FACULTY OF MEDICINE

STUDY PROGRAM 0912.1 MEDICINE

CHAIR OF MOLECULAR BIOLOGY AND HUMAN GENETICS

APPROVED
at the meeting of the Commission for Quality Assurance and Evaluation of the Curriculum faculty _____
Minutes No. 6 of 23.02.18

Chairman, Associate professor, PhD

Suman Serghei _____

APPROVED
at the Council meeting of the Faculty

_____
Minutes No. 4 of 20.03.18

Dean of Faculty Medicine 2,
Associate professor, PhD

Betiu Mircea _____

APPROVED
approved at the meeting of the chair of Molecular Biology and Human Genetics
Minutes No.5 of 02.11.2017
Head of chair, Associate professor, PhD

Cemortan Igor _____

SYLLABUS

DISCIPLINE **MOLECULAR BIOLOGY**

Integrated studies

Type of course: **Compulsory discipline**

Chisinau, 2017

I. INTRODUCTION

- **General presentation of the discipline: place and role of the discipline in the formation of the specific competences of the professional / specialty training program**

  The course of molecular biology is an important part of preclinical education and its main objective is to study the molecular structure of the cell - the basic structural, biochemical, functional level of the human body.
  The content of the course is structured to demonstrate that living organisms, regardless of their complexity, including the human organism, have a common organizational principle, which determines them to be self-reproducing, self-renewing and self-regulating systems; the peculiarities of an organism structure and functions are encoded in DNA molecules and expressed through the synthesis of RNA molecules and proteins, which are the molecular substrate of all structures, properties and functions of the human body; DNA replication, repair, encoding genetic information, transcription and translation - fundamental processes that explain vitality; the dynamics of cellular components and molecular processes depending on cell cycle period, cell type and ontogenetic period of the body - the basis of human body development, cell differentiation and transformation.

- **Mission of the curriculum (aim) in professional training**

  One of the main objectives of the course is to demonstrate the link between the structure and function of biopolymers, cell compartments, different cell types. The second objective is to evaluate the relationship in the chain: the function of a cellular component at the molecular →cellular → organism level. The third objective is to understand the medical role of DNA, RNA and proteins. It is important that any pathological process can be based on cellular changes: metabolic defects; structural defects; signaling defects; defects in cellular contacts; etc.
  Knowing the organization and functioning of the cell / cells provides the medical student the chance to understand the mechanisms of human disease production and ways of solving pathological processes. 21st Century Medicine is MOLECULAR MEDICINE.
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- **Language (s) of the course**: English.

- **Beneficiaries:** students of the Ist year, faculty Medicine 2, Specialty Medicine.

II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		F.01.O.004.	
Name of the discipline		**Molecular Biology**	
Person(s) in charge of the discipline		Associate professor **Igor Cemortan**	
Year	**I**	Semester/Semesters	**1**
Total number of hours, including:			**150**
Lectures	**34**	Practical/laboratory hours	**25**
Seminars	**26**	Self-training	**65**
Clinical internship			
Form of assessment	**E**	Number of credits	**5**

III. TRAINING AIMS WITHIN THE DISCIPLINE

At the end of the discipline study the student will be able to:

at the level of knowledge and understanding:

- know the organization of biological systems;
- know the fundamental properties of life and its molecular organization;
- understand the principles of human cell compartmentalization, the characteristic features of each compartment, the set of characteristic molecules and the interrelationships between different cell organelles and the cells of a multicellular organism;
- know the relationship DNA-RNA-protein --- cellular structures and functions and their effects at the body level; to know the relationship Genome → Transcriptome → Proteome → Metabolome → Phenome;
- understand how the human genome is organized, the particularities of the storage, transmission and realization of genetic information at the molecular, cellular and body level;
- know the principles of basic molecular processes: transcription, translation, replication and repair;
- know the particularities of organization and functioning of the human cell vs. the bacterial cell;
- understand the basic processes that ensure the growth of the multicellular organism, cell differentiation, renewal and regeneration of tissues - mitosis and apoptosis.
- understand the basis of diversity of living organisms, intra- and inter-familial variability of the human organism – intra-chromosomal, inter-chromosomal and genomic recombination;
- know the basics of DNA technology, the principles of human gene study techniques.

