and pass on to offspring part of the hereditary information of the parents. Although the leading role in the inheritance of most traits belongs to nuclear genes, the role of cytoplasmic heredity is also significant. *It is associated with two types of genetic phenomena:*

- inheritance of traits encoded by extranuclear genes located in certain organelles (mitochondria, plastids);
- manifestation in the offspring of traits caused by nuclear genes, but the formation of which is influenced by the cytoplasm of the egg.

The existence of genes in organelles (mitochondria and plastids) capable of self-replication became known in the early twentieth century during the study of green and colorless plastids in some flowering plants with mosaic coloration of leaves. Extranuclear genes interact with nuclear ones and are under the control of nuclear DNA. Cytoplasmic heredity associated with plastid genes is characteristic of different plant species (eg, mouths). Among such plants there are forms with variegated leaves, and this feature is transmitted through the maternal line. The variegation of the leaves is due to the inability of some plastids to form the pigment chlorophyll. After cell division with colorless plastids, white spots appear in the leaves, which alternate with green areas. The transmission of variegation through the maternal line is explained by the fact that during the formation of gametes, plastids get to the eggs, not to the sperm. Plastids that reproduce by division have genetic continuity: green plastids give rise to green, and colorless - colorless. During cell division, plastids are distributed randomly, resulting in the formation of cells with colorless, green, or both types of plastids simultaneously.

Topic 10. Genotype and phenotype.

Individuals of any species differ in many respects. And man in this respect is no exception. People are different in color of skin, eyes, hair, weight and linear size of body and organs, number of blood cells, blood pressure and venous pressure, erythrocyte antigens (blood groups, rhesus system), enzyme activity, histocompatibility complex. These and other differences determine a person's personality, which must be taken into account in transplant surgery, transfusiology, forensic practice, medical and genetic counseling.

The differences are due to genetic and environmental factors. Both factors are equally important. But their relative role in the development of symptoms is different. Any traits are genetically determined. But some of them have a purely genetic nature, i.e. under all environmental conditions compatible with life, this genotype gives the same phenotype (blood group). Other differences are also genetically determined, but the degree of their phenotypic manifestation is influenced by the environment. Thus, the number of erythrocytes in the peripheral blood is often associated with the altitude above sea level, although the body's ability to change within certain limits depending on the partial pressure of oxygen in the atmosphere is determined by genotype. There are many differences that are due to both heredity and environment. Human growth is controlled by several dominant non-allelic genes (polygens), and also depends on the nature of the diet. The occurrence of hereditary diseases is caused by mutations that occur spontaneously or under the influence of mutagenic factors at the cellular and molecular levels. Knowledge of such mutations, their mechanisms, and frequencies in populations help to predict the manifestation of pathological signs in offspring, to determine the degree of genetic risk and the need for prenatal diagnosis.

Therefore, the same hereditary information in the changed conditions can be shown differently. Thus, in Himalayan rabbits and Siamese cats, the nature of hair pigmentation on different parts of the body is determined by the external temperature (in cold areas the coat is dark, because these organisms have a mutant enzyme - tyrosinase. environment.

The range of variability, within which, depending on environmental conditions, the same genotype is able to give different phenotypes, is called the response rate. In some cases, the same gene, depending on the entire genotype and external conditions, may have a different form of phenotype: from the almost complete absence of gene-controlled traits in the phenotype to its complete manifestation. In primroses, the genotype is such that the red color of flowers appears at a temperature of 15-20 ° C, white - at a higher temperature, but not at any temperature there are no blue, blue, purple or yellow flowers. This is the rate of reaction of this plant on the basis of pigmentation of the flower.

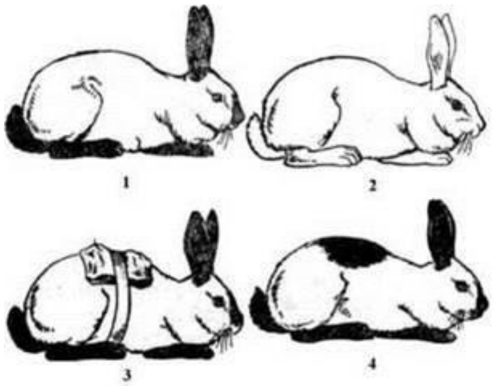


Fig. 18. Change in the color of the fur of the Himalayan rabbit under the influence of temperature: 1 - rabbit, which grew at normal ambient temperature (about 20°C); 2 - rabbit, which grew at a high temperature (about 32°C); 3— a rabbit with a shaved part of the fur on its back and the skin was cooled under a sterile bandage; 4 - rabbit with pigmented fur on the body area, which was cooled.

The degree of manifestation of the trait in the implementation of the genotype in different environmental conditions is called expressiveness. Under the expression means the degree of phenotypic expression of the gene. It is associated with the variability of the sign within the normal response. Expressiveness can be manifested in changes in morphological features, biochemical, immunological, pathological and other indicators. Thus, the chlorine content in human sweat usually does not exceed 40 mmol / l, and in hereditary disease - cystic fibrosis (with the same genotype) ranges from 40 to 150 mmol / l.

Hereditary disease - phenylketonuria (impaired amino acid metabolism) may have varying degrees of manifestation (ie different variable expression), primarily - it is determined by different amounts of phenylalanine in the blood, secondarily - from mild mental retardation, to deep imbecility (ie the ability to only basic self-care skills). Expression can be constant (presence of erythrocyte antigens) and variable (chlorine, blood sugar, changes in the number of metabolic products in phenylketonuria, galactosemia and other hereditary diseases).

The same trait may appear in some organisms and not in others that have the same gene. Quantitative indicator of the phenotypic manifestation of the gene is called penetrance.

Penetration - the frequency of phenotypic expression of a gene among individuals who have this gene in the genotype. This is a quantitative trait characterized by the ratio of individuals in which the gene is phenotypically to the total number of individuals in which the gene could appear (if the recessive gene is taken into account, then in homozygotes, if dominant - then in dominant homozygotes and heterozygotes). If, for example, the mutant gene is manifested in all individuals, say about 100% penetrance, in other cases - about incomplete and indicate the percentage of individuals in which the gene is manifested. Thus, the determination of blood groups in humans by ABO, MN, rhesus has one hundred percent penetrance, hereditary diseases: epilepsy

- 67%, diabetes - 65%, congenital hip dislocation - 20%, gout - 20% in men and 0% in women penetrance, etc.

The terms "expressiveness" and "penetrance" were introduced in 1927 by M.V. Timofeev-Resovsky.

Expressiveness and penetrance of signs are defined:

a) the presence of specific genes and their alleles in the genotype of the organism;
b) a system of interacting genes in the genotype, in particular the presence of polygenic systems:
c) the influence of environmental factors that have a modifying effect on the manifestation of

symptoms.

The fact that the same genotype can be a source of development of different phenotypes is essential for medicine. This means that the burdened heredity does not necessarily have to manifest itself, it all depends on the conditions in which a person is. In many cases, the disease, as a phenotypic manifestation of hereditary information, can be prevented or alleviated by preventive measures: the use of diet, physical therapy or the use of drugs. The implementation of hereditary information directly depends on the environment, their interdependence can be formulated by certain provisions:

1) Since organisms are open systems that exist as a whole in the environment, the realization of hereditary information is under the influence of the environment.
2) The same genotype is able to give different phenotypes, which is determined by the conditions in which the genotype of the individual is realized in the process of ontogenesis.
3) Organisms can develop only those traits that are due to genotype.
4) Phenotypic variability within the reaction rate occurs for each specific trait.
5) Environmental factors can affect the severity of hereditary traits in organisms (expressiveness), or the quantitative manifestation of traits (penetrance).

Variability- the property of organisms within a species to exist in different variants of traits, to acquire in the process of development of new properties and traits. There are two forms of variability - hereditary and non-hereditary. The first of them is associated with a change in genotype, the second - the phenotype.

Darwin called hereditary variability definite and hereditary variability indefinite. Non-hereditary variability includes phenotypic (modification), hereditary - genotypic variability.

Forms of variability

Non-hereditary, or phenotypic (occurs without changes in genotype and does not persist during sexual reproduction)	**Hereditary, or genotypic (associated with a change in genotype and therefore stored for generations)**

Modification (phenotype changes under the influence of certain conditions of existence of organisms)	Ontogenetic (phenotype changes due to the functioning of different genes at different stages of ontogenesis)	Mutational (genotype changes due to mutations)	Combinatorial (genotype changes due to the formation of new combinations of genes)

Genotypic variability is divided into mutational and combinatorial. In all forms of variability the phenotype changes, but in the case of genotypic variability the changes in the phenotype are caused by changes in the genotype, in the case of phenotypic variability - by environmental factors.

Phenotypic variability (modification).Modifications are phenotypic changes that occur under the influence of environmental conditions. The size of the modification variability is limited by the reaction rate. Modification changes in the trait are not inherited, but its range, the rate of reaction is genetically determined and inherited. Modification changes are not associated with changes in genotype. Modification variability is usually appropriate. It corresponds to the conditions of existence, is adaptive.

Under the influence of external conditions, the growth of animals and plants, their weight, color, etc. change phenotypically. The emergence of modifications is due to the fact that environmental conditions affect the enzymatic reactions that occur in the body, and in some way change their course. This, in particular, explains the appearance of different colors of primrose flowers and the deposition of pigment in the hair of Himalayan rabbits. Examples of modification variability in humans may be increased pigmentation under the influence of ultraviolet radiation, the development of muscular and skeletal systems as a result of exercise and the like.

