FACULTY OF MEDICINE

STUDY PROGRAM 0912.1 MEDICINE

DEPARTMENT OF MOLECULAR BIOLOGY AND HUMAN GENETICS

APPROVED
at the meeting of the Commission for Quality Assurance and Evaluation of the Curriculum faculty
Minutes No. 7 of 6.03.18

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 **MEDICAL GENETICS**

Integrated studies

Type of course: Compulsory course

Chişinău, 2017

I. PRELIMINARY

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

Human genetics is a clinical discipline that studies the relationship between heredity and disease or, more specifically, the role of mutations in the production of disease or predisposition to disease. There are over 10,000 genetic conditions that affect 5-8% of new-borns and probably 30-40% of individuals throughout their lives; they have a great diversity and are found in almost all medical specialties. Genetics is the field of activity of some specialists, but every practitioner must use a genetic approach in his relationship with the patient and his family.

The content of courses and practical lessons include aspects related to: 1) highlighting the genetic mechanisms that maintain the body's homeostasis and determine the individual's health; 2) the importance of genetic factors (mutations and correlation of certain genes) in the aetiology of pathologies; 3) the role of genetic factors in determining the clinical manifestations of diseases (hereditary and non-hereditary); 4) specificity of the genetic diseases: chromosomal anomalies, monogenic and multifactorial diseases, mitochondrial diseases and somatic cell genome; 5) methodology of genetic counselling and its value for medical practice; 6) new techniques of genetic investigation, 7) the importance of prophylaxis of genetic pathologies and methods of prenatal and postnatal diagnosis, 8) reproductive health and family planning; 9) the role of heredity in determining the specificity of pharmacological therapy and other types of treatment.

- **The mission of the curriculum (purpose) in professional training**

The integration of medical genetics into the medical education curriculum has become an indispensable discipline for the complex and modern training of the future physician. The course is addressed to future physicians from various specialties in the context of integrating genomic medicine into medical practice, becoming an essential tool for acquiring knowledge, vocabulary and especially a broad concept about the role of genomics in medicine to avoid the risks of not understanding the medicine of the near future. Discoveries of the last decade have had important effects on medical theory and practice. In the diagnostic plan, the perfecting of molecular analysis methods at the genetic level allows improvement of the ability to identify diseases, regardless of the age of the patient (foetus, newborn, child, adult) and often before the clinical manifestation of the disease (pre-symptomatic). "Genomic" pharmacology has emerged whereby the synthesis of gene transcription inhibitors is attempted to block the functioning of the mutant genes. It has become operational (since 1991) the gene therapy, through which the production and introduction of normal genes in somatic cells of patients with serious genetic disorders can improve / control the effect of mutant genes. Disease prophylaxis, due to genetics, gets a new dimension. It is addressed to families or people with genetic risk and prophylaxis becomes personalized.

Identifying genes that determine the susceptibility of healthy people to certain diseases opens the way for predictive medicine, based on prenatal or premorbid "predictions." Medical Genetics can form the main paradigm in the medical education of student doctors.

- **Languages of the discipline:** Romanian
- **Beneficiaries: 4th year students, Department of general Medicine No. 1, Medicine specialty**

II. ADMINISTRATION OF THE DISCIPLINE

Code of discipline		S.08.O.071	
Name of the discipline		**Medical Genetics**	
Responsible for discipline		PhD, associate professor, **Igor Cemortan**	
Year	**IV**	Semesters	**VII şi VIII**
The number of total hours, including:			**30**
Course	**10**	Practical lessons	**5**
Seminars	**5**	Individual work	**10**
Clinical training (number of total hours)			
Evaluation form	**CD**	Number of credits	**1**

III. OBJECTIVES OF THE DISCIPLINE

✓ ***At the level of knowledge and understanding:***

- To know the organization and functioning of genes, structure of chromosomes and human genome;
- To understand the role of genetic and environmental factors in the etiopathogenesis of human diseases;
- To know the international nomenclature of chromosomal anomalies and gene mutations;
- To know the general clinical signs and genetic particularities of chromosomal syndromes, monogenic diseases, multifactorial diseases and mitochondrial diseases;
- To know etiopathogenesis, clinical signs, diagnosis, principles of treatment and prophylaxis of frequently encountered genetic diseases;
- To know the principles, indications and limits of different methods of genetic testing;
- To know the role of genetic counseling in family planning;
- To understand the principles of gene therapy.

