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 "Genetics of complex traits" includes several topics of human and medical genetics that focus on the genetic component in the determination and expression of normal and pathological traits in humans at different ontogenetic periods and environmental conditions.

Evaluation of genetic imprinting, chromosomal and gene mosaicism, and chimerism in the development of the human organism explains the role of maternal and paternal genetic material in normal development and the production of malformations. Understanding the mechanisms of production of genetic and teratogenic congenital anomalies is the basis of various methods of prenatal diagnosis. Evaluation of chromosomal abnormalities, sexualization gene mutations and environmental factors allow the appropriate management of sexualization disorders. Understanding the role of genetic, epigenetic and environmental factors in the formation and manifestation of multifactorial traits allows the assessment of genetic predisposition in common diseases of the adult, multifactorial polygenic diseases with continuous population distribution. The correlation between the drug - metabolic pathway and the body's response, the identification of genetic variations associated with side effects of drugs opens the path to personalized medicine.

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

The course "Genetics of Complex Traits" complements the knowledge gained in the Medical Genetics course and is designed for the medical student for a genetic approach to patient diagnosis and treatment, disease prevention and family planning. Genetics is a science in continuous perpetuation, daily adding to the data on disease etiology and pathogenesis, diagnostic biomarkers and therapeutic targets, personalized medicines and pharmacogenetic tests. Familiarizing the medical student with genetic phenomena and their impact on the production and manifestation of various normal and pathological traits is a continuing concern of the course "Genetics of Complex Traits".

- **Language (s) of the course:** Romanian, Russian, English, French.

- **Beneficiaries:** students of the 2nd year, faculties of Medicine 1 and Medicine 2, Specialty Medicine.

II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		S.06.A.054.3	
Name of the discipline		**Genetics of Complex Traits**	
Person(s) in charge of the discipline		**Associate professor Igor Cemortan, PhD**	
Year	**II**	Semester	**4**
Total number of hours, including:			**30**
Lectures	**10**	Practical/laboratory hours	
Seminars	**10**	Self-training	**10**
Clinical internship (total hours)			
Form of assessment	**E***	Number of credits	**1**

III. TRAINING AIMS WITHIN THE DISCIPLINE

- ***at the level of knowledge and understanding:***

- Knowledge of genetic phenomena involved in development;
- Knowledge of the role of chromosomes and genes responsible for sexual determinism and differentiation;
- Knowledge of the role of genetic and teratogenic factors in the production of birth defects;
- Understanding the determinism of monogenic and polygenic traits;
- Understanding genetic predisposition in the manifestation of common adult pathology;
- Understanding the principles of pharmacogenomics.

- ***at the application level:***

- To appreciate the consequences of epigenetic changes in human pathology;
- To establish the origin of gene or chromosomal mosaics, generalized or tissue-limited;
- To appreciate the genetic causes of various intersex conditions;
- To evaluate the indications and limits of prenatal diagnosis;
- To analyse the contribution of mutations and environmental factors in the calculation of risk for common adult diseases.

- ***at the integration level:***

- To apply the genetic approach in the evaluation of the patient with common diseases;
- To value the role of pharmacogenetic testing;
- To be aware of the practical importance of genetic counselling in assessing the risk of inheriting or transmitting pathological mutations.

IV. Provisional terms and conditions

The third-year student, semester 6 requires the following:

- knowledge of the language of instruction;
- competence in molecular biology and human genetics;
- competence in biochemistry, physiology, histology and anatomy;
- digital skills (use of the internet, document processing, electronic spreadsheets and presentations, use of graphic software);
- communication and teamwork skills;
- qualities - tolerance, compassion, autonomy.
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V. THEMES AND ESTIMATE ALLOCATION OF HOURS

Lectures (L) /Seminars and Practical Lessons (PL) / Self-training (ST):