Phenocopies should also be included in the modification variability. (R. Goldschmid, 1935) non-hereditary changes in the phenotype, which are due to environmental influences, but are similar to changes in the phenotype of genetic nature (mutations). That is, in the process of development under the influence of external factors, a trait that depends on a certain genotype may change so that the traits that are characteristic of other changes - mutations - are copied. The development of phenocopies can be influenced by various environmental factors - climatic, physical, chemical, biological. Some infectious diseases (rubella, toxoplasmosis), which the mother suffered during pregnancy, can also cause phenocopies of a number of hereditary diseases and malformations in newborns. Phenocopies occur with high frequency at certain (phenocritical) stages of ontogenesis,

Phenocopies- is a violation of the normal course of ontogenesis under the influence of various factors without a specific change in genotype. The presence of phenocopies often complicates the diagnosis, so the doctor should be aware of their existence that phenocopies are not inherited and require treatment other than hereditary diseases.

In addition to phenocopies, there is the concept of «genocopy».

Gene Copies- these are the same phenotypic traits, the appearance of which is associated with the action of different genes. For example, these are different types of hemophilia caused by mutations in different genes.

A special group of modification variability consists of long-term modifications. Thus, when exposed to high or low temperatures on the pupae of the Colorado potato beetle, the color of adult animals changes. This feature is observed in several generations, and then the previous color returns. This trait is transmitted to offspring only under the influence of temperature on females and is not transmitted if the factor acted only on males. Thus, long-term modifications resemble cytoplasmic heredity.

Ontogenetic variability observed during the individual development of the individual, in the period from fertilization to death.

Ontogenesis is a complete cycle of individual development of each individual, which is based on the realization of hereditary information at all stages of existence in certain environmental conditions; it begins with the formation of the zygote (during sexual reproduction) and ends with death.

Genotypic, or hereditary, variability is divided into combinatorial and mutational.

Combinatorial variability associated with obtaining new combinations of genes in the genotype.

Naturally occurs during sexual reproduction. This is achieved mainly due to the following mechanisms:

a) independent chromosome divergence during meiosis;

b) their accidental combination during fertilization;

c) gene recombination due to crossover; the genes themselves do not change, but a random new combination of them, which leads to the emergence of organisms with a different genotype and phenotype.

Combinatorial variability is widespread in nature. In microorganisms that reproduce asexually, there are peculiar mechanisms (transformation and transduction) that lead to combinatorial variability. All this suggests the great importance of combinatorial variability for evolution, the process of speciation. In human populations, phenotypic polymorphism is achieved as a result of combined variability.

The phenomenon of heterosis belongs to combinatorial variability. Heterosis (modification, transformation), or "hybrid force", can be observed in the first generation during hybridization between representatives of different populations, breeds or varieties. It manifests itself in the form of increased viability, increased growth and other manifestations.

Mutational variability

Mutation- sudden abrupt change of hereditary trait due to a change in genetic material. Mutagenesis the process of mutations. A mutant is an organism that has changed its phenotype due to a mutation. Mutations were first described in evening primrose plants (Oenothera lamarckiana) and introduced to science by the Dutch botanist G. de Vries (1901), one of three scientists who rediscovered the patterns of inheritance of traits established by Mendel. Evolution is associated with mutational variability - the process of formation of new species, varieties, breeds. Mutations are known in all classes of animals, plants, viruses. Mutations cause polymorphism in human populations: different pigmentation of the skin, hair, eye color, shape of the nose, lips, etc. Clinically, mutations manifest as hereditary diseases.

Law of homologous series of hereditary forms of variability (MI Vavilov, 1920)

The law of homologous series of hereditary forms of variability reflects the general direction of the mutation process in all living organisms, which is determined by:

a) the universality of the genetic code, the general scheme of gene organization, the processes of realization of genetic information;
b) chromosomal organization of hereditary material;
c) the same for eukaryotes cell division processes;
d) homologous mechanisms of recombination, mutation;
e) homologous processes of germ cell formation and fertilization ...

Comparing the characteristics of different varieties of cultivated plants and related wild species, MI Vavilov noticed that the compared plants had many common hereditary changes, which gave him the opportunity to formulate the law of homologous series in hereditary variability:

1. Genetically related species and genera are characterized by similar series of hereditary variability with such correctness that knowing a number of forms within one species, it is possible to predict the existence of parallel forms in other species and genera. The genetically closer the organisms in the general system of genera and species, the more complete the similarity in the series of their variability.

His law MI Vavilov expressed the formula:

$$\begin{gathered} G1\,(a + b + c\ldots\ldots\ldots), \\ G2\,(a + b + c\ldots\ldots\ldots), \\ G3\,(a + b + c\ldots\ldots\ldots), \end{gathered}$$

where G - different species (genera) of organisms, a, b, c - different variable features.

2. Whole families of organisms in general are characterized by a certain cycle of homologous forms of variability, which are observed in all genera and species belonging to this systematic group.

The law of homologous series in hereditary variability is directly related to the study of hereditary human diseases. The treatment and prevention of hereditary diseases cannot be solved without research on animals with hereditary anomalies that are similar to those observed in humans.

According to the law MI Vavilov, similar to hereditary human diseases, phenotypes should be found in animals. Indeed, many pathological conditions found in animals can be models of hereditary human diseases. Yes, dogs have hemophilia, which is linked to sex. Albinism has been reported in many species of rodents, cats, dogs, and a number of birds. Mice, cattle, and horses are used to study muscular dystrophy; epilepsy - rabbits, rats, mice; abnormalities in the structure of the eye - many species of rodents, dogs, pigs and other animals. Hereditary deafness exists in guinea pigs, mice and dogs. Defects in the structure of the human face, which are homologous to the cleft lip (cleft upper lip) and wolf's mouth (cleft upper jaw and hard palate), are observed in the facial skull of mice, dogs and pigs. Hereditary metabolic diseases, such as obesity and diabetes, mice get sick. In addition to already known mutations, many new anomalies similar to those found in humans can be obtained from laboratory animals by exposure to mutagenic factors and studied experimentally.

Questions for Preparation

1. Subject and tasks of human genetics and medical genetics. Heredity and variability.
2. Allelic genes. Homozygotes, heterozygotes.
3. Genotype, phenotype.
4. Patterns of inheritance in monohybrid crossing.
5. Mendel's first and second laws. Mendelian traits.
6. Patterns of inheritance in dihybrid and polyhybrid crossing. Mendel's third law.
7. Multiple alleles. Inheritance of human blood groups according to the AB0 antigenic system.
8. The Rh factor. Significance for medicine. Rh conflict.
9. Pleiotropy.
10. Linked inheritance of genes (Morgan's law). Crossing over.
11. Chromosomal theory of heredity.
12. Sex genetics. Chromosomal diseases caused by a change in the number of sex chromosomes.
13. Variability, its forms, significance in ontogenesis and evolution.
14. Modification variability, its characteristics. Reaction rate. Phenocopies.
15. Genotypic variability, its forms. Combinatorial variability.
16. Mechanisms of occurrence and significance.
17. Mutational variability and its phenotypic manifestations.
18. Classification of mutations by genotype.

Substantial module 3 «Molecular Genetics. Mutations».

Topic 11. The structure of nucleic acids. DNA repair.

Cells are able to maintain a high order of their organization due to genetic information that is stored, reproduced, realized and improved. At the heart of these fundamental phenomena are molecular processes that occur with the help of DNA and RNA. In the cell, in the organization of the flow of biological information, DNA of chromosomes of the nucleus, information RNA molecules, which transfer it to the cytoplasm, then ribosomes, transport RNA and enzymes of amino acid activation are sequentially involved. Finally, proteins are synthesized that have a certain structure and function.

The main role in the storage and transfer of information belongs to nucleic acids. ***Nucleic acids*** were first discovered by F. Mischer in 1869. Convincing evidence that it is DNA associated with the transmission of hereditary information obtained in the study of viruses. The role of DNA in the transmission of hereditary information has also been obtained in experiments on microorganisms due to the phenomena of transformation, transduction and conjugation.

Transformation (transformation) - the inclusion of foreign DNA in the genome of the host cell, which leads to changes in its structural and functional properties.

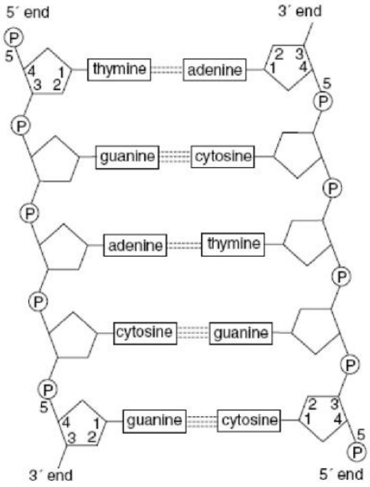
Transduction (displacement) - is that viruses, leaving the bacterial cells in which they parasitized, can capture part of their DNA and, getting into new cells, transmit to new hosts the properties of the previous ones.

Conjugation (compound) - the transfer of genetic material from one bacterium to another by forming a cytoplasmic bridge, moving part of the DNA and its integration with the genome of the recipient cell.

The structure of nucleic acids

Establishing the structure of DNA has opened a new era in biology, as it has made it possible to understand how living cells, and therefore organisms, accurately reproduce their counterparts and how they encode the information needed to regulate their vital functions.

There are two groups of these acids - **RNA** and **DNA**. They differ in chemical structure and biological properties. Some viruses contain only RNA, others only DNA, but the cells of bacteria and all eukaryotes contain nucleic acids of both types. DNA and RNA in the cell are localized differently. **DNA** is found mainly in the nucleus, is part of chromatin, concentrated in chromosomes. **DNA** is also part of mitochondria, centrosomes and plastids. The main **RNA** reservoirs are the nucleoli and ribosomes, which are located in the cytoplasm. In addition, RNA is in the cytoplasmic matrix.



