



**CD8.5.1 DISCIPLINE SYLLABUS FOR
UNIVERSITY STUDIES**

Edition: 09

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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

in Medicine 1

Minutes No. 1 of 16.09.21

Chairman PhD, associate professor,

Suman Serghei _____

APPROVED

at the Council meeting of the Faculty Medicine 2

Minutes No. 1 of 16.09.21

Dean of Faculty of Medicine 2,

PhD, associate professor,

Bețiu Mircea _____

APPROVED

at the meeting of the Department of Molecular Biology and Human Genetics

Minutes No. 1 of 29.08.2022

Head of chair PhD, associate professor

Cemortan Igor _____

SYLLABUS

DISCIPLINE MEDICAL GENETICS

Integrated studies

Type of course: **Optional discipline**

Curriculum developed by the team of authors:

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Chisinau, 2022



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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 Medical Genetics course is, throughout the world, one of the basic components in the curriculum of medical schools and can form the main paradigm in the medical education of medical students. This course highlights the role of the genome vs. environmental factors in the formation, development and functioning of the human body. The genotype of a person is unique and unrepeatable, it is set at the moment of fertilization - the combination of maternal and paternal genes. Genetic individuality determines biological individuality - the phenotype - the set of specific traits of a body, produced by permanent interaction, in different proportions of heredity and environment. Changes in genetic material - mutations - can cause different pathological conditions with the involvement of one or more systems, which can explain the occurrence of genetic diseases or syndromes. There are two important genetic phenomena considered: family aggregation and hereditary transmission of normal and pathological characters; different vulnerability of people to external aggression, variable manifestations of a disease in different people, different reaction to certain pharmacological preparations.

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

The course is structured to demonstrate that *genetics* can be the core of *modern medicine* that studies biological development and possible variations of the entire life cycle; *genetics is of major importance in calculating genetic risk and preventing human disease; high resolution molecular techniques* used in human genetics *are the primary tool for studying diseases* in medical specialties. Medical Genetics ensures the possibility of

- elucidation of pathogenic mechanisms of genetic diseases (about 1,000 chromosomal syndromes and about 10,000 monogenic diseases) and diseases with genetic predisposition (cancers, diabetes mellitus, high blood pressure, mental deficiencies, etc.);
- genotypic diagnosis: prenatal and pre-symptomatic;
- genomic pharmacology - the right dose of the right medicine for a particular patient;
- gene therapy - blocking the expression or replication of mutant genes, introduction of normal genes into somatic cells of patients with mutant genes;
- individualized disease prevention;
- changing the doctor-patient relationship - "*There are no sick people, but only families of sick people*".

- **Language (s) of the discipline:** Romanian, Russian, English.
- **Beneficiaries:** students of the 2nd year, faculties of Medicine 1 and Medicine 2, Specialty Medicine.



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II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		F.02.O.015	
Name of the discipline		Medical Genetics	
Person(s) in charge of the discipline		Associate professor Igor Cemortan, PhD	
Year	II	Semester	IV
Total number of hours, including:			150
Lectures	30	Practical/laboratory hours	25
Seminars	20	Self-training	75
Form of assessment	E	Number of credits	5



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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:*

- have knowledge of the processes of storing, transmitting and expressing genetic information through which the morpho-functional traits specific to each individual are realized;
- know the molecular and cellular substrate of heredity - DNA and chromosomes - that contain, express and transmit hereditary information;
- understand the transmission of hereditary information in the succession of generations of cells and organisms;
- understand phenomena that cause genetic differences between individuals of a population and between different populations: mutations, genetic recombination in meiosis and fertilization, migration - the flow of genes in the receiving population;
- know the nomenclature of mutations;
- know of the heredity laws for normal and pathological monogenic, polygenic and multifactorial traits;
- understand the genetic basis of human body development;
- understand the genetic basis of the immune response;
- know the genetic mechanisms of carcinogenesis;
- know the principles of different techniques used in human genetics.