✓ ***At the level of application:***

- To perform a family survey by collecting the hereditary anamnesis and calculate the genetic risk;
- To distinguish methods for assessing the genetic character of pathologies in the medical-genetic consultation;
- To interpret the results of cytogenetic and molecular-genetic tests;
- To distinguish the particularities of manifestation and criteria for recognition of dominant vs. recessive and autosomal vs. X-linked diseases.
- To interpret the congenital and multisystemic character of chromosomal syndromes;
- To interpret the chronic and progressive character of multifactorial pathology with genetic predisposition;
- To evaluate methods of prophylaxis of hereditary pathologies, prenatal genetic diagnosis, prenatal screening tests (biochemical and ultrasound) and their diagnostic value.

✓ ***At the integration level:***

- To be able to deduce the role of genetic and environmental factors in the etiopathogenesis of human pathologies;
- To be competent to use the knowledge and methodology of genetic counseling at any patient;
- To be able to link genetic modification to phenotypic consequences;
- To be competent to deduce the evolution of pathological conditions and initiate the early diagnosis of monogenic hereditary pathologies;
- To be able to deduce the patient's individual character and the family approach of each case;
- To be able to deduce the particularities of diagnosis, treatment and prophylaxis of hereditary pathologies with multisystemic impairment;

- To be competent to indicate prenatal and postnatal diagnosis methods, to indicate medical-genetic counseling in families with rare diseases.

IV. CONDITIONS AND REQUIREMENTS

Student of the fourth year requires the following:

- to know the language of teaching;
- proven competencies in preclinical sciences (molecular biology, biochemistry, human genetics, embryology, propedeutics, normal and pathological physiology);
- digital competences (use of the Internet, document processing, electronic tables and presentations, use of graphic programs);
- ability to communicate and team work;
- qualities - tolerance, compassion, autonomy.

V. TOPICS AND ORIENTAL DISTRIBUTION OF LESSONS

Courses / Seminars (S) / Practical Lessons (PL)/ Individual work:

Nr.	Topic	Hours			
		Courses	S	PL	Individual work
1.	Classification and peculiarities of genetic pathologies. Methods of assessing the genetic character of the pathology.	1	1		1
2.	Clinical and cytogenetic particularities of the most common chromosomal diseases.	1	1		1
3.	Diagnostic cytogenetic methods of chromosomal pathologies.	1		1	1
4.	Monogenic diseases versus monogenic syndromes. Mendelian transmission and genealogical method.	1	1		1
5.	The molecular, genetic and clinical aspects of the most common monogenic diseases.	1	1		1
6.	Molecular-genetic methods in the diagnosis of genetic diseases.	1		1	1
7.	Polygenic, multifactorial diseases. The role of genetic predisposition in cancers in adult common diseases.	1	1		1
8.	Reproductive disorders - primary sterility, spontaneous abortions, new-borns with congenital malformations , diagnosis, family planning.	1		1	1
9.	Congenital anomalies - genetic and teratogenic causes, prenatal diagnosis, prevention.	1		1	1
10.	Genetic counseling. Prophylaxis of genetic pathology. Prenatal diagnosis. Invasive and non-invasive screening methods. Principles of gene therapy.	1		1	1
		10	5	5	10
Total		30			

