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 in Medicine
Minutes No._4_ of 21.03.24
Chairman , Associate profesor, PhD

Padure Andrei _____

APPROVED

at the Council meeting of the Faculty

_____

Minutes No.7 of 26.03.24
Dean of Faculty Medicine No.2,
Associate profesor, PhD

Betiu Mircea_____

APPROVED

approved at the meeting of the chair_____

Minutes No.15 of 18.03.2024

Head of Chair of Molecular Biology and Human Genetics
Associate professor, PhD

Cemortan Igor _____

SYLLABUS

DISCIPLINE

APPLICATIONS AND LIMITS IN MOLECULAR TESTING

Integrated studies

Type of course: **Optional discipline**

Curriculum developed by:

Lesanu Mihai, PhD, dr. in biol, associate professor

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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 discipline *Applications and limits in molecular testing* is an optional course, intended for first year students within the Program of integrated higher education in Medicine. It is complementary to the content of the compulsory discipline Molecular Biology and is focused on the field of research in accordance with the results of scientific investigations in that field at national and international level.

It is based on general principles about the structure and functions of the main biopolymers of the human cell, the particularities of organization and expression of the genetic information in the cell, molecular methods of analysis and the medical fields in which these methods can be applied. In the optional course, the particularities of investigating medical problems through research at the molecular level are reflected.

The discipline *Applications and limits in molecular testing* will contribute to the development of learning and communication skills in the native language by applying knowledge in the field of molecular biology, generalization of the accumulated information and evaluating molecular-biological methods, proposing modern solutions for the management of various problems in medicine.

At the end of the course, students will know the diversity of DNA, RNA and protein analysis methods; they will understand the principles of isolation, separation, amplification, hybridization, visualization of nucleic acids; they will apply the acquired knowledge to solve certain medical problems; they will perform the synthesis of molecular-biological data at the level of the cell, human organism and populations, etc.

- Mission of the curriculum (aim) in professional training

The optional discipline *Applications and limits in molecular testing* has as its mission the strengthening of knowledge in the field through active involvement in research and the application of the obtained results to the analysis and solution of medical problems. It will be achieved through:

- Studying and understanding the role of biopolymers in the normal and pathological development of the human organism;
- Knowing and mastering the basic methods applied in molecular biology for the analysis of biological processes and phenomena at the level of the cell and human organism;
- Application of molecular-biological investigation methods of clinical importance and the formation of the skills of analysis and interpretation of laboratory data focused on research.

- Language (s) of the discipline: _____;

II. Beneficiaries: students of the 1st year, faculties of Medicine 1, Medicine 2, specialty Medicine.

II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		**F.02.A.018.5**	
Name of the discipline		Applications and limits in molecular testing	
Person(s) in charge of the discipline			
Year	**I**	Semester/Semesters	**II**
Total number of hours, including:			**30**
Lectures	**10**	Practical/laboratory hours	**10**
Seminars		Self-training	**10**
Form of assessment	**E**	Number of credits	**1**

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:**
  - to define notions related to molecular biology;
  - to explain the mechanisms of the expression of hereditary information within the framework of gene expression;
  - to know investigation methods in molecular biology, their advantages and limits;
  - to identify ways of analyzing biopolymers, cell components, products of gene expression;
  - to distinguish molecular diagnostic algorithms in the detection of pathological mutations;
  - to distinguish fields of application of molecular-biological testing in medicine.
- **at the application level:**
- to isolate and quantify nucleic acids;
- to use different molecular biology methods of investigation in the research and diagnosis of certain diseases;
- to apply knowledge in molecular biology to solving medical problems;
- to demonstrate the possibilities of applying molecular-biological methods in medical research;
- to use the knowledge of molecular biology in research and diagnosis.
- **at the integration level:**
- to appreciate the role of molecular biology in medical investigation;
- to propose solutions for the application of molecular tests in the study of human heredity;
- to develop projects related to the use of molecular biology data in the protection of human health;
- to interpret the results obtained in molecular testing;
- to develop strategies for the integration of molecular biology in solving current medical problems.