at the application level:

- distinguish cellular forms of life from acellular;
- distinguish the eukaryotic from the prokaryotic cell;
- model basic genetic processes: replication, transcription, translation;
- evaluate the practical role of recombinant DNA technology;
- distinguish separation of DNA and mRNA from human cells;
- interpret the results obtained by different DNA sequencing methods;
- interpret the results obtained by the PCR technique;
- interpret the results obtained by the Southern blot technique;
- read out the results of electrophoresis of DNA fragments obtained by various techniques.

at the integration level:

- assess the place and role of molecular biology in the pre-clinical training of the medical student;
- use the knowledge and methodology of molecular biology to explain the nature of physiological or pathological processes;
- make the link between structure and function at molecular level → at cellular level → at tissue level → at organism level;
- deduce the possible causes of blocking the basic molecular processes and the consequences on the cell, tissue, organism as a whole;
- implement the knowledge gained in the research activity;
- use critically and with confidence the scientific information obtained using the new information and communication technologies;
- use multimedia technology to receive, evaluate, store, produce, present and exchange information, and communicate and participate in networks via the Internet;
- learn to learn, which will contribute to the management of the professional development.

IV. PROVISIONAL TERMS AND CONDITIONS

Requirements for first year students:
• knowledge of the language of studies;
• confirmed competences in sciences (biology, chemistry, physics) at the school level;
• digital competences (use of the Internet, document processing, electronic tables and presentations, use of graphics programs);
• ability to communicate and work in a team;
• qualities - tolerance, compassion, autonomy.

V. THEMES AND ESTIMATE ALLOCATION OF HOURS

Lectures, practical hours/ laboratory hours/seminars and self-training

No. d/o	THEME	Number of hours		
		Lectures	Practical hours	Self-training
1.	Molecular biology as biological science. Importance of Molecular biology for medicine. Biological systems and their proprieties. Levels of organization of biological systems. The cell as structural and functional unit of life. Acellular forms of life: viruses and prions. Comparative characterization of prokaryotic and eukaryotic cells. Chemical organization of cell. Main cell components. Cytosol and cytoskeleton. Compartmentalization of eukaryotic cells. Methods of cell analysis. Microscopic methods of cell investigation.	2	3	4
2.	Macromolecules. Proteins: structure, functions and their location in the cell. Activation and inactivation of proteins. Carbohydrates structure, functions of deposition and signalling. Lipids. Phospholipids. Cholesterol. Nucleic acids.	2	3	4
3.	Nucleic acids – structure, properties, functions. Peculiarities of DNA organization in prokaryotes and eukaryotes. Mitochondrial DNA. Types of RNA. Functions of different types of RNA. Functions of different types of RNA. Functions and interactions of macromolecules in biological systems.	2	3	3
4.	Biological membranes and their molecular organization. Plasma membrane and intracellular membranes. Particularities of the internal cell membranes and their biogenesis. Transmembrane transport of substances. Membrane receptors. Cell junctions.	2	3	3
5.	Compartmentalization of eukaryotic cells. Cell organelles: structure and functions. Biogenesis of membrane. Endocytosis, exocytosis and their biological role. Cytoskeleton.	2	3	3
6.	Main characteristics of prokaryotes. General structure of bacteria. Cell envelope: structure and peculiarities. Genetic apparatus of bacteria: nucleoid and plasmids. Bacterial cell cycle. Biological importance of bacteria.	2	3	4