Nucleic acids are polymers whose monomers are nucleotides. Each nucleotide consists of:

- a monosaccharide (ribose or deoxyribose),
- a phosphoric acid residue,
- and one of four nitrogenous bases: adenine (A), guanine (D), cytosine (C), and thymine (T), or uracil (B). Nucleotides are connected by phosphodiester bonds to form polymer chains. DNA strands are interconnected by hydrogen bonds and form a double helix of DNA.

Fig. 19. Antiparallel DNA strands.

This model of DNA structure was proposed in 1953 by J. Watson and F. Crick. The two polynucleotide strands of DNA are antiparallel. That is, the 5 'end of one chain (free phosphate residue at the fifth carbon of ribose or deoxyribose) is connected to the 3' end of the other (free hydroxyl group at the third carbon of ribose or deoxyribose), and vice versa. Genetic information is recorded by a sequence of nucleotides in the direction from the 5'- to the 3'-end.

The strand is called a «content» strand, and its nucleotide sequence coincides with the mRNA sequence. The second chain in the 3'-5 'direction is called "antisense", it is a matrix chain in the process of transcription.

Two long antiparallel polymer chains are firmly connected by hydrogen bonds. Adenine of one chain is connected to the thymine of another chain by two hydrogen bonds, and guanine is connected to cytosine by three hydrogen bonds. They are complementary to each other. Then a double spiral is formed, twisted around the central axis clockwise (right spiral).

Studying the chemical composition of DNA in 1950, ***E. Chargaff*** formulated important ***provisions for the structure of DNA:***

I The molar fraction of *purines* (adenine - A and guanine - D) is equal to the molar fraction of *pyrimidines* (cytosine - C and thymine - T):

A + G = C + T, or A + G / C + T = 1

II The amount of adenine and cytosine is equal to the amount of guanine and thymine: A + C = G + T, or A + C / G + T = 1

III The amount of adenine is equal to the amount of thymine, and the amount of guanine is equal to the amount of cytosine:

A = T, or A / T = 1, G = C, or G / C = 1

IV The ratio of the sum of molar concentrations of A + T in different species varies considerably: G + C / A + T is called the specificity coefficient. For bacteria, the specificity coefficient is 0.45–2.8, for higher plants, animals and humans - 0.45–0.94.

Spatial organization of DNA.

You can select the *primary structure* - the sequence of nucleotides in the chain, interconnected by phosphodiester bonds, *secondary structure* - two complementary antiparallel chains connected by hydrogen bonds, *tertiary structure* - three-dimensional spiral.

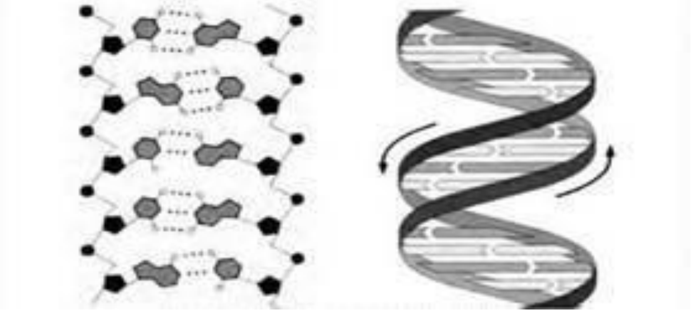


Fig. 20. Spatial structure of DNA.

X-ray diffraction analysis showed that the diameter of the double helix is 2 nm, the total rotation of the helix is 3.4 nm. Each round contains 10 nucleotide pairs. The contribution of one nucleotide in the length of the helix is 0.34 nm.

DNA is not directly involved in cell life. The role of mediators in the transfer of information from DNA to the cytoplasm is played by ribonucleic acids. The relationship between DNA, RNA and proteins can be represented as a diagram:

DNA → RNA → white.

In this case, one of the DNA strands is a template for RNA molecules, which in turn are templates for protein synthesis or are part of ribosomes or carry amino acids.

RNAs have the form of long unbranched polymer molecules consisting of a single strand. In some viruses, RNA is a carrier of hereditary information in the absence of DNA. RNA is a polymer of ribonucleotides consisting of phosphoric acid, ribose and nitrogenous bases (adenine, guanine, cytosine, uracil). Ribose together with phosphoric acid residues forms the skeleton of the molecule on which the nitrogenous bases are located. All types of RNA are synthesized on DNA molecules with the participation of RNA polymerase enzymes based on the principle of complementarity. In the synthesized molecule, uracil RNA is complementary to adenine DNA, and guanine is complementary to cytosine. If the DNA content in cells is constant, then the RNA content varies greatly depending on the type of cells, the intensity of metabolism and protein synthesis.

RNA molecules have much in common with the structure of DNA, but have a number of features: a) RNA carbohydrate is ribose; b) RNA does not contain thymine, its place in the molecule is occupied by uracil (only in tRNA there is thymine); c) RNA - a single-stranded molecule; d) Chargaff's rules are not followed.

RNA types

Based on the size, structure and function of molecules, there are three types of RNA, characteristic of both prokaryotes and eukaryotes.

Information RNA (mRNA). Its molecules are formed on certain sections of DNA, carry information from structural genes and have the form of a complementary copy of a section of one of the DNA strands. They carry encoded information about the primary structure of proteins in the cytoplasm, where they attach to ribosomes and implement this information.

Information RNA is a template for the synthesis of polypeptides (proteins), so it is also called a template (mRNA). Matrix RNA is a template on which polypeptides are built according to the underlying genetic information. Information RNA contains information about the order of amino acids in the synthesized protein. The location of the amino acids is encoded by a clear nucleotide sequence in the mRNA molecule. Each amino acid corresponds to its own triplet of nucleotides (codon). MRNA molecules consist of 300-3000 nucleotides. They make up 0.5–3.0% of the mass of all RNA cells. Information RNA is formed in the nucleus in the form of pro-mRNA, which contains exons (informative nucleotide sequences) and introns (non-informational sequences). As a result of processing (cutting of intron sites) it "matures" and arrives in cytoplasm where at once joins ribosomes.

Transport RNA (tRNA).tRNA molecules are formed on special genes. Transport RNAs are short, single-stranded, have the shape of a clover leaf due to the complementary combination of bases in different parts of the chain, and consist of a small number of nucleotides - 75-90. Of the total mass of RNA, tRNA accounts for about 10-15%. In the cytoplasm, tRNA molecules transfer to the site of protein synthesis only the corresponding amino acids. Each amino acid corresponds to its own tRNA due to the peculiarities of the nucleotide sequence and spatial structure.

tRNA molecules have four important sites:

a) transport - to which a specific amino acid is attached;
b) an anticodon, which is a three specific ribonucleotides (triplet) and is complementary to the triplet
on mRNA (codon);
c) the site of attachment of the enzyme that catalyzes the attachment of the amino acid to the tRNA;
d) ribosome binding site - a specific nucleotide sequence required for attachment to ribosomes.

Ribosomal RNA (rRNA).Ribosomal RNA is formed in the nucleolus on special DNA genes. rRNA is a large single-stranded unbranched molecule that contains 3000–5000 nucleotides. Of the total mass of RNA, it accounts for up to 90%. In the karyoplasm, rRNA and various proteins combine in a 1: 1 ratio to form small and large ribosome subunits.

Functions of rRNA in the structure of the ribosome: provides the process of protein synthesis; provides binding of mRNA to ribosomes by means of certain sequences of nucleotides.

DNA repair

To ensure the basic characteristics of cells and organisms of this population requires accurate preservation of the structure and stability of the functions of genetic material for thousands and millions of years, despite the action of various factors. There are several mechanisms for maintaining the stability of DNA functions. First, it is the high chemical stability of the DNA molecule itself, and secondly, the presence of special mechanisms of self-correction and repair of emerging changes. Genetic information can be reliably stored in the nucleotide sequences of DNA only because a wide range of different replication enzymes continuously "scans" DNA and removes damaged nucleotides.

Under the influence of physical and chemical factors, as well as in the normal biosynthesis of DNA, it can be damaged. It turned out that the cells have mechanisms to repair damage in DNA strands. The ability of cells to repair damage in DNA molecules is called ***repair*** (from the Latin reparatio - recovery).

The process of DNA repair is that genetic information is presented in DNA in two copies - one in each of the two strands of the DNA double helix. Due to this, accidental damage in one of the chains can be removed by the replication enzyme and the damaged part of the chain is resynthesized in its normal form due to the information contained in the intact chain. Not all types of DNA damage are repaired, some of them are manifested in the form of mutations, which can cause cell death. There are several mutations that manifest as severe congenital diseases due to disruption of the repair process. For example, xeroderma pigmentosum is a rare recessive autosomal mutation. Babies homozygous for this mutation have a normal appearance at birth, but at an early age under the influence of sunlight they have skin damage: freckles, capillary dilation, keratinization, there are eye injuries. Later develop atrophic skin changes, benign and then malignant tumors.

The ability of cells to alter the repair efficiency of genetic material may also be important in the cellular mechanisms of aging. There are observations that indicate a decrease in the intensity of DNA repair processes with age. But it is difficult to say whether these changes are the cause of aging or its consequence.

Diseases associated with impaired DNA repair

Different genes are responsible for the synthesis of enzymes for DNA repair. When the structure of at least one of these genes is disrupted, the consequences for the human body can be very serious.