IV. PROVISIONAL TERMS AND CONDITIONS

Requirements to the first year student:

- Knowledge of the teaching language;
- Confirmed competences in sciences at high school level (biology, chemistry, physics, mathematics, informatics);
- Confirmed competences in university subjects (molecular biology, biochemistry, biophysics);
- Digital skills (use of the Internet, processing of documents, electronic tables and presentations, use of computer programs);
- Communication skills and teamwork;
- Qualities: motivation, autonomy, tolerance, compassion.

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.	Physicochemical properties of biopolymers *in situ*, *in vivo* and *in vitro*.	2	2	2
2.	Isolation of DNA, RNA, proteins - principles, stages, particularities. Quantification of nucleic acids.	2	2	2
3.	Principles and techniques of nucleic acid amplification. Diversity, applications and limits of PCR techniques.	2	2	2
4.	Principles and techniques of nucleic acid hybridization. Diversity, applications and limits of hybridization techniques: blotting, *in situ*, colonial.	2	2	2
5.	Applications of molecular techniques in gene identification, gene localization, gene expression, detection of pathological mutations, identification of gene therapy targets, genomic editing targets.	2	2	2
Total		**10**	**10**	**10**

VI. PRACTICAL TOOLS PURCHASED AT THE END OF THE COURSE

Mandatory essential practical tools are:

- Knowing and understanding the molecular organization of different cellular compartments, explaining the principles of their specialization and interaction in the process of genetic information expression in the human cell;
- Modeling the molecular-genetic processes underlying the functioning of the human cell: replication, transcription, processing, translation;
- Knowing the principles of molecular biology techniques and understanding the interpretation of their results;
- Preparing and presenting a scientific project using molecular-biological methods in scientific research and medical diagnosis.

VII. OBJECTIVES AND CONTENT UNITS

Objective	Content units
Module 1. Physico-chemical properties of biopolymers *in situ, in vivo* and *in vitro*.	
• to identify the particularities of DNA, RNA and proteins organization; • to briefly describe the stages of the expression of the genetic information in the human cell; • to use the accumulated information to solve various problems related to the structure of nucleic acids and proteins; • to compare genes, processes and phenomena related to the organization of hereditary material in the human organism based on certain criteria of similarities and differences; • to estimate the consequences of affecting the structure of proteins and nucleic acids; • to propose methods for the analysis of proteins and nucleic acids.	1. Nucleic acids: DNA, RNA. General aspects, types, genesis mechanisms, significance. Peculiarities of the structure of human genes. 2. Proteins. General aspects, diversity, biological significance, role in molecular medicine. 3. Expression of the genetic information in the human cell: transcription, processing, translation. ***Key terms:*** *nucleic acids, proteins, replication, transcription, processing, translation* ***Practical classes:*** ***1. Analysis of the physico-chemical properties of nucleic acids***
Module 2. Isolation of DNA, RNA, proteins - principles, stages, particularities. Quantification of nucleic acids.	
• To distinguish methods of nucleic acid and protein isolation; • to describe steps of isolation and quantification of nucleic acids; • to establish links between the content of nucleic acids and proteins and the physiological state of the cell, organism; • to compare different methods of isolation of nucleic acids and proteins, techniques	1. Principles of collecting and preparation of nucleic acid and protein samples. Peculiarities. 2. Isolation of nucleic acids. Steps: cell lysis, deproteinization, DNA extraction, DNA precipitation. 3. Methods of DNA, RNA and protein isolation. Peculiarities and perspectives of use.