No. d/o	THEME	Number of hours		
		Lectures	Practical hours	Self-training
7.	Structure and functions of the nucleus. Nuclear DNA, coding and non-coding sequences. Chromatin: euchromatin and heterochromatin. Molecular organization of chromatin. Levels of condensation of chromatin. Nucleolus: molecular organization and functions. Steps of ribosomes biogenesis.	2	3	4
8.	Structure of prokaryotic and eukaryotic genes. Coding, non-coding, regulatory and modulatory sequences. Structure and functions of the Ist, IInd, IIIrd class genes. Mitochondrial genes. Prokaryotic genes.	2	3	4
9.	Gene expression. Transcription. Steps of transcription. Apparatus of transcription. Peculiarities of transcription in prokaryotes and eukaryotes. Processing of RNA. Transcription of 1^{st}, 2^{nd} and 3^{rd} class genes. RNA splicing. Alternative splicing and its biological importance. editing. Modeling of transcription and translation.	2	3	4
10.	Translation. Genetic code. Steps and apparatus of translation. Modelling of translation.	2	3	4
11.	Modelling of the Ist, IInd, IIIrd class gene expression. . Control of gene expression. Blocking of transcription and translation, its possible causes and consequences. Defects of splicing and their consequences.	2	3	4
12.	Replication and its biological role. Apparatus of replication. Peculiarities of replication in prokaryotes. Replication in eukaryotes. DNA repair in prokaryotes and eukaryotes: mechanisms and biological role.	2	3	4
13.	Cell cycle. Steps of cell cycle: interphase in mitosis. Apoptosis. Examination of microscopic slides, images with different phases of mitosis. Dynamic of chromosomes during cell cycle.	2	3	4
14.	Meiosis and its periods. Crossing-over and its biological importance. Molecular mechanism of crossing-over. Dynamic of chromosomes during meiosis. Biological importance of meiosis.	2	3	4
15.	Recombinant DNA methods. Restriction enzymes. Restriction maps. Cloning vectors: plasmids and bacteriophages. Isolation and purification of DNA and RNA. Cloning in vivo and in vitro.	2	3	4
16.	Methods of gene analysis.	2	3	4
17.	Application of the molecular-genetic methods in medicine: indication and limits.	2	3	4
Total		**34**	**51**	65

VI. REFERENCE OBJECTIVES OF CONTENT UNITS

Objectives	Content units
Theme (chapter) 1. „Molecular organization of human cell"	
• To define e biopolymers and cell compartments • to know the structure, properties and functions of biopolymers and their location in the cell • to demonstrate the principles of cell compartmentalization and the interaction between different compartments • to comment on the medical significance of biopolymers • to apply knowledge to other disciplines • to formulate conclusions, to develop own views on the biological and medical role of biopolymers and cell compartments	1. Cell as a structural, functional and pathological unit of human organism. 2. Nucleic acids as carriers of genetic information about organization and functions of cell. 3. Proteins – substrate of all structures, properties and functions at the level of cell, tissue, organism. **4.** Interactions between macromolecules, their role in integrity and normal activity of human cells.
Theme (chapter) 2. Main molecular processes in cell	
• To define gene, gene expression, transcription, processing, splicing, alternative splicing, translation, genetic code, replicon, replication, NER repair; BER repair • To know the peculiarities of organization of different human vs. prokaryotes genes; the peculiarities of the expression of nuclear vs mitochondrial vs bacterial genes; • to know the principles and the apparatus of transcription, processing and translation; • to know the peculiarities of nuclear vs. mitochondrial vs. prokaryotic DNA replication; • to demonstrate the peculiarities of GI expression and the importance of this knowledge in eukaryotes vs. prokaryotes • to model the expression of Class I, Class II, Class III genes and prokaryotic genes • to model the translation of the genetic code • to apply the gained knowledge in other subjects	1. Structure and functions of genes. Coding, non-coding, regulatory and modulatory sequences. Mobile genetic elements. 2. Transcription of genetic material. Steps of transcription. Apparatus of transcription. Processing of RNA. RNA splicing. Alternative splicing and its biological importance. 3. Translation. Genetic code. Steps and apparatus of translation. Control of gene expression in eukaryotes. Levels of the control of gene expression. Control of gene activity on ontogenesis and cell specialization. 4. DNA replication. Apparatus of replication. Peculiarities of replication in prokaryotes and eukaryotes. Synthesis of telomeres. Replication of mitochondrial DNA. 5. DNA repair.