A classic example of damage to the repair system is ***xeroderma pigmentosum***. Pigmented xeroderma was first described in Vienna in 1874, and in the 1960s the connection of this disease with disorders of DNA repair, or more precisely, with the lack of enzymes for dark repair, was discovered. Xeroderma pigmentosum occurs with a frequency of 1 in 250,000 and is inherited by *autosomal recessive* type. A little sun exposure can easily lead to skin wounds and skin cancer. ***Ataxia-telangiectasia*** also reveals a deficiency of topoisomerase enzymes required for repair. This disease first appears in childhood as a lack of muscle control (ataxia), which increases when the child begins to walk. Red spots (telangiectasia) appear on the face and neck due to dilation of small blood vessels under the skin. The child is prone to various lung infections. Symptoms of Fanconi's anemia are the result of impaired ability to excrete thymine dimers formed after UV irradiation (deficiency of dark repair enzymes). In some populations, the incidence of Fanconi anemia reaches 1 in 22,000.

Anemia damages all types of blood cells. Correction of the disease can be carried out only with the help of a bone marrow transplant. A child with Fanconi anemia of small stature, with a triangular face, dark skin and missing or
«Chopped» thumbs. Other accompanying symptoms are mental retardation and learning disabilities. Like individuals with other DNA repair disorders, a child with Fanconi anemia has chromosome breaks and a high risk of developing leukemia.

Topic 12. DNA replication. Transcription.

The unique property of a DNA molecule to double before cell division is called replication. Semi-conservative path of DNA replication. It is established (M. Mezelson, F. Steel) that in the process of replication two strands of DNA are separated, each of them is a template (matrix) for a new strand.

The sequence of bases that should be in the new threads can be easily predicted because they are complementary to the bases that are present in the old threads. Thus, two daughter molecules are formed that are identical to the parent. Each daughter molecule consists of one old (mother) thread and one new thread. Because only one mother thread is stored in each daughter molecule, this type of replication is called semi-conservative.

The mechanism of DNA replication.

DNA replication is a complex, multi-step process that requires the involvement of a large number of special proteins and enzymes. For example, initiator proteins form a replication fork, DNA topoisomerases untwist strands, DNA helicase and destabilizing protein cleave DNA into two separate strands, DNA polymerase and

DNA primase catalyze the polymerization of nucleotide triphosphates and the formation of a new chain. lagging DNA strands, etc.

The process is similar in both prokaryotes and eukaryotes, although slightly different in speed, direction, number of replication points, and so on. The rate of replication in eukaryotes is very high and is 50 nucleotides per second, and in prokaryotes - up to 2000 nucleotides per second.

The main stages of replication:

1) ***Initiation*** (from the Latin initialis - primary, initial).

Activation of deoxyribonucleotides. Deoxyribonucleotide monophosphates (AMP, GMF, CMF, TMF) are in a state of «free float» in the nucleus and are a «raw material» for DNA synthesis.

Initiation point recognition. The promotion of DNA begins at a certain point. This particular point is called the replication initiation point or the initiation genome (special nucleotide sequence). Specific initiator proteins are required to determine the initiation point. Viruses and prokaryotes have only one point of initiation. Eukaryotes that have large DNA molecules may have many replication initiation points that eventually merge with each other when the DNA strands are completely separated. Replication of both strands of DNA occurs simultaneously and continuously.

Untwisting of the DNA molecule. The double helix of DNA is untwisted and unfolded into individual strands of DNA by breaking the weak hydrogen bonds between complementary nucleotides. This process is provided by enzymes - helicases. Bare bases A, T, D and C of both chains are projected into the karyoplasm. Enzymes, called topoisomerases, break and re-stitch individual strands of DNA, helping to untwist the helix. Due to the separation of DNA strands, replication plugs appear. New strands of DNA are formed on each of the released chains, their growth occurs in opposite directions.

2) ***Elongation.*** Free triphosphates of deoxyribonucleotides with their nitrogenous bases are attached by hydrogen bonds to the nitrogenous bases of both DNA strands, in accordance with the rule of complementarity, ie A – T, C – G.

Elongation is the addition of deoxyribonucleotide to the 3 'end of a growing chain. The process is catalyzed by DNA polymerase. Deoxyribonucleotide triphosphates (trinucleotides), joining each DNA strand, break their internal high-energy bonds and form deoxyribonucleotide monophosphates (mononucleotides), which are normal components of DNA. The released pyrophosphate molecules (PP) enter the nucleoplasm.

3) ***Formation of new DNA strands.***

4) Subsequently, the attached adjacent nucleotides bind to each other with phosphorus residues and form a new DNA strand. The process is catalyzed by the enzyme DNA polymerase. The presence of metal ions Mn^{2+} or Mg^{2+} is required.

DNA polymerase can polymerize deoxyribonucleotides in the 5-3 'direction, i.e. from the carbon 5'-end to the carbon 3'-end of DNA molecules. Because the two strands of DNA are antiparallel, new strands must form on the old (mother) strands in opposite directions. One new thread is formed in the direction 5'-3 '. This thread is called the lead. On the second mother thread, short DNA segments are formed in the 3'-5 'direction. Eventually, they join together to form a long lag.

5) ***Formation of primers.***

On the lagging strand, a short strand of RNA is first formed according to the DNA pattern. It is called an RNA primer and contains a sequence of 10-60 nucleotides. The primer enzyme catalyzes the polymerization of RNA blocks (A, B, D, C) in the primer. RNA primer is formed because DNA polymerase cannot initiate the synthesis of a new strand of DNA in the lag chain in the direction 3'-5 ', it can only catalyze its growth. The primers are later removed, and the resulting cavities are filled with DNA deoxyribonucleotides in the 5'-3 'direction, which completes the construction of the second strand. In place of the primers, fragments of a new strand of DNA are formed, which are called Okazaki fragments and consist of 1000-2000 (prokaryotes) or 100-200 (eukaryotes) nucleotides. These fragments are doped (crosslinked) by DNA ligases, resulting in the formation of a second complete chain.

6) ***Editing.*** Clear complementarity of base pairs ensures accurate DNA replication. However, sometimes there are errors in joining the basics. They are removed by DNA polymerase, which re-binds to DNA molecules (repair).

7) ***Termination*** (from the Latin terminalis - final).

Upon completion of the replication process, the resulting molecules are separated, and each daughter strand of DNA is twisted together with the mother into a double helix. This creates two DNA molecules that are identical to the mother. They are formed by individual fragments along the length of the chromosome.

Such a single fragment of DNA, which is doubled on one chromosome, is called a replicon. There are several replicons at once, and asynchronously and in its various sites.

The replication process affects the entire chromosome and runs almost simultaneously, at the same rate. After replication in replicons, they are crosslinked by enzymes into a single DNA molecule. The areas of chromosomes where replication begins are called initiation points. It is believed that these are probably the sites of attachment of interphase chromosomes to the proteins of the lamella of the nuclear envelope. The process is activated by a cytoplasmic factor of unknown nature that enters the nucleus. Replication follows a certain order, i.e. first some parts of chromosomes begin to replicate, and later - others. In the synthetic period of the interphase, the number of histone proteins that associate with the synthesized DNA and form the classical structure of chromatin also doubles. Disruption of replication leads to disruption of protein synthesis and the development of pathological changes in cells and organs.

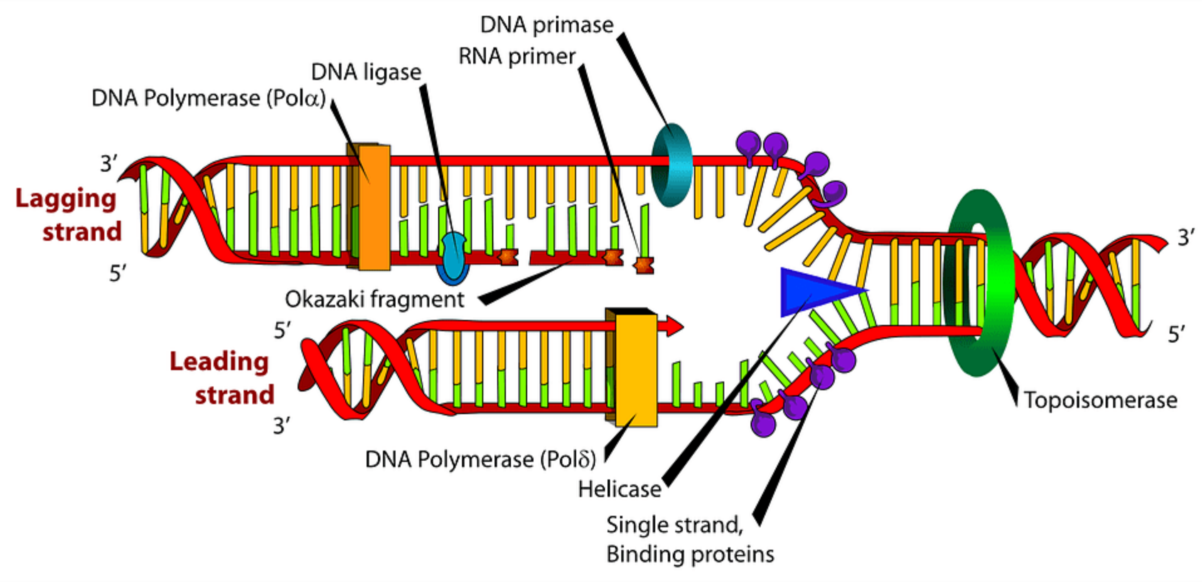


Fig. 21. Scheme of DNA replication.

Replication value:

a) the process is an important molecular mechanism underlying all types of cell division of pro- and eukaryotes;
b) provides reproduction of both unicellular and multicellular organisms;
c) maintains the stability of the cellular composition of organs, tissues and the body due to genetic
regeneration;
d) ensures the long-term existence of individuals and species of organisms;
e) contributes to the exact doubling of information;
e) in the process of replication possible errors (mutations), which can lead to disorders of protein synthesis with the development of pathological changes.