VI. REFERENCE OBJECTIVES AND UNITS OF CONTENTS

Objective	Units of contents
Chapter 1. „Introduction to medical genetics"	
• to demonstrate the knowledge on organizing and functioning of human genome; • to comment medical significance of heredity of normal and pathological characters; • to know definitions of gene mutations, point mutations, balanced and imbalanced chromosomal aberrations, autosomal aneuploidies, and gonosomal aneuploidies; • to possess the methods of evaluation of genetic character of pathology; • to know the classification of genetic pathologies; • to apply knowledge to other clinical disciplines; • to formulate a conclusion on genetic character of pathology. • to develop your own opinion on role of hereditary and environmental factors in development of pathology.	1. Discourse into the history of medical genetics. Organizing and functioning of human genome. 2. Role of hereditary and environmental factors in etiology and pathogenesis of human pathologies. 3. Classification of genetic pathologies. 4. Features of clinical manifestations and evolution of genetic diseases. 5. Genetic determinism and hereditary transmittance. 6. Hereditary, family and congenital nature of genetic diseases. 7. Evolution of hereditary pathologies: chronic, progressive, relapsing etc.
Chapter 2. „Chromosomal diseases"	
• to define normal human karyotype. • to know classification and nomenclature of chromosomal numerical and structural abnormalities. • to know clinical and cytogenetic features of more prevalent chromosomal abnormalities such as: Down, Edwards, Patau syndromes, i. e., 21, 13, and 18 trisomies, Klinefelter and Turner syndromes. • to know clinical and cytogenetic features of syndromes of partial aneuploidies. • to know clinical and cytogenetic features of syndromes of submicroscopic chromosomal syndromes. • to know risk factors of giving birth of children with chromosomal abnormalities. • to apply accumulated knowledge to others clinical disciplines.	1. Normal human karyotype. 2. Etiology and classification of chromosomal abnormalities. 3. Consequences of numerical and structural abnormalities. 4. Reproductive disorders caused by chromosomal abnormalities. 5. Clinical and cytogenetic features of more prevalent chromosomal abnormalities, such as: Down, Edwards, Patau syndromes, i. e., 21, 13, and 18 trisomies, Klinefelter and Turner syndromes. 6. Clinical and cytogenetic features of syndromes of partial aneuploidies. Clinical and cytogenetic features of submicroscopic chromosomal abnormalities. 7. Risk factors of giving birth of children with chromosomal abnormalities.

Objective	Units of contents
Chapter 3. „**Single gene (molecular) diseases"**	
• to know etiology, classification, basic features of pathogenesis of SGD; • to know nomenclature gene mutations; • to know features of clinical pictures of single gene disorders; • to define genetic heterogeneity, expressivity, clinical polymorphism of single gene disorders; • to know enzymopathies, such as phenylketonuria, galactosemia, adrenogenital syndrome, and alkaptonuria; • to know syndromes with nervous system involvement, such as Duchenne-Becker muscular dystrophy, neurofibromatosis (Von Recklinhausen's disease), fragile X syndrome, Wilson's disease, etc.; • to know syndromes with connective tissue's involvement, such as Ehlers-Danlos disease, Marfan syndrome, osteogenesis imperfecta; • to know pathologies such as: cystic fibrosis, familial hypercholesterolemia, autosomal-dominant polycystic kidney disease, hemophilia A and B, clinical and genetics features of more prevalent mitochondrial diseases; • to demonstrate medical role of knowledge of genetic counseling, risk grade in single gene pathologies.	1. Etiology. Classification. Basic features of pathogenesis. 2. Mendelian transmittance. 3. Clinical polymorphism and its causes. 4. Genetic heterogeneity.Expressivity. 5. Phenylketonuria; Cystic fibrosis; 6. Adrenogenital syndrome. 7. Syndromes with nervous system involvement: 8. Duchenne-Becker muscular dystrophy; 9. Neurofibromatosis (Von Recklinhausen's disease); 10. Fragile X syndrome; Wilson's disease; 11. Syndromes with connective tissue's involvement: 12. Ehlers-Danlos syndrome; 13. Marfan syndrome. Familial hypercholesterolemia. Autosomal-dominant polycystic kidney disease. Hemophilia A and B. Clinical and genetic features of more prevalent mitochondrial diseases; 14. Techniques of analysis of mutant genes; 15. Genetic counseling, risk grade in single gene pathologies.
Chapter 4. „**Laboratory methods in genetic pathologies"**	
• to determine cytogenetic methods such as karyotyping, Barr test, FISH and techniques of obtaining of samples of metaphase chromosomes; • to know practical indications for studying of sex chromatin and human chromosomes; • to understand the principles of genomic DNA and RNA isolation for the different analytic techniques; • to understand the principles of gene analysis; • to interpret the obtained results of PCR technique; • to interpret the obtained results of Southern blot hybridization; • to know practical indications and limits for molecular genetic prenatal and postnatal study in high risk group of single gene diseases.	1. Cytogenetic methods such as karyotyping, Barr test, FISH. 2. Techniques of obtaining of samples of metaphase chromosomes. Standard steps of obtaining of samples of chromosomes from different cells, i. e., blood, chorionic villi, amniocytes. 3. Practical indications for studying of sex chromatin and human chromosomes. 4. Biochemical methoss in diagnosis of enzymopathies, i. e., selective method and screening. 5. Methods of molecular genetics. Direct and indirect detection of gene mutations. 6. DNA polymorphism. Molecular markers of genetic diseases. 7. Molecular-genetic prenatal diagnosis of