Objectives	Content units
Theme (chapter) 3. Transmission of the genetic information from cell to cell, from parents to offspring	
• To define interphase, mitosis, meiosis, gametogenesis, crossing-over, gametocyte, gamete, G0 period, somatic cell, STEM cell, apoptosis • to know the particularities of the cell cycle, the dynamics of the chromosomes in G1, S, G2, prophase, metaphase, anaphase, telophase; • to know the modality and particularities of the meiosis, the dynamics of the chromosomes during the reductional and equational divisions; • to know the particularities of apoptosis; • to understand the mechanisms of cell cycle control and cell transformation pathways; • to understand the particularities of the development of meiosis in oogenesis vs spermatogenesis; • to demonstrate the medical role of knowing the cell cycle, apoptosis;	1. Cell cycle. Steps of cell cycle: interphase and mitosis. Interphase: sequence of main events. Mitosis. Dynamic of chromosomes during mitosis. Control of cell cycle. Restriction points. Types of cell proliferation. Period G_o. Malign transformation. 2. Apoptosis programmed cell death. Mechanisms of apoptosis. Biological importance of apoptosis. Control of apoptosis. 3. Recombination. Steps of meiosis: Reductional and equational divisions. Crossing-over and its biological importance. Dynamics of chromosomes during meiosis. Peculiarities of gametogenesis in male and female.
Theme (chapter) 4. Basics of the genetic engineering	
• To define recombinant DNA, DNA cloning, in vivo cloning, in vitro cloning, restriction enzymes, molecular markers, synthetic primers, PCR • to know the principles, stages and components needed for recombinant DNA technology; • to know the particularities of cloning vectors and hosts; • to know the particularities of DNA cloning in vitro; • to understand the principles of genomic DNA and RNA isolation for different techniques; • to understand the principles of gene analysis techniques; • to model *in vivo* cloning and *in vitro* cloning of DNA • to model the PCR and the Southern-blot techniques • to interpret the results obtained by the PCR technique; • to interpret the results obtained by the Southern blot technique.	1. Recombinant DNA technology. Restriction enzymes. Restriction maps. Cloning vectors: plasmids and bacteriophages. 2. Isolation and purification of DNA and RNA. DNA and genomic libraries. 3. Cloning in vivo and in vitro. 4. Methods of gene analysis. Gene sequencing. Southern, Northern and Western-blot analysis. PCR and its applications.

VII. PROFESSIONAL (SPECIFIC (SC)) AND TRANSVERSAL (TC) COMPETENCES AND STUDY OUTCOMES

✓ Professional (specific) (SC) competences

PC1. Knowing, understanding and use of language specific to molecular biology, molecular medicine;

PC2. Knowing and understanding the molecular organization of different cell compartments, explaining the principles of their specialization and interaction;

PC3. Explaining and interpreting molecular processes (replication, repair, transcription, translation, mitosis, meiosis, apoptosis).

PC4. Knowing the principles of gene engineering techniques and understanding the interpretation of their results.

FP5. Modeling of genes expression, replication, mitosis, meiosis.

FP6. Solving situation problems and formulating the conclusions.

FP7. Classification of different cellular, molecular elements and identification of grouping criteria.

FP8. Comparing different cellular and molecular elements and processes.

PC9. Analysis of various cellular, molecular and cellular elements and pathways leading to pathological conditions.