Transcription, processing, splicing

The DNA molecules of each cell contain information for the synthesis of all the proteins it needs. DNA molecules are contained in the nucleus, and protein synthesis occurs in the cytoplasm. DNA cannot move to the site of protein synthesis in the cytoplasm. It transmits information about the structure of proteins with the participation of specific mRNA molecules that are formed on DNA and transferred from the nucleus into the cytoplasm to the site of protein synthesis. Other RNAs (tRNA and rRNA) are also involved in protein synthesis. The formation of RNA molecules on the DNA matrix is called transcription (from the Latin transcription - transcription). This process occurs during the interphase. All three types of RNA are formed on the genes of the DNA matrix - informational, transport and ribosomal.

The molecular mechanisms involved in the «maturation» of different types of RNA are called processing. They are carried out in the nucleus before the release of RNA from the nucleus into the cytoplasm. It turned out that complementary DNA is only a precursor molecule of messenger RNA (pro-mRNA). Pro-mRNA molecules are much larger than mature mRNAs. During the «maturation» of messenger RNA in bacteria, only the ends of molecules are cleaved, and in eukaryotes and some viruses, this process is much more complicated. The pro-mRNA molecule contains a number of inert regions (introns) that do not carry information about the structure of the protein.

In the process of «maturation» of mRNA, special enzymes cut out nitrons and crosslink the remaining active areas (exons). This process is called splicing. Therefore, the nucleotide sequence in mature mRNA is not completely complementary to DNA nucleotides. Splicing is a very precise process, its violation changes the reading frame during translation, which leads to the synthesis of another peptide.

Topic 13. Translation. Regulation of gene expression.

Proteins -these are organic compounds, polymers, monomers in which are amino acids. Amino acids are small organic compounds that contain both an amino group and a carboxyl group. (Fig. 1) Proteins are also called proteins.

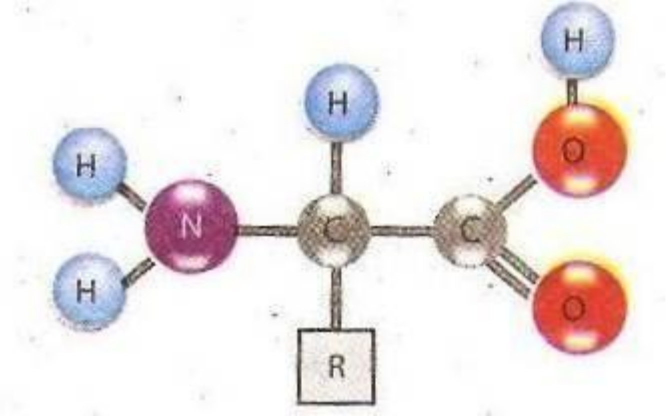


Fig. 22. General formula of amino acids.

In the process of protein biosynthesis, it includes 20 amino acids (eg, alanine, glycine, serine, tyrosine and others).

There are amino acids which organisms of the person and an animal cannot synthesize, they are called irreplaceable and necessarily have to arrive to an organism with food.

Amino acids can combine with each other. If there are several amino acids in such a compound, this bond is called a peptide; if a large number - polypeptide.

Levels of organization of a protein molecule

- **The primary structure of the protein represented** by a polypeptide chain. In this structure all communications between amino acids are covalent, and consequently, strong.
- **Secondary structure of protein is** a method of packing the primary structure in an alpha helix or beta layer. The alpha helix arises as a result of formation of hydrogen communications between groups -CO- and -NH located on various turns of a helix. The beta layer is formed as a result of formation of hydrogen bonds between CO groups of one polypeptide chain and NH groups of another polypeptide chain.
- **Tertiary structure -**it is a way of packing an alpha helix into a spatial globule. It is formed due to additional hydrogen bonds, hydrophilic-hydrophobic interactions and covalent disulfide bonds -SS-, which occur between two cysteine molecules.

- **Quaternary structure-** a method of joint packaging of several polypeptide chains.

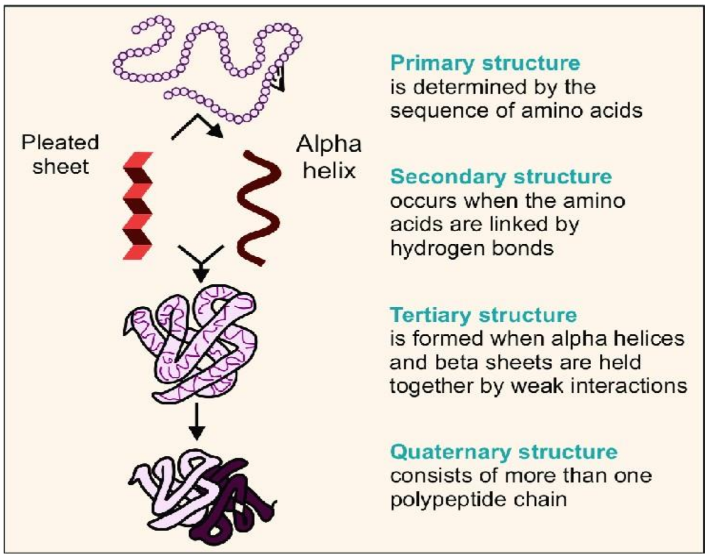
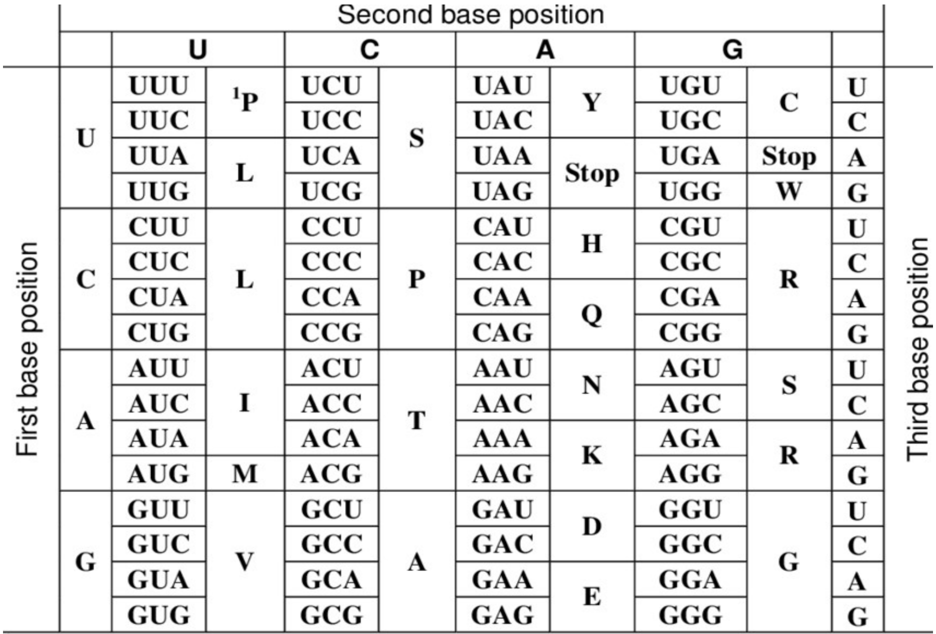


Fig. 23. Levels of structural organization of proteins.

Genetic code, its properties

The uniqueness of each cell lies in the uniqueness of its proteins. Cells that perform various functions are able to synthesize their own proteins using the information recorded in the DNA molecule. The information contained in DNA is transmitted to a protein molecule that is synthesized through RNA. A region of DNA that contains information about the structure of any one protein is called a genome. This information exists as a special sequence of nitrogenous bases in DNA.

Genetic code - a system for recording hereditary information, the correspondence between the three nucleotides of mRNA (codon) and amino acid in protein synthesis.



First base position	Second base position								Third base position
	U		C		A		G		
U	UUU	[1]P	UCU	S	UAU	Y	UGU	C	U
	UUC		UCC		UAC		UGC		C
	UUA	L	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG		UGG	W	G
C	CUU	L	CCU	P	CAU	H	CGU	R	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Q	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	I	ACU	T	AAU	N	AGU	S	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	K	AGA	R	A
	AUG	M	ACG		AAG		AGG		G
G	GUU	V	GCU	A	GAU	D	GGU	G	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	E	GGA		A
	GUG		GCG		GAG		GGG		G

[1] The one letter symbol of amino acids.

Fig. 24. Genetic code.

Characteristics of the genetic code of DNA:

1. Triplet - three adjacent nitrogenous bases are called codons and encode one amino acid.
2. Specificity - each individual triplet encodes only one specific amino acid.
3. Continuity - no nitrogenous base of one codon is ever part of another codon.
4. Versatility - this codon in DNA or mRNA determines the same amino acid in the protein systems of all organisms from bacteria to humans.
5. Redundancy - one amino acid often has more than one code triplet.