Objective	Units of contents
	hereditary pathology.
Chapter 5. „**Prophylaxis of genetic pathology. Medical genetics counseling”**	
• to know methods of prenatal diagnosis of congenital and hereditary diseases. • to know pre-symptomatic diagnosis of hereditary diseases. • to know invasive and non-invasive methods of prenatal diagnosis. Biochemical and ultrasonic screening in pregnancy. • to know postnatal screening of genetic diseases: phenylketonuria, congenital hypothyroidism, adrenogenital syndrome, cystic fibrosis etc. • to know symptomatic and pathogenetic treatment. • to know primary, secondary and tertiary prophylaxis of genetic diseases. • to know medical genetic counseiling. Clinical examination and pedigree analysis. Pedigree construction and studying.	1. Prenatal diagnosis of congenital and hereditary diseases. 2. Pre-symptomatic diagnosis of hereditary diseases. 3. Invasive and non-invasive methods of prenatal diagnosis. 4. Biochemical and ultrasonic screening in pregnancy. 5. Postnatal screening of genetic diseases: phenylketonuria, congenital hypothyroidism, adrenogenital syndrome, cystic fibrosis etc. 6. Principles of symptomatic and pathogenetic treatment. 7. Primary, secondary and tertiary prophylaxis of genetic diseases. 8. Medical genetic counseling.

VII. PROFESSIONAL COMPETENCY (SPECIFIC (SC) AND TRANSVERSE (TC)) AND OUTCOMES OF STUDY

✓ **PROFESSIONAL COMPETENCIES:**

PC1. Knowledge of genetic mechanisms, organization and functioning of human genome;
PC2. Knowledge the role of genetic and environmental factors in etiology and pathogenesis of genetic pathology;
PC3. Understanding of genetic and clinical features of genetic diseases: chromosomal, single gene, complex or multifactorial, and mitochondrial diseases;
PC4. Explaining the role of syndromologic approach in genetic pathology;
PC5. Knowledge of principles of medical genetic counseling, clinical examination and pedigree construction and analysis;
PC6. Knowledge of indications and limits of methods of prenatal and postnatal diagnosis, medical genetic counseling in hereditary pathology;
PC7. Knowledge of principles of diagnosis, treatment and prophylaxis of hereditary pathology with multi-systemic lesions;
PC8. Prognosing of evolution of genetic diseases and methodology of early diagnosis of hereditary single gene pathologies;
PC9. Resolving the situation problems and development the conclusions.