✓ Transversal competences (TC)

TC1. Improving the capacity of decisional autonomy;
TC2. Formation of personal attitude;
TC3. Ability to social interaction, group work with different roles;
TC4. participating in interdisciplinary projects, extracurricular activities;
TC5. Improving digital skills;
TC6. Developing different learning techniques;
TC7. Selection of digital materials, critical analysis and conclusions;
TC8. Presentation of individual scientific projects.

✓ Study outcomes

- To know the organizational features, fundamental properties of life and the molecular basis of biological systems;
- To understand the principles of human cell compartmentalization;
- To understand the relationship Genome → Transcriptome → Proteinome → Metabolome → Phenome;
- To know the principles and model the basic molecular processes: transcription, translation, replication and repair;
- To know the particularities of organization and functioning of the human cell vs. the bacterial cell;
- To understand the basic processes that ensure the growth of the multicellular organism, cell differentiation, renewal and regeneration of tissues - mitosis and apoptosis.
- To know the bases and the practical role of recombinant DNA technology, the principles of human gene study techniques.

- To be able to assess the place and role of molecular biology in the pre-clinical training of the medical student;
- To be competent to use the knowledge and methodology of molecular biology to explain the nature of physiological or pathological processes;
- To be able to deduce the possible causes of blocking the underlying molecular processes and their consequences on the cell, the tissue, the body as a whole;
- To be able to implement the knowledge gained in the research activity;
- To be competent to use critically and with confidence the scientific information obtained using the new information and communication technologies.

VIII. STUDENT'S SELF-TRAINING

No.	Expected product	Implementation strategies	Assessment criteria	Implementation terms
1.	Working with information sources:	Reading the lecture or the material from the textbook on the topic carefully. Reading questions on the topic, which require a reflection on the subject. To get acquainted with the list of additional information sources on the topic. Select the source of additional information for the topic. Reading the text entirely, carefully and writing the main content. Writing generalizations and conclusions regarding the importance of the topic / subject.	Ability to extract the main information; interpretative skills; the volume of work	During the semester
2.	Working with the Workbook:	Before solving the tasks in the workbook to analyze the information and images from the respective subject in the lecture and textbook. Solving consecutive tasks. Formulate conclusions at the end of each lesson. Verifying the final conclusions of the lesson and appreciating their fulfilment. Selection of additional information, using electronic addresses and additional bibliography.	Workload, problem solving, ability to formulate conclusions	During the semester

3.	Working with online materials	Online self-assessment, study of online materials on the Chair site, expressing own opinions on forum and chat	Number and duration of chair site entries, self-evaluation results	During the semester
4.	Preparing and presenting presentations / portfolios	Selection of the research topic, establishing the research plan, setting the terms of realization. Establishing the components of the project / PowerPoint presentation - topic, goal, results, conclusions, practical applications, bibliography. Peer reviews. Teacher reviews	The volume of work, the degree of understanding of the essence of the project topic, the level of scientific argumentation, the quality of the conclusions, the elements of creativity, the personal attitude, the coherence of the exposure and the scientific correctness, the way of presenting	During the semester

IX. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

- ***Teaching and learning methods used***

In teaching Molecular Biology are used various didactic methods and techniques, oriented towards the efficient learning and achievement of the objectives of the didactic process. During theoretical lectures, along with traditional methods (lecture-exposure, lecture-conversation, synthesis lecture), modern methods (lesson-debate, lecture-conference, problem-lesson) are also used. Forms of individual, frontal, group, virtual lab work are used in the practical classes. To learn the material in depth, different semiotic systems (scientific language, graphical and computerized language) and teaching materials (tables, diagrams, micro-pictures, transparent films) are used. During the lessons and extracurricular activities are used Communication Information Technologies - PowerPoint presentations, on-line lessons.