Translating

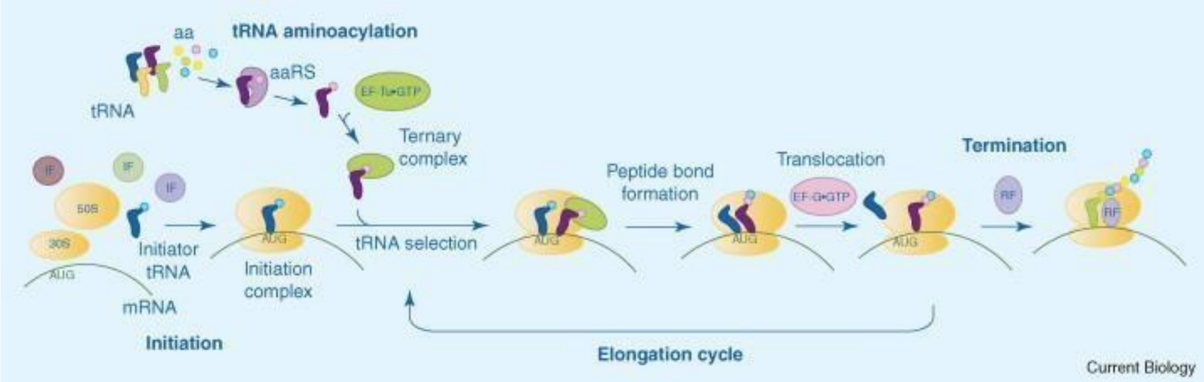
Translation, or protein biosynthesis, is the stage during which the polypeptide chain of a protein molecule is synthesized according to the information contained in the mRNA.

The translation process takes place in the ribosome, which is contained in the cytoplasm of the cell. It should be noted that several ribosomes can «work» on one molecule of IRNA at the same time. Each of them synthesizes one protein molecule. And all of them together with mRNA form a structure called a polyribosome. The synthesis takes place according to the genetic code, i.e. each amino acid triplet corresponds to a specific amino acid (see the table of the genetic code on the second cover). For example, the amino acid methionine (Met) corresponds to the AUG triplet, the isoleucine (Ile) amino acid triplet, and the UAA, UAG, and UGA nucleotides are stop codons, indicating the end of polypeptide chain synthesis.

At the time of synthesis a protein molecule in the cytoplasm must be a complete set of essential amino acids. Recall that they are formed as a result of the breakdown of proteins that enter the body with food or synthesized in the body.

Protein biosynthesis, like all previous stages of the implementation of hereditary information, is provided by energy due to the cleavage of ATP molecules.

The translation process consists of three stages: initiation, elongation and termination.



Current Biology

Fig. 25. General scheme of translation.

<u>General broadcast scheme:</u>

Initiation. 1. Recognition of the start codon (AUG), accompanied by the binding of tRNA aminoacylated methionine (M) and the assembly of the ribosome from large and small subunits.

Elongation. 2. Recognition of the current codon of the corresponding aminoacyl-tRNA (complementary interaction of the mRNA codon and the anticodon of tRNA is increased). 3. Attachment of the amino acid brought by tRNA to the end of the growing polypeptide chain. 4. The advancement of the ribosome along the matrix, accompanied by the release of the tRNA molecule. 5. Aminoacylation of the released tRNA molecule by its corresponding aminoacyl-tRNA synthetase. 6. Attachment of the next aminoacyl-tRNA molecule, similar to stage (2). 7. The movement of the ribosome by the mRNA molecule to the stop codon (in this case UAG).

Termination. Recognition of the stop codon by the ribosome is accompanied by (8) detachment of the newly synthesized protein and in some cases (9) dissociation of the ribosome.

The first stage of broadcasting is initiation

Initiation is the beginning of the synthesis of a polypeptide chain of a protein molecule. At this stage, the small subunit of the ribosome is attached to the mRNA chain, the start codon is recognized, the large ribosomal subunit is attached, and the first amino acid that initiates the polypeptide chain is attached to the ribosome.

The start codon is always the AUG codon. It is joined by a tRNA molecule that brings the amino acid methionine to the ribosome, which will be the first amino acid of the future polypeptide chain. The tRNA molecule attaches to the mRNA molecule through its triplet, called the anticodon, on the principle of complementarity.

The second stage of translation is elongation

Elongation - building a polypeptide chain of a protein molecule. After the start codon, the ribosome analyzes the next codon, recognizes it, and attaches to it the corresponding tRNA molecule, which transports the next amino acid to the ribosome. A peptide bond is formed between two amino acids, and the peptide chain is extended to this amino acid. The tRNA molecule is released and leaves the ribosome.

The ribosome then moves to the next mRNA triplet, recognizes it, and attaches the next tRNA molecule, which brings the corresponding amino acid to the ribosome. It attaches to the previous amino acid, and the polypeptide chain is extended by another amino acid.

The process of lengthening the polypeptide chain of a protein molecule is repeated until the ribosome encounters one of the stop codons - UAA, UAG or UGA.

The third stage of translation is termination

The third stage of translation - *termination* - completion of translation begins with the recognition of the stop codon by the ribosome. At this stage, the synthesis of the polypeptide chain of the protein molecule is completed, the ribosome is again broken down into small and large subunits, tRNA and mRNA molecules are released. Ribosome subunits, upon completion of polypeptide chain synthesis, can join a new mRNA molecule, and tRNA molecules can capture new amino acid molecules and transport them to the site of synthesis of another protein.

Maturation of protein

After the synthesis, the process of protein maturation can take place. During this process, some parts of the protein may be excreted by special enzymes, the protein may change its shape, combine with other proteins or join a non-protein part.

Maturation is required because the protein that has just been synthesized is not yet able to perform its functions. Maturation results in the loss of some amino acids located at the ends of the chain, and the final formation of secondary, tertiary and Quaternary structures of the molecule.

Protein synthesis is the basis of division, differentiation, growth and development, and provides features of metabolism and functions. Proteins help to unite cells into groups, which leads to the formation of tissues and organs. Any disturbances in the translation and synthesis of proteins cause disturbances in metabolism and function, and this leads to diseases.

Regulation of gene expression

Regulation of gene expression refers to a complex set of molecular mechanisms by which cells can increase or decrease the expression of certain genes (RNA or proteins) in response to changes in external conditions and factors. Regulation of expression allows the existence of different phenotypes in cells with identical genomes; this in turn determines the flexibility of living systems and the ability to adapt to changing environmental factors. Regulation of gene expression plays a key role in biological phenomena such as the adaptation of bacteria to a new environment with an alternative set of nutrients. The information encoded in the genes is transcribed in RNA, which after appropriate processing is broadcast on ribosomes in polypeptide products (protein). In general, any part of this process can be regulated; therefore, it is customary to distinguish between gene regulation at the transcription level, gene regulation at the translation level, and so on.

A key event in the study of the regulation of gene expression was the discovery of the lactose operon (lac operon) in 1961 by Jacques Mono. It has been shown that a group of enzymes that are required for lactose metabolism are expressed in bacteria *E. coli* only in the presence of lactose and the absence of the main source of energy - glucose. That is, the example of the lactose operon showed how organisms adapt to adverse environmental conditions by changing the set of genes expressed in the body at a certain point in time.

In multicellular organisms, due to the regulation of gene expression, such complex phenomena as cell differentiation and morphogenesis occur. As a rule, the initiator of changes in gene expression is the activation of certain receptors.

Topic 14. Genes and genomes. Horizontal gene transfer.

All organisms have heredity - the ability to transmit their characteristics and features of individual development to offspring. The unit of heredity is the gene.

***Gene* -** it is a region of the DNA molecule that contains information about the primary structure of the protein or RNA molecule and determines the possibility of the development of the trait.

The gene encodes hereditary information about the structure of a particular protein, nucleic acid or performs regulatory functions.

Any gene is a part of a DNA molecule. The gene is responsible for the formation of one or more traits in the body. However, most traits are formed by the interaction of several genes.

History of gene study:

1) in 1865 Gregor Mendel proved the existence of hereditary «inclinations»;
2) the term «gene» was proposed in 1909 by the Danish scientist Wilhelm Ludwig Johansen;
3) in the first half of the twentieth century, Thomas Morgan found that genes are linearly located on the chromosomes of the nucleus;
4) In 1953, James Watson and Francis Crick discovered the spatial structure of DNA.

According to the functional value, there are structural genes (containing 100, 1000 and more nucleotides) encoding the structure of proteins and RNA; and regulatory (containing several tens of nucleotide pairs) control the activity of structural genes – provide activation or inhibition of information reading.

Regulatory genes:

1) serve as a place of attachment of enzymes and other biologically active substances;
2) affect the activity of structural genes;
3) participate in the processes of DNA replication and transcription.

Genome – a set of hereditary material in the cells of an organism of a certain species. The term «genome» was proposed by Hans Winkler in 1920 to describe a set of genes.

The main provisions of modern gene theory:

1) Each gene occupies a certain position in the chromosome - a locus.
2) Gene – a part of a DNA molecule that has a specific nucleotide sequence and is a functional unit of hereditary information. The number of nucleotides that are part of different genes is different. Genes are located in a chromosome along its length in a linear order: one after another. At the same time they do not overlap.
3) Within the gene can occur recombination (redistribution of genetic material) and mutations (changes in genetic material).
4) There are structural genes – which encode protein synthesis and regulation - which control and direct the activity of structural genes.
5) The gene is not directly involved in protein synthesis, it is a matrix for the formation of mediators of various RNA molecules that are directly involved in synthesis.
6) The location of nucleotide triplets in structural genes is corresponding (collinear) to the amino acids in the polypeptide chain encoded by this gene.
7) DNA molecules are capable of repair (correction of DNA damage), so not all gene damage leads to mutations.
8) Genotype consists of individual genes, but functions as a whole. The function of genes is influenced by factors of both internal and external environment.

Gene functions are determined by the following properties:

1) **specificity**- the gene contains hereditary information only about a certain product or regulates the synthesis of only one specific protein;
2) **stability**- genes are able to maintain their inherent order of nucleotides;
3) **lability**- genes are capable of change and can mutate;
4) **gene interaction**- genes are able to influence each other with the participation of proteins that are products of the implementation of hereditary information encoded in them;
5) **multiple action of genes**- one gene can affect the development of several traits;
6) **polymeric action of genes**- several genes can affect the formation of one trait.