• *at the application level:*

- determine normal vs abnormal karyotype;
- establish the nature of aneuploidy: mitotic error or meiotic error;
- determine the type of mutation, possible consequences, identification methods;
- evaluate the genetic phenomena involved in the phenotypic manifestation of normal and pathological genes: gene interactions, pleiotropy, penetrance, expressivity, heterogeneity, imprinting, anticipation.
- know the principles and practical applications of the karyotyping technique;
- evaluate the Barr body test;
- apply the laws of heredity to polymorphic normal **monogenic** traits:
 - blood groups (variations of erythrocytes Ag);
 - serum groups (variations of plasma proteins);
 - enzymatic groups (isoenzyme variations of an enzyme);
 - tissue groups (HLA);
- analyze the genealogical transmission of normal or pathological characters, determine the type of transmission, genotype, and calculate the risk of recurrence of a monogenic disorder;
- evaluate the results of different molecular-genetic techniques: PCR, Southern blot and DNA sequencing;
- apply the methods of studying the hereditary characters in different case studies:
 - genealogical method
 - twin method;
 - statistical population method.



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- **at the integration level:**

- Understand the theoretical importance of studying hereditary characters:
 - different vulnerability to external aggression;
 - genetic predisposition to certain diseases;
 - variable manifestations of a disease;
 - Different treatment response.
- Understand the practical importance of studying hereditary characters:
 - genetic approach to the patient in various clinical disciplines: cardiology, neurology, pediatrics, nephrology, pulmonology, psychiatry, oncology, etc.
 - prevention of hemolytic disease of the newborn caused by Rh system incompatibility;
 - paternity and parentage tests;
 - people identification;
 - diagnosis of the type of twins.

IV. PROVISIONAL TERMS AND CONDITIONS

Requirements for second year, second semester students:

- knowledge of the language of studies;
- confirmed competences in sciences (biology, chemistry, physics) at the school level;
- competences in molecular biology;
- competences in biochemistry, physiology, histology and anatomy;
- 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.



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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.	Introduction. The genetic apparatus of the human cell. Base of heredity and variability. Heredity and the environment in the manifestation of normal and pathological traits in humans. Mutations - types, origin, phenotypic consequences.	2	3	5
2.	Chromosomes - the morphological base of heredity and variability. Characteristic of the human karyotype. Peculiarities of X and Y chromosomes. Chromosomes polymorphisms. Uniparental disomy. Classification of chromosomal abnormalities. Nomenclature of normal and pathological variations of the karyotype.	2	3	5
3.	Numerical and structural chromosomal abnormalities. Causes, mechanisms of production and their consequences: reproductive abnormalities, birth defects and mental retardation	2	3	5
4.	Chromosomal syndromes - diversity, causes, manifestations and cytogenetic diagnosis. Cytogenetic methods - diversity, indications and limits.	2	3	5
5.	Human genes - organization, properties, functions, diversity, examples. Autosomal genes and X-linked genes. Allelic and non-allelic genes. Linkage groups. Haplotypes. Gene-genotype-phenotype relationship.	2	3	5
6.	Gene mutations - mechanisms, nomenclature, consequences at molecular, cellular and organism level. Pathological vs positive vs neutral gene mutations. AD, AR, XD, XR, mitochondrial monogenic diseases.	2	3	5
7.	Phenomena in the expression of human genes. Parental fingerprinting of human genes and monoallelic expression. Epigenetic changes and their role in human pathology.	2	3	5
8.	Methods of studying genes. Direct and indirect gene testing. Principles of PCR, RFLPs and dideoxy sequencing techniques. Advantages and limitations of human gene testing. Prenatal and postnatal testing of human genes.	2	3	5
9.	Mendelian monogenic traits. Heredity of ABO, Rh, MN and Xg blood groups. Allelic and non-allelic interactions. Genetics of HDNB. Non-mendelian monogenic traits. Allelic and non-allelic heterogeneity. Complete and incomplete penetration. Variable expressivity. Anticipation. Mendelian (AD, AR, AD, XR) and non-Mendelian (mitochondrial, fingerprinting) monogenic diseases, common polygenic diseases.	2	3	5
10.	Peculiarities of normal vs. pathological hereditary traits. Methods for assessing the genetic nature of human diseases. Genealogical, twins, linkage, genomic studies.	2	3	5