- ***Recommended learning methods***
  - **Observation** - Identification of elements characteristic to some structures or biological phenomena, describing these elements or phenomena.
  - **Analysis** - Imaginary decomposition of the whole into component parts. Highlighting the essential elements. Studying each element as part of the whole.
  - **Diagram / picture analysis** - Selection of required information. Recognition based on knowledge and selected information of the structures indicated in the diagram, drawing. Analysis of the functions / role of recognized structures.
  - **Comparison** - Analysis of the first object / process in a group and determining its main features. Analysis of the second object / process and determining its main features. Comparing objects / processes and highlighting common features. Comparing objects / processes and determining differences. Establishing distinguishing criteria. Formulating conclusions.

- **Classification** - Identification of the structures / processes to be classified. Determining the criteria on which classification is to be made. Distribution of structures / processes by groups according to established criteria.
- **Scheme drawing** - Selection of elements, which must be included in the scheme. Showing the selected elements through different symbols / colors and showing their relationships. Formulating an appropriate title and legend for the symbols used.
- **Modeling** - Identifying and selecting the elements needed for modeling the phenomenon. Imaging (graphically, schematically) the phenomenon studied. Realizing the phenomenon using the developed model. Formulating conclusions, deduced from arguments or findings.
- **Experiment** - Formulating a hypothesis, based on known facts, on the process / phenomenon studied. Verifying the hypothesis by performing the processes / phenomena studied under laboratory conditions. Formulation of conclusions, deduced from arguments or findings.

- ***Applied teaching strategies / technologies*** *(specific to the discipline)*

"Brainstorming", "Multi-voting"; "The round table"; "Group Interview"; "Case Study"; "Creative Controversy"; "Focus-group technique", "Portfolio".
Virtual Practices

- ***Methods of assessment*** *(including the method of final mark calculation)*

✓ **Current**: frontal and / or individual control through

- (a) applying docimological tests,
- (b) solving problems / exercises,
- (c) analysis of case studies
- (d) performing role-plays on the topics discussed.
- (e) tests

Final: exam

The **final mark** will consist of the average mark of three concluding tests and the semester scientific project (50%), and the final test in computerized system (50%).

The average mark and the marks of all the final exam stages (computer, written test) - will be expressed in numbers according to the marks scale (as in the table) and the final mark obtained will be expressed in two decimals and will be written in the marks book.

Method of mark rounding at different assessment stages

Intermediate marks scale (annual average, marks from the examination stages)	National Assessment System	ECTS Equivalent
1,00-3,00	**2**	**F**
3,01-4,99	**4**	**FX**
5,00	**5**	**E**
5,01-5,50	**5,5**	
5,51-6,0	**6**	
6,01-6,50	**6,5**	**D**

6,51-7,00	**7**	
7,01-7,50	**7,5**	**C**
7,51-8,00	**8**	
8,01-8,50	**8,5**	**B**
8,51-8,00	**9**	
9,01-9,50	**9,5**	**A**
9,51-10,0	**10**	

The average annual mark and the marks of all stages of final examination (computer assisted, test, oral) - are expressed in numbers according to the mark scale (according to the table), and the final mark obtained is expressed in number with two decimals, which is transferred to student's record-book.

Absence on examination without good reason is recorded as "absent" and is equivalent to 0 (zero). The student has the right to have two re-examinations.

X. RECOMMENDED LITERATURE:

A. Compulsory:

1. Molecular biology. Exercise book Capcelea S., Perciuleac L., Cemortan I, 2017
2. Presentations of lectures: www.biologiemoleculară.usmf.md
3. Reading materials: www.biologiemoleculară.usmf.md
4. On line-tests: e.usmf. md
5. www.ncbi.nih.gov

B. Additional

1. Information about the Human Genome Project. www.ornl.gov
2. Free online books www.freebooks4doctors.com
3. Online scientific journals www.pubmed.com
4. Online scientific journals www.freemedicaljournals.com
5. www.nature.com
6. www.genome.org
7. http://www.genecards.org/
8. Cell biology Pollard Th., Earnshaw W., 2017
9. Molecular Biology of the Cell. B. Alberts 2016
10. Genes B.Lewin, 2017
11. Biologie moleculaire en biologie clinique V.2. M. Bogart 2005