Horizontal gene transfer- any process during which an organism transmits genetic material to another organism (cell), which is not necessarily its descendant. In contrast, during vertical transmission, an organism receives genetic material from its ancestor, such as its father or the species from which the organism evolved. The artificial form of horizontal gene transfer is called ***genetic engineering.***

Gene therapy

The concept of gene therapy is the obvious statement that the most radical way to combat various diseases caused by changes in the genetic information of cells should be to correct or destroy the very genetic cause of the disease, not its consequences. This may be a mutation in the germ cell line that is passed onto offspring; or a somatic mutation that causes, for example, malignant transformation; or the appearance in the cell of foreign genetic material due to a viral infection. A way to combat these genetic changes is to artificially introduce into the affected cell new genetic information designed to correct the one associated with the disease.

Gene therapy strategies can be divided into three large blocks.

The first type of strategy is used in cases where the cells to be treated have lost the function of a particular gene. Then a gene capable of providing it must be delivered to the cell suffering from loss of function. Often the disease, on the contrary, is caused by excessive function, not inherent in a normal cell. This occurs, in particular, in infections or tumor transformations. Then you should focus on suppressing unnecessary functions. These two strategies can be considered purely gene-therapeutic: they are aimed at correcting the cell defect by 'its genetic modification.

The third type of approaches are those that aim to strengthen the body's immune response to adverse events. It also carries out genetic modification of either those cells against which they want to increase the immune response, or cells of the immune system, with which they want to enhance this effect.

There are several ways to introduce new genetic information into mammalian cells. Usually use two main approaches, which differ in the nature of the target cells:

1) ***fetal gene therapy*** - in which foreign DNA is injected into the zygote or embryo at an early stage of development; it is expected that the introduced material will get into all cells of the recipient, including sexual, thus providing transmission to the next generation);
2) ***somatic gene therapy*** - in this case, the genetic material is injected only into somatic cells and it is not transmitted to germ cells.

There is a third approach - activation of the body's own genes in order to completely or partially overcome the action of the mutant gene. A clear example of such an approach is the use of hydroxyurea to activate hemoglobin F synthesis in patients with sickle cell anemia and thalassemia.

There are various methods of introducing foreign DNA into target cells - the choice depends in part on the disease. The delivery of genetic material is carried out using vectors based on viruses (retroviruses that are not capable of self-replication, adenoviruses, herpesviruses, etc.) or using vector-free systems, in particular liposomes.

There are two approaches to somatic gene therapy.

The first is ex vivo gene therapy: first, the genetic material is injected into cells grown in culture, and then the transgenic cells are administered to the recipient.

The second is gene therapy in vivo: the vector carrying the desired gene is injected directly into the recipient's body. The first approach is especially effective if hematopoietic stem cells and other cells are used for delivery, which can be grown in culture in large quantities.

Up to 80% of all modern developments in gene therapy account for tumors. The following promising areas of cancer control are considered to be the most promising today:

1) increasing the immunogenicity of tumor cells, for example, by introducing genes encoding a foreign antigen to these cells;
2) introduction into tumor cells of «killer genes» that trigger the death program or are responsible for the synthesis of the product, which under certain conditions leads to the death of tumor cells;
3) blocking the expression of oncogenes by, for example, the introduction into cells of structures that encode the synthesis of antisense RNA or antibodies to oncoproteins;
4) protection of stem cells from the toxic effects of chemotherapy by introducing drug resistance genes into them.

A special place is occupied by developments aimed at combating AIDS. AIDS is an unusual infectious disease, because in this case the genetic material of the pathogen enters the genome and remains there until the end of the cell's existence. Today, two main approaches are used for AIDS gene therapy: intracellular immunization and boosting immunity against the virus using genetically modified cells. The term «intracellular immunization» means the process of creating cells capable of producing intracellular antibodies against the pathogen after the introduction into the cell of relevant genetic information. Intracellular antibodies open a unique means of influencing from within the cell on any intracellular objects - proteins, sugars or nucleic acids.

Finally, one of the most important areas of application of molecular genetics in medicine is the molecular diagnosis of hereditary diseases, including prenatal (prenatal diagnosis). Genes of almost all hereditary diseases are already known, methods for their determination are widely used in medicine to prevent the birth of a sick child. Molecular diagnostic methods can detect not only the genes of hereditary (monogenic) diseases (hemophilia, cystic fibrosis, Duchenne myodystrophy, phenylketonuria, etc.), but also the genes of predisposition to a disease: diseases that develop in old age

(Alzheimer's disease, breast cancer) neurodegenerative diseases), and those arising from the action of certain external factors (diabetes, atherosclerosis, some cancers).

Topic 15. Mutations.

Mutation is called a change in the amount or structure of DNA of a given organism. The mutation changes the genotype, which can be inherited by cells that are formed from the mutant cell as a result of mitosis or meiosis. The idea of mutation as the cause of the sudden appearance of a new trait was first put forward in 1901 by the Dutch botanist Hugo de Vries.

There are several principles for classifying mutations:

a) by the nature of changes in the genome mutations are divided into: genomic mutations (changes in the number of chromosomes), chromosomal mutations, or chromosomal rearrangements (changes in the structure of chromosomes) and gene mutations (changes in genes);
b) by manifestation in the heterozygote mutations are dominant and recessive;
c) by deviation from the norm of mutation is divided into direct mutations and reversals;
d) depending on the causes of mutations, they are divided into spontaneous, arising without a cause, ie without any inducing effects from the experimenter, and induced mutations.

These classifications of changes in genetic material are of universal importance. Each of the approaches in these classifications reflects some aspect of the occurrence or manifestation of mutations in any organism: eukaryotes, prokaryotes and non-cellular forms.

There are more careful approaches to the classification of mutations:

a) by localization in the cell mutations are divided into nuclear and cytoplasmic
b) in relation to the possibility of inheritance mutations are generative, occurring in germ cells, and somatic, observed in somatic cells.

Probably, the last two classifications of mutations are characteristic only for eukaryotes.

Very often mutations are classified according to their phenotypic manifestation, i.e. depending on the changing trait. Then consider mutations lethal, morphological, biochemical, behavioral, etc.

Mutations occur spontaneously, i.e. any gene can mutate at any time. The frequency of mutations in different organisms is different, but is obviously related to the duration of the life cycle: in organisms with a short life cycle, it is higher.

Genomic mutations include changes in the number of chromosomes. Some types of genomic mutations alter the action of some genes and affect the phenotype much more than gene mutations. Changes in the number of chromosomes usually occur due to errors in meiosis, but they are possible under conditions of mitosis. These changes are expressed either in aneuploidy - the loss or addition of individual chromosomes, or in polyploidy - the addition of whole haploid sets of chromosomes.

Aneuploidy may occur if in anaphase I of meiosis homologous chromosomes of one or more pairs do not diverge. In this case, both members of the pair are directed to the same pole of the cell, and then meiosis leads to the formation of gametes that contain one or more chromosomes more or less than normal. This phenomenon is known as discrepancy. When a gamete with a missing or excess chromosome merges with a normal haploid gamete, a zygote with an odd number of chromosomes is formed: instead of any two homologues in such a zygote, there may be three or only one. A zygote in which the number of chromosomes is less than diploid does not usually develop, but zygotes with extra chromosomes are sometimes capable of development. However from such zygotes in most cases persons with sharply expressed anomalies develop.

Gametes and somatic cells with an increased number of chromosomes, a multiple of the haploid number, are called polyploid; prefixes tri-, tetra-, etc. indicate how many times the number of chromosomes is increased, ie the degree of ploidy. The relative rarity of polyploidy in animals is explained by the fact that the increased number of chromosomes significantly increases the probability of errors in meiosis during gametogenesis.

Chromosomal mutations.

At crossing over during prophase I of meiosis there is an exchange of genetic material between homologous chromosomes. This causes changes in the sequence of alleles in the parental coupling groups, resulting in recombinants, but without the loss of any gene loci. Similar effects occur with chromosomal rearrangements such as inversions and translocations. In rearrangements of other types — deletions and duplications — the number of gene loci on chromosomes changes, and this can affect phenotypes. Structural changes in chromosomes associated with inversions, deletions, duplications, and in some cases translocations, can be observed under a microscope, when in prophase I of meiosis homologous chromosomes begin to conjugate. Homologous chromosomes conjugate, and in those areas affected by rearrangement, one of the homologous chromosomes forms a loop or is twisted. Which of the chromosomes forms a loop and how its genes are located depends on the type of rearrangement.

Inversion occurs due to the excision of a portion of the chromosome that rotates 180°, and then re-inserted in the same place. There are no changes in the genotype, but phenotypic changes are possible. This indicates that the sequence of genes in a given chromosome may be indifferent to their action (position effect).

At translocation from one of the chromosomes the site comes off and joins or to the other end of the same chromosome, or to another, nonhomologous chromosome.

The simplest form of chromosomal mutation is a ***deletion*** or deficiency, i.e. the loss of a chromosome of any region, intermediate or final. At the same time, some genes are already missing in the chromosome. Deletion can occur in one of two homologous chromosomes; in this case, alleles located on another normal chromosome will be expressed, even if they are recessive. If the deletion affected the same gene loci on both homologous chromosomes, it usually leads to death.

Sometimes a part of a chromosome doubles, so there is a ***duplication*** - a repetition of a set of genes that are localized in that part. This extra set can be found inside the same chromosome or at one end, and sometimes joins any other chromosome.

Gene mutations.

Genna, or a point (because it belongs to a specific gene locus) ***mutation*** is the result of a change in the nucleotide sequence of a DNA molecule in a specific region of a chromosome. This change in the sequence of bases in this gene is reproduced by transcription in the structure of mRNA and leads to a change in the sequence of amino acids in the polypeptide chain formed by translation on ribosomes.