✓ **TRANSVERSE COMPETENCIES:**

TC1. Improvement of abilities in autonomy of decisions;
TC2. Development of personal attitude;
TC3. Ability in social interaction, group activity with different roles;
TC4. Including in inter-disciplinary projects, extra-curricular activities;
TC5. Improvement of skills in digital technologies;
TC6. Development of different teaching techniques;
TC7. Selection of digital materials, critical analysis and making conclusions;
TC8. Presentation of individual scientific projects.

✓ **OUTCOMES OF DISCIPLINE**

- Learning methods of evaluation of genetic character of pathology, method of classification of genetic pathologies, features of genetic pathologies, medical genetic counseling and clinical and pedigree analysis.
- Knowledge of etiology and classification of chromosomal abnormalities; clinical and cytogenetical features of more prevalent chromosomal diseases; factors and groups of genetic risk.
- Knowledge of etiology and classification of single gene diseases; basic features of pathogenesis, clinical manifestations, clinical polymorphism and genetic heterogeneity.
- Knowledge and application of cytogenetic methods of diagnosing of chromosomal pathology; methods of molecular genetics in diagnosis of genetic pathologies.
- Knowledge the principle of prophylactic methods of genetic pathology and therapy; establishing correct role of prenatal and postnatal diagnosis.
- Competency in using the knowledge and methodology of medical genetics in explication of nature of some physiological and pathological processes;
- Ability to implement accumulated knowledge in research activity;
- Competency in critical using the scientific information obtained using new informational and communicating technologies.

VIII. INDIVIDUAL WORK OF STUDENTS

Nr.	The product envisaged	Strategies of realization	Criteria of evaluation	Term of realization
1	***Work with information–nal resources:***	Visiting the lectures or carefully reading the materials on corresponding topic. Reading the topics of the theme, which are necessary for reflecting the subject. Acquaintance with the list of sources of supplementary information concerning respective theme. Selection the sources of supplementary information concerning the topic. Comprehensive reading the text, with attention to the essential content. Making generalization and conclusions concerning to importance of the theme/subject.	Ability to extract the essential information; ability to interpret; volume of work	Throughout the module
2	***Work with online materials***	Online autoevaluation, studying the materials online on the website of cathedra, examining the own opinions on forums and chat	Number and duration of entering the website, results of autoevaluation	Throughout the module
3	***Work with patients' records***	Selection of come patients with genetic pathology, completing of general data concerning the patient, concerning history of antecedents and family. Inputting the results of clinical evaluation in the ystem, including laboratory data, resulta of paraclinical data, results of genetic testing (if applicable). Establishment of clinical diagnosis. Realizing the differential diagnosis and counseling the literature on the topic. Recommendations for confirming the diagnosis. Establishment the conclusion about etiology, presenting evolution and treatment of disease; perspectives in contacts with family of patient.	Volume of work, grade of understanding the essence of genetic pathology, quality of completing of records, correctness of conclusions, capacity of completing of virtual records	Throughout the module
4	***Preparing and presenting the presentations /portfolios***	Selection of theme of research, establishment of plan of research, determining the term of realization. Determining the components of the project / PowerPoint presentation – theme, scope, results, conclusions, practical applications, bibliography. Reviews from the colleagues. Reviews from the teachers.	Volume of work, grade of understanding the essence of the project, level of argumentation, quality of conclusions, creativity, establishment of personal attitude,	Throughout the module

Nr.	The product envisaged	Strategies of realization	Criteria of evaluation	Term of realization
			exposure consistency and scientific correctness, graphic presentations, modality of presentation	