Objective	Content units
of sampling and preparation of biological samples; • to propose fields of application of the results of the quantification of the nucleic acids and proteins in biological samples; • to evaluate the benefits and limitations of different nucleic acid and protein isolation methods.	4. Determination of protein and nucleic acid content in biological samples. Quantification of nucleic acids by photo- and spectrometric techniques. ***Key Terms:*** *DNA isolation, cell lysis, homogenization, precipitation, purification, electrophoresis, DNA quantification, optical density* ***Practical lesson:*** *1. Isolation of DNA from a biological sample.*
Module 3. Principles and techniques of nucleic acid amplification. Diversity, applications and limits of PCR techniques.	
• to distinguish enzymes and vectors with implications in gene transformation; • to describe the technologies for obtaining recombinant DNA molecules; • to establish links between PCR techniques and different fields of research and medical diagnosis; • to compare different methods of amplification of nucleic acid sequences, principles of DNA cloning; • to interpret the results of PCR techniques; • to reevaluate the benefits and limitations of PCR techniques in medicine.	1. Multiplication of nucleic acid molecules by repeated replication. *In vivo* and *in vitro* cloning of nucleic acid sequences. 2. Recombinant DNA technique. Restriction enzymes, DNA-ligases, vector systems. Transfer and expression of genetic information in host cells. 3. Polymerase chain reaction. Stages: denaturation of template DNA, hybridization of primers, synthesis of the new DNA strand. Diversity of PCR-based analysis methods. 4. The practical applicability of PCR techniques in research and diagnosis. Advantages of using and limits of PCR techniques. ***Key terms:*** *recombinant DNA, restrictases, ligases, vectors, DNA cloning, PCR, primer, cloning, amplification* ***Practical lesson:*** *1. Analysis of nucleic acids from a biological sample.*
Module 4. Principles and techniques of nucleic acid hybridization. Diversity, applications and limits of hybridization techniques: blotting, *in situ*, colonial.	
• To distinguish hybridization techniques and nucleic acid sequencing methods • to describe the procedures for preparing genetic probes and marking nucleotides; • to interpret the results obtained based on DNA fingerprints; • to compare different DNA sequencing methods, hybridization techniques; • to propose DNA sequencing methods for biological research and medical diagnosis;	1. Detection and analysis of nucleic acids. Principles of nucleic acids hybridization. Applications and limits of hybridization reactions for medicine and biology. 2. Nucleic acid hybridization techniques: blotting, *in situ*, colonial. Obtaining genetic probes. Preparation of DNA and RNA samples. Marking and incorporation of marked nucleotides into the genetic probe. Genetic analysis. 3. DNA sequencing. Sequencing methods. Applications in research and diagnosis. Genomic fingerprinting. Molecular

Objective	Content units
• to evaluate the benefits and limitations of nucleic acid hybridization and sequencing techniques in medicine.	techniques for identification and quantification of genetic variations. Human genome sequencing and personalized medicine. ***Key Terms:*** *DNA hybridization, DNA sequencing, blotting, molecular labeling, genomic fingerprinting* ***Practical lesson:*** *1. Gene expression detection techniques (mRNA, cellular proteins)*
Module 5. Applications of molecular techniques in gene identification, gene localization, gene expression, detection of pathological mutations, identification of gene therapy targets, genomic editing targets.	
• To distinguish areas of application of molecular techniques in modern medicine; • To recognize molecular markers, viral and non-viral vectors, genome editing techniques; • to determine directions for using the molecular techniques in research and medical diagnosis; • to argue the necessity of using modern molecular-biological methods in medical and diagnostic research; • to evaluate the possibilities of applying molecular techniques to solving of certain problems in medicine; • to recommend fields of application of modern molecular-biological methods in contemporary medicine.	1. Practical applications of molecular techniques. The study of the peculiarities of gene organization and expression. Identification of genes and formation of gene libraries. 2. Molecular markers. Detection of people carrying pathological mutations. Detection of foreign DNA and diagnosis of infectious diseases. The relevance of molecular techniques for pathology. 3. Gene therapy *in vivo* and *ex vivo*. Target gene selection. Viral and non-viral vectors. Methods of gene therapy. Achievements and perspectives. Examples of targeted therapy. 4. Genome editing. Basic techniques applied in genome editing: benefits and limits. The CRISPR Cas9 technique. Genome editing technologies as a component of gene therapy. ***Key terms:*** *gene libraries, molecular markers, gene therapy, genome editing* ***Practical lesson:*** *5. Application of molecular-biological methods in research and diagnosis (case study/project).*

VIII. PROFESSIONAL (SPECIFIC (SC)) AND TRANSVERSAL (TC) COMPETENCES AND STUDY FINALITIES

Professional (specific) (SC) competences

- ✓ SC1. The responsible execution of professional tasks with the application of the values and norms of professional ethics, as well as the provisions of the legislation in force
- ✓ SC2. Adequate knowledge of the sciences about the structure of the body, the physiological functions and the behavior of the human body in various physiological and pathological states, as well as the existing relationships between the state of health, the physical and the social environment
- ✓ SC6. Carrying out scientific research in the field of health and in other branches of science