There are different types of gene mutations that involve the addition, loss, or rearrangement of nitrogenous bases in a gene. These are duplications, insertions, deletions, inversions or substitutions of bases. In all cases, they cause changes in the nucleotide sequence, and sometimes the formation of an altered polypeptide.

Gene mutations that occur in gametes are transmitted to all progeny cells and can affect the future of the population. Somatic gene mutations that occur in the body are inherited only by those cells that are formed from the mutant cell by mitosis. They can affect the organism in which they originated, but as a result of death, individuals disappear from the gene pool of the population. Somatic mutations are likely to occur very frequently and go unnoticed, but in some cases, cells with increased growth and distribution rates are formed. These cells can give rise to tumors – either benign, which have little effect on the whole body, or malignant, which causes cancer.

The effects of gene mutations are extremely diverse. Most small gene mutations are not phenotypically detected because they are recessive, but there are a number of cases where the change of only one base in a particular gene affects the phenotype.

Mutagens

Mutagens (mutagenic factors)- these are the factors that cause mutations. Many of them are carcinogenic, i.e. they can cause malignant tumors. There are the following types of mutagens - physical, chemical, biological.

Physical mutagens include all types of ionizing radiation (gamma and X-rays, electrons, positrons, protons, neutrons), ultraviolet radiation, high and low temperatures. The most dangerous is ionizing radiation (ionizing radiation). All types of ionizing radiation have high permeability and are characterized by biological action. Penetrating through the tissues of the human body, they transfer their energy to the atoms of these tissues, causing their excitation and ionization. Particularly sensitive are proliferating tissues - lymphoid and hematopoietic. Ionizing radiation affects all components of the cell, but the chromosomes of the nucleus are particularly vulnerable. In DNA molecules there are gaps, chromosomal aberrations, point mutations.

Induction of mutations occurs at action of any dose, and with increasing dose, the number of mutations increases proportionally. The genetic effect of small doses is summed up. Any use of ionizing radiation requires compliance with the rules of radiation safety and radiation protection of patients and medical staff.

Ultraviolet rays do not cause ionization, but only excite the electronic shells of atoms, which increases their reactivity and can lead to mutations. UV rays with a wavelength of about 260 nm have the greatest mutagenic activity, because DNA absorbs just this part of the spectrum.

Chemical mutagens- various chemicals used in agriculture as herbicides (maleic acid hydrazide), pesticides (DDT), medicine as drugs (cytostatic and antimitotic agents), industry (benzene, heavy metals: cadmium, mercury, lead, nickel) in including food (food additives), in everyday life (varnishes, paints). In order to prevent mutagenesis, each chemical compound to be used is tested for mutagenicity.

The strongest mutagens (super mutagens) are ethylene diamine, diethyl sulfate, nitrosomethylurea, nitrosomethylurea, hydrogen peroxide, and mustard gas. The second group consists of substances that are similar in structure to the nitrogenous bases of nucleic acids and act on them: 5-bromouracil, 5-fluorodeoxyuridine, 5-bromodeoxyuridine. The third group includes acridines and their derivatives: acridine yellow, ethidium bromide. The fourth group includes nitric acid, formaldehyde, hydroxylamine.

Biological mutagens- viruses, live vaccines, toxins of some organisms, especially molds, bacteria, protozoa, helminths. Live vaccines are biological products made from bacteria or viruses with reduced virulence.

Genetic monitoring

The condition of atmospheric air, water and soil in many regions of Ukraine is unsatisfactory. It has been found that many contaminants are able to induce gene mutations in experiments on Salmonella test strains. In some cases, water intended for drinking purposes was genotoxic. The unsatisfactory environmental situation in Ukraine has been exacerbated by the Chernobyl disaster (1986). The demographic situation in Ukraine has taken the form of an acute crisis. Since 1991, mortality has prevailed over birth rate. The number of people with genetic disorders has increased as a result of the combined action of chemical and physical mutagens. Genetic load in populations has increased. Burdened heredity has become a significant factor that negatively affects the health of the population. Damage to the hereditary material of somatic cells can lead to a sharp increase in malignant diseases, premature aging, and weakening of the body's defenses. All this reduces the birth rate and leads to biological regression. Damage to the hereditary material of germ cells can lead to gradual degeneration and even death of individual populations.

The demographic situation and the state of health of the population in Ukraine require immediate measures at the state level to protect the gene pool of the population. By his Decree, the President approved the Targeted Comprehensive Program of Genetic Monitoring (Genetic Surveillance, Genetic Control) in Ukraine. One of the most important divisions of this program is the creation of a state genetic monitoring service. The purpose of genetic monitoring is to analyze the mutagenic state of the environment, to observe mutagenic changes in human populations.

In order to reduce the risk of mutations:

1) test all new chemicals, drugs for mutagenicity;
2) use antimutagens. Antimutagens are factors that reduce the frequency of mutations.

They neutralize the mutagen before it reacts with the DNA molecule, or remove the DNA damage caused by the mutagen. Vitamins, glutamine, serotonin, reserpine, and also some physical factors (daylight) have antimutagenic action. Com Mutagens are substances that increase the effects of environmental mutagens, although they themselves are not capable of mutagenic action, do not have their own mutagenic activity. This effect has compounds of natural and artificial origin, inorganic and organic nature. Mutagenesis is the growth of the damaging effect of mutagens under the action of non-mutagenic compounds. So, ascorbic acid (vitamin C) enhances the cytogenetic effects of mutagens (cyclophosphamide) in human lymphocyte culture; caffeine increases the induction of methotrexate by sister chromatid exchanges, the formation of micronuclei, and so on. The presence of commutagens in the environment can increase the negative effects of chemical, physical, biological and other mutagens with which a person comes into contact.

Questions for Preparation

1. Nucleic acids. DNA, structure and functions.
2. RNA, structure and functions. Types of RNA.
3. Structure of the eukaryotic gene. Classification of genes.
4. DNA replication, its significance. Self-correction and DNA repair.
5. Genetic code, its properties.
6. Main stages of protein biosynthesis in the cell.
7. Features of gene regulation in proto- and eukaryotes. Operon.
8. Gene mutations, mechanisms of occurrence. The concept of monogenic diseases.
9. Chromosomal aberrations. Mechanisms of occurrence and examples of diseases that are their consequence.
10. Hereditary diseases that are a consequence of a violation of the number of autosomes and sex chromosomes.
11. Mutations in germ and somatic cells, their significance. Mosaicism.
12. Spontaneous and induced mutations. Mutagenic factors, their types.
13. Mutagenesis. Genetic monitoring.

Recommended reading:

1. Yu. I. Bazhora [et al.]. / Бажора Ю.И., Булик Р.Е., Чеснокова М.М. Medical biology. textbook. – Vinnytsia: Nova Knyha, 2019. – 448 p.
2. Smirnov O. «Medical Biology: A Short Course. Vol. 1», Chapter 1. 2. Bazhora Yu. et al. «Medical Biology». Vinnytsia: Nova Knyha, 2021). – 86 p.
3. Test Bank of Licensin exam «Krok-1» in Medical biology: Manual for independent learning of students of VI faculty for international students / autors: V.V. Myasoyedov, Yu.A. Sadovnychenko, O.B. Khromenkova, I.P. Meshcheryakova. – Kharkiv: KNMU, 2017. – 57 p.
4. Smirnov O. Yu. Test Items for Licensing Examination: «Krok-1 General Medical Training: Medical Biology» (For Medical Students). – Sumy: Sumy State University, 2016.
5. Smirnov O. Medical Biology: A Short Course. Vol. 1. 2 nd Ed. – Sumy: Korpunkt Publishers, 2011. – 181 p.
6. Lazarev K. L. Medical Biology. – textbook. - 2nd ed. - Simferopol_ IAD CSMU, 2003. – 592 p.

Reference to information resources on the Internet, video lectures, other methodological support:

https://activepresenter.online/pluginfile.php/22999/mod_resource/content/2/GUIDE%20TO%20PRACTICAL%20CLASSES%20IN%20MEDICAL%20BIOLOGY%20by%20Dr.%20Oleg%20Smirnov.pdf

https://www.google.com/search?sca_esv=4c75ca2344971d57&q=Lazarev+K.+L.+Medical+Biology.+%E2%80%93+textbook.+-+2nd+ed.+-+Simferopol+IAD+ZSMU,+2003.+%E2%80%93+592+p.&spell=1&sa=X&ved=2ahUKEwjjx_n_os6MAxVGKRAIHet0IrkQBSgAegQIDBAB&biw=1280&bih=593&dpr=1.5

https://repo.knmu.edu.ua/server/api/core/bitstreams/c1b4b36f-0ef4-41ee-8d46-acbf49171690/content

Електронне навчальне видання комбінованого використання
Можна використовувати в локальному та мережному режимі

Шерстюк Сергій Олексійович
Наконечна Світлана Анатоліївна
Зотова Алла Борисівна
Панов Станіслав Ігорович

МЕДИЧНА БІОЛОГІЯ

У двох частинах

ЧАСТИНА І

Методичні рекомендації для самостійної
роботи студентів 1-го курсу навчання медичного факультету
з дисципліни «Медична біологія»

(Англ. мовою)

В авторській редакції

Підписано до розміщення 21.05.2025. Гарнітура Times New Roman.
Ум. друк. арк. 3,88. Обсяг 2,496. Зам. 445/25.

Харківський національний університет імені В. Н. Каразіна,
61022, м. Харків, майдан Свободи, 4
Свідоцтво суб’єкта видавничої справи ДК № 3367 від 13.01.2009
Видавництво ХНУ імені В. Н. Каразіна