	Lectures	Hours L	Hours PL	Hours ST
1	Genetic phenomena in development. Genetic control of growth, cell differentiation and the genetic basis of embryogenesis, organogenesis and physiogenesis.	2	2	2
2	Congenital abnormalities and prenatal diagnosis. Genetic and teratogenic causes of congenital malformations, disruptions, dysplasias and deformities.	2	2	2
3	Intersex conditions. The role of chromosomes and genes in hermaphroditism, female and male pseudohermaphroditism.	2	2	2
4	Multifactorial traits. The role of genes and environmental factors in controlling the manifestation of normal and pathological polygenic traits.	2	2	2
5	Pharmacogenetics and genetic variations in individual response to drugs.	2	2	2
Total hours		10	10	10

VI. REFERENCE OBJECTIVES AND CONTENT UNITS

Objectives	Content units
Topic 1. Genetic phenomena during development	
• To define maternal genome, paternal genome, epigenome, genomic imprinting, mosaicism, chimerism; • to know the biological and medical role of epigenetic phenomena in development; • to know the genetic characteristics of monozygotic and dizygotic twins; • to demonstrate the mechanism of chromosomal and gene mosaicism and chimerism; • to interpret the consequences of mUPD and pUPD; • to apply the knowledge to other subjects; • to formulate conclusions; • to develop their own opinions and attitudes.	• Epigenetic changes and programmed activation/inactivation of genes responsible for morphogenesis. • DNA methylation, histone modification, ncRNA • Genomic imprinting, role in development and examples • Uniparental disomy and consequences • Mechanism of production and impact of chromosomal, gene and biochemical placental, generalized and tissue-limited mosaicism • Mechanism of production and impact of generalized and tissue-limited chimerism • Genetic characteristics of monozygotic and dizygotic twins.
Topic 2. Congenital abnormalities and prenatal diagnosis	
• To define congenital abnormality, malformation, mutagenic factor, teratogenic factor, amniocentesis; • to know the teratogenic timing and risks of congenital disorders; • to know the indications and limitations of invasive and non-invasive prenatal tests for the first trimester of pregnancy, for the second trimester of pregnancy. • to demonstrate the weight of genetic factors in different categories of congenital anomalies; • to interpret the results of different prenatal tests in relation to the terms of achievement; • to apply knowledge to other disciplines; • to formulate conclusions; • to develop their own opinions and attitudes.	• Genetic definition of congenital disorders • The ethico-pathogenetic classification of congenital abnormalities • The etiology of congenital malformations, disruptions, dysplasias and deformations. • Teratogenic timing, risk factors and congenital defects • Malformations - causes, examples. • Disruptions - causes, examples. • Dysplasias - causes, examples. • Deformations - causes, examples. • Prenatal diagnosis and genetic counselling in families with children with congenital abnormalities
Topic 3. Intersex conditions	
• To define genetic sex, gonadal sex, hermaphroditism, pseudohermaphroditism; • to know the causes of sexual determinism anomalies and sexual differentiation anomalies; • to demonstrate the role of genetic counselling in sexual ambiguities; • to interpret the sexual inversion 46,XX - male phenotype and 46,XY - female phenotype; • to apply their knowledge to other disciplines; • to formulate conclusions;	• Defining intersex conditions • Characteristics of sex-determinism abnormalities • Characteristics of sexual differentiation abnormalities • Role of chromosomes and genes in sexualisation • Molecular basis of intersex conditions • Genetics of hermaphroditism

Objectives	Content units
• to develop own opinions and attitudes	• Genetics of male and female pseudohermaphroditism • Genetic counselling in sexualization abnormalities
Topic 4. Multifactorial traits	
• To define multifactorial character, polygenic character, genetic predisposition, continuous distribution, cumulative risk; • to know the particularities of monogenic vs polygenic traits; • to know the causes of common adult diseases; • to demonstrate the association of dermatoglyph variations with various chromosomal syndromes; • to interpret genetic predisposition in multifactorial pathology; • to apply knowledge to other disciplines; • to formulate conclusions; • to develop their own opinions and attitudes.	• Normal and pathological polygenic traits • The role of genes in the formation of different human traits • The role of mutations in genetic predisposition and environmental factors in the determinism of common adult diseases • Characteristics of genes and environmental factors in controlling skin color • Characteristics of dermatoglyphs • Characterization of genes involved in control of hearing • Genetic conditioning in type 2 diabetes mellitus • Genetic conditioning in hypertension • Genetic conditioning in osteoporosis • Genetic conditioning in varicose vein disease • Population distribution of normal and pathological multifactorial traits
Topic 5. Pharmacogenetics	
• To define pharmacogenetics, pharmacogenomics, pharmacokinetics, pharmacodynamics; • to know the stages of biotransformation of drugs and the consequences of the enzyme defects involved; • to demonstrate the role of polymorphisms of enzyme coding genes involved in phase I or II of drug metabolism; • to interpret pharmacogenetic tests; • to apply their knowledge to other disciplines; • to formulate conclusions; • to develop their own opinions and attitudes.	• Definition and compartments of pharmacogenetics • Peculiarities of pharmacokinetics and pharmacodynamics • Molecules and genes involved in the various steps of drug metabolism • Genetic polymorphisms in individual drug response • Enzymes and genes involved in phase I of drug biotransformation • Enzymes and genes involved in phase II of drug biotransformation • Genetic testing for polymorphism of genes involved in side effects of some drugs • Limits of pharmacogenetics.