Transversal competences (TC)

- ✓ TC1. Autonomy and responsibility in activity
- ✓ TC4. Personal and professional development, the formation of the critical spirit
- ✓ TC5. Developing the skills of efficient time and informational resources management

✓ **Study finalities**

Upon completion of the course, the student will be able:

1.1. to define the notions related to molecular biology;
1.2. to establish the correlation between molecular biology and strengthening the health of the human population;
1.3. to formulate the objectives of molecular biology in medical research;
1.4. to describe the possibilities of applying molecular biology in accordance with the values and norms of professional ethics;
1.5. to apply knowledge in the field of molecular biology to strengthen the health of the human organism;
2.1. to identify the fields of application of molecular biology in medical research;
2.2. to use various modern techniques and methods of molecular-biological analysis to solve certain health problems;
2.3. to compare molecular-biological methods of analysis applied in scientific research and diagnosis;
2.4. to develop strategies for the integration of modern molecular-biological methods in different medical fields;
2.5. to propose projects for the application of molecular biology in the investigation of the state of health of the human body;
6.1. to identify the main directions of application of molecular biology in contemporary medicine;
6.2. to describe molecular-biological methods applied in research and diagnosis;
6.3. to determine conditions for the application of molecular biology techniques in health care;
6.4. to interpret the data obtained as a result of scientific research;
6.5. to propose solutions to solve health problems by applying molecular biology.

Note. Discipline finatities (are deduced from the professional competences and the formative valences of the informational content of the discipline).

IX. STUDENT'S SELF-TRAINING

No.	Expected product	Implementation strategies	Assessment criteria	Implementation terms
1.	Working with information sources:	• Selecting a topic from the field • Formulating objectives • Generalization of the selected information • Formulation of conclusions • Preparing a report/presentations on the selected topic Public defense of the report/presentation	• Depth of study • Diversity of sources • Critical analysis of the presented results • Volume of the report/presentation • Identifying the possibilities of applying the results The quality of the report/presentation	During the semester
2.	Working with online materials	• Studying online materials on the department's website • Online self-assessment • Evaluation of activities through forum and chat	• The number and duration of site visits • The result of the self-assessments	During the semester
3.	Research project through investigating a medical situation	• Selecting a topic from the field • Formulating objectives • Carrying out investigations on the selected topic by applying molecular-biological methods • Formulation of conclusions Public defense of the research project	• Actuality of the research topic • Appropriate methods/techniques used • Analysis/processing of the obtained data • The originality of the form of presentation • The relevance of the conclusions The answers to the questions	At the end of the semester

X. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

Teaching and learning methods used

The forms of organization of studies in the discipline *Applications and limits in molecular testing* are:

- theoretical courses, in which the content of the discipline is systematically presented, using for training both classical and traditional methods - explanation, description, conversation, exercise, demonstration, as well as modern methods - problematization, speech accompanied by Power Point presentation, posting course support on the Moodle electronic platform;
- practical lessons, in which laboratory experiments; description and interpretation of the methods and techniques used; collecting, evaluating, processing and interpreting the results; the elaboration and presentation of scientific information regarding the application of modern molecular-biological methods in research and diagnosis are carried out, with the description of the

working method and the interpretation of the results, using as training methods demonstration, observation, experiment, exercise, algorithmization, problematization, etc.

In order to increase students' access to information, to ensure transparency regarding the content of the course, the analytical program of the course lectures and practical lessons, course notes, tasks for individual work, the Moodle electronic platform is used.

Individual activities of the students involve creation of reports, online self-evaluations and research projects based on the analysis of information from the specialized literature on the investigated topics. The products are publicly presented and analyzed during practical classes

The main **learning methods** are:

- *didactic speech* – involves the verbal presentation of a volume of information by the teacher to the student in accordance with the curriculum provisions and the objectives of the discipline;
- *didactic conversation* - involves the didactic use of questions and answers in accordance with the objectives of the discipline;
- *demonstration* – involves achieving the objectives of the discipline through the application of objects, actions, technical means, etc.;
- *observation* - involves the systematic follow-up by the student of the objectives and phenomena that constitute the learning content;
- *working with the textbook* - involves the use of the textbook, course materials and electronic sources in the learning process;
- *the exercise* - involves the conscious execution of some activities in order to learn the subject or improve a performance;
- *algorithmization* – involves achieving the objectives of the discipline by developing and applying an algorithm;
- *didactic modeling* – involves mastering the content and achieving the proposed objectives by proposing certain models;
- *problematization* – involves the presentation of content by solving problems or problematic situations;
- *programmed training* – involves reflecting the content of the discipline in a determined order;
- *case study* – involves the application of case situations to the understanding of certain processes and phenomena;
- *simulation* – involves the use of games and simulator learning;
- *discovery* - involves learning through research and discovery.

Applied didactic strategies/technologies *(discipline specific)*

Didactic strategies are selected depending on the learning objectives and include a complex system of means, methods, materials and other educational resources aimed at achieving these objectives.

The use of didactic strategies depends on the logic of applied thinking (inductive, deductive, analogical, mixed, transductive didactic strategies), the degree of guidance/non-guidance of learning (algorithmic, non-algorithmic).

In accordance with the mission of the discipline, the emphasis is placed on non-algorithmic didactic strategies, namely, heuristic strategies, focused on research and discovery: the experiment, the practical work, researching a problem situation, group investigation, carrying out a research project.

Evaluation methods *(including the method of calculating the final grade)*

During the course, different forms of assessment are applied: initial, current and final.

Initial assessment: At the beginning of the course, a self-assessment is carried out on the material of the basic course in *Molecular Biology* to determine the level of students' knowledge.

Current evaluation: During the semester, 2 tests are carried out on the material covered during the course. It includes application of docimological tests, solving of didactic tasks, analysis of case studies, carrying out of practical works, etc.

Final evaluation: The final evaluation is carried out during the exam by testing with didactic tasks on the computer.

The student's final grade is made up of the semester grade (50%) with which the student is admitted to the exam and the exam grade (50%). The semester grade is made up of the arithmetic mean of two tests and the semester scientific project. The exam grade represents the grade of the final computerized test. The final grade is indicated in hundredths and is reflected by the ECTS qualification.

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**
8,51-9,00	**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 in the failed exam.

XI. RECOMMENDED LITERATURE:

A. Compulsory :

1. Covic M., Ştefănescu D., Sandovoci I. Genetica medicală (ed. III), Iaşi, Polirom, 2017.
2. Israil Anca-Michaela. Biologie moleculară. Prezent şi perspective, Bucureşti, Humanitas, 2000.
3. Seidman Lisa A. Basic laboratory calculations for biotechnology, San Francisco, Pearson Education, 2008.
4. Seidman Lisa A., Moore Cynthia J. Basic laboratory methods for biotechnology, San Francisco, Pearson Education, 2009.
5. Thieman W.J., Palladino M.A.. Introduction to Biotechnology, Edinburgh, Pearson Education Limited, 2014.
6. www.biologiemoleculară.usmf.md (suport de curs la Biologia moleculară)

B. Additional

1. Cotrutz C. E., Cotrutz C., Petreuş T. Biologia celulară şi moleculară, Iaşi, Sedcom Libris, 2011.
2. Curticapean M. Tehnici de biologie moleculară şi genetică, Bucureşti, University Press, 2016.
3. Frenţescu L. Tehnici de biologie moleculară cu aplicaţii în laboratorul medical, Cluj-Napoca, UMF, 2011.
4. Mihăşan M., Ştefan M., Olteanu Z. Biologie moleculară, Iaşi, UAIC, 2013.
5. Necula L-G., Dragu D., Pitica I., Tanase C. Tehnici de biologie celulară şi moleculară, Bucureşti, Hamangiu, 2023
6. Rakeeb Ahmad Mir, Sheikh Mansoor, Sajad Zargar. Principkes of Genomics and Proteomics, Elsevier – Health Sciences Division, 2022.
7. Rădulescu M.S. Metodologia cercetării ştiinţifice, Bucureşti, Ed. Didactică şi Pedagogică, 2011.
8. Vior C. Biotehnologii medicale, București, ed. România de mâine, 2000.
9. Введение в молекулярную медицину (под ред. Пальцева М.А.), М., Медицина, 2004.
10. www.genecards.org.