IX. METHODOLOGIC SUGGESTIONS FOR TEACHING – TRAINING – EVALUATION

- ***Used methods of teaching***

For the teaching of medical genetic disciplines were used various methods and didactic processes, oriented towards effective learning and achieving the objectives of the didactic process. In theoretical lessons, besides the traditional methods such as lesson – exposure, lesson – conversation, synthesis lesson, were also used modern methods, such as lesson – debate, lesson – conference, lesson – problems. In practical works were used forms of individual, frontal, group activity, virtual laboratory work, discussion of cases – children with various genetic pathologies or congenital anomalies admitted in the IMC, children and adults admitted to the genetic counseling. For the deeper mastering of the material, were used different semiotic systems such as scientific language, graphic and computerized language, and didactic materials, such as tables, diagrams, microphotographs, transparencies. In extracurricular lessons and activities were used communication information technologies, such as PowerPoint presentations, online lessons.

- ***Recommended methods of teaching***

- **Observation** – Identifying the pathologic signs in patient, description of this phenomena.
- **Analysis** – Clinical examining of patient, observation of essential pathologic signs. Studying of each symptom as component of nozological entity.
- **Analysis of medical record of patient** – Selection of information necessary for establishing of the diagnosis, recognition of pathology or syndrome on the basis of knowledge and selected information.
- **Comparison** – Analysis of clinical case, selection of diagnostic criteria, realization of differential diagnosis. Establishment of conclusions.
- **Classification** – Identifying of different patients. Determining of criteria on the basis of which it is necessary to establish the diagnosis. Distribution of cases by groups using established criteria for different categories of genetic pathologies.
- **Development of record form** – Patients' selection, completing the form according to the requirements of a genetic consult form, the elements chosen by different symbols/colors and the indication of the relationships between them. Formulating an appropriate title and legend of the symbols used.
- **Modeling** – Identifying and selection some single gene syndrom necessary for modeling of virtual record form. Imaging of studied patient. Realizing some record form using proposed model. Establishing conclusions.
- **Experiment** – Formulation of the hypothesis based on known facts, related to process /phenomenon studied. Verification of the hypothesis by realizing the process/phenomenon in laboratory condition. Establishment of conclusions, deduced from the arguments or findings.

- ***Strategies/applied didactic technologies (specific disciplines);***

„Brainstorming", „Multi-voting"; „Round table"; „Group interview"; „Case study"; „Creative controversies"; „Focus Group Technique", „Portfolio".

Virtual practice working.

- ***Methods of assessment*** *(including with indication of modalities of calculation of final note).*
  - ✓ **Current**: frontal control or/and individual control by:
    - (a) application of docimologic tests,
    - (b) resolving the problems/exercises,
    - (c) analysis of case study
    - (d) realizing some role games on the disputed subject.
    - (e) control work
  - ✓ **Final:** differential colloquium
  - ✓ *complex attesting in 3 stages – media note of study course, project and test-control notes.*

Scale of assessment

TABLE OF INTERMEDIATE NOTES (medium annual, notes from the stages of examinations)	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	

Absence in the exam without valid reasons is registered as "absent" and is equivalent to note 0 (zero). Student have 2 attempts to re-exam in the case of non-passing of exam.

X. RECOMMENDED BIBLIOGRAPHY

A. Obligatory:

1. Lecture materials published on the site www.biologiemoleculară.usmf.md, e.usmf.md
2. Support course on medical genetics published on the site www.biologiemoleculară.usmf.md
3. Genetica medicală Covic M., Ştefanescu D., Sandovici I. 2004, 2011
4. https://ghr.nlm.nih.gov

B. Suplimentary:

1. Sprincean M. Bolile genetice. Elaborare metodică. Chişinău, 2013, 70 p. ISBN 978-9975-113-86-1.
2. Sprincean M. Consultul medico-genetic şi diagnosticul prenatal în contextul Geneticii Medicale. Elaborare metodică. Chişinău, 2013, 41 p.
3. www.ornl.gov
4. www.freebooks4doctors.com
5. www.pubmed.com
6. www.genome.org