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

✓ **PROFESSIONAL COMPETENCES:**

- PCI. Responsible execution of professional tasks with the application of the values and rules of professional ethics and the provisions of the legislation in force.
- PC2. Adequate knowledge of the sciences about the structure of the body, physiological functions and behavior of the human body in various physiological and pathological states, as well as the relationships between health, physical and social environment.

✓ **TRANSVERSAL COMPETENCES:**

- TC1. Autonomy and responsibility in the activity.

✓ **STUDY OUTCOMES**

- ✓ to understand the role of the maternal genome, the paternal genome and the epigenome in the development and functioning of the human organism;
- ✓ to appreciate the importance of genetic and environmental factors in the formation and functioning of the human organism;
- ✓ to know the genetic phenomena that can disrupt embryogenesis - gene imprinting defects, uniparental disomy, mosaicism, chimerism;
- ✓ to know the ethico-pathogenetic classification of congenital anomalies;
- ✓ to know the role of autosomes, sex chromosomes and genes in sexualization;
- ✓ to know the gene-environment relationship in controlling the formation and manifestation of multifactorial traits;
- ✓ to know the role of polymorphisms of genes encoding enzymes involved in drug biotransformation.
- ✓ to understand the role of genetic counselling in the assessment of couples at genetic risk and healthy/diseased individuals from families at genetic risk.
- ✓ to form personal opinions, conclusions and attitudes regarding normal or pathological monogenic or polygenic, mono- or multifactorial traits.

VIII. STUDENT'S SELF-TRAINING

Nr.	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 course
2	Working with online materials	Online self-assessment, study of online materials on Google Forms, expressing own opinions on forum and chat	Number and duration of online entries, self-evaluation results	During the semester

IX. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

- ***Teaching methods used***

In teaching Genetics of complex traits 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 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) are used. During the lessons and individual 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".

- ***Methods of assessment*** *(including the method of final mark calculation).*
  - ✓ **Current**: frontal and / or individual control through
    - (a) applying docimology 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 five concluding tests and self-training activities (50%), and the final test (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**	

Absence from an 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 failed exams.

RECOMMENDED LITERATURE

- *A. Mandatory:*

1. Lecture materials on www.biologiemoleculară.usmf.md
2. Reading materials in medical genetics on www.biologiemoleculară.usmf.md
3. Genetica medicală Covic M., Ştefanescu D., Sandovici I., Gorduza E.V. 2017

- *B. Additional:*

1. https://ghr.nlm.nih.gov
2. Jameson J. L., Fauci A. S., Kasper D. L., Hauser S. L., Longo D. L., Loscalzo J. Harrison's principles of internal medicine. 20e. PART 16 Genes, the Environment, and Disease, 2019
3. Curs de biologie moleculară Cemortan I., Capcelea S., 2000 Ţaranov L., Amoaşii D.
4. Medicina genomică și bolile comune ale adultului. Covic A., Gorduza V.E., Covic M. 2020
5. http://www.genecards.org/
6. https://www.malacards.org/
7. https://www.ncbi.nlm.nih.gov/pubmed/
8. https://genome.cshlp.org/
9. Biologie moleculaire en biologie clinique V.2. M. Bogart 2005