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No. d/o	THEME	Number of hours		
		Lectures	Practical hours	Self-training
11.	Developmental genetics. Genetic basis of congenital anomalies.	2	3	5
12.	The genetics of sex. Major masculinizing and feminizing genes. Sex development disorders.	2	3	5
13.	Immunogenetics. Genetic mechanisms of Ac and TcR diversity. Genetic immunodeficiencies.	2	3	5
14.	Cancer - a genetic disease of somatic cells. Mutations of proto-oncogenes and GST in carcinogenesis.	2	3	5
15.	Genetic counseling in the prevention of genetic diseases. Principles of gene therapies in the etiological treatment of genetic diseases. Pharmacogenomic perspectives.	2	3	5
Total		30	45	75



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VI. OBJECTIVES AND CONTENT UNITS

Objectives	Content units
Chapter 1. Normal and pathological human karyotype	
<ul style="list-style-type: none"> • To define genome, genotype, plasmotype, phenotype; • to know the normal karyotype and the chromosomal polymorphisms; • to know the nomenclature and consequences of numerical and structural chromosomal abnormalities; • to demonstrate the difference between autosomal and gonosomal abnormalities, balanced and unbalanced abnormalities; • to know the dynamics of chromosomes in mitosis and meiosis, errors and their cytogenetic consequences; • to comment on the medical significance of knowing the mitotic or meiotic origin of the chromosomal abnormality; • to know the cytogenetic and phenotypic peculiarities of autosomal and gonosomal chromosomal syndromes. • to know the principles and stages of different cytogenetic techniques; • to interpret the karyogram, the Barr body test, the F body test, the FISH test; • to apply knowledge to other disciplines; • to formulate conclusions; • to develop own opinions 	<ol style="list-style-type: none"> 1. Genetic apparatus of human cell. Nuclear and mitochondrial genome. 2. Human chromosomes, structure and nomenclature. Sexual chromosomes peculiarities. Normal human karyotype. 3. Techniques for studying human chromosomes. 4. Numeric and structural chromosomal abnormalities. 5. Dynamics of chromosomes in mitosis. Errors of genetic information distribution during mitosis. Chromosomal mosaics. 6. Chromosome dynamics in meiosis. Transmission of genetic material from parents to offspring. Meiosis errors and their consequences. 7. Evaluation of the normal and pathological human karyotypes. 8. Autosomal chromosomal syndromes (Down, Patau, Edwards, Cri-du-chat, Angelman, Prader-Willi) - cytogenetic, phenotypic, diagnostic, prophylactic aspects. 9. Gonosomal chromosomal syndromes (Turner s., Klinefelter s.) - cytogenetic, phenotypic aspects, diagnosis, prophylaxis.
Chapter 2. Peculiarities of human genes	
<ul style="list-style-type: none"> • To define gene, gene expression, genotype, homozygote, heterozygote, hemizygote, phenotype • to know the peculiarities of organization, properties and functions of different genes; • to know and understand the causes, mechanisms and nomenclature of gene mutations; • to know the consequences of mutations of coding, regulatory and modulating regions of human genes; • to demonstrate the dominant, codominant or recessive effect of molecular mutations at the molecular, cellular and organism levels. • to understand the genetic phenomena that can appear in the manifestation and transmission of some traits: incomplete penetration, variable 	<ol style="list-style-type: none"> 1. Human genes. Structure, location and identification of genes. 2. Methods of direct and indirect gene analysis. 3. Gene mutations. Classification. Point mutations consequences. 4. Normal monogenic hereditary traits (I). Human blood types genetics (AB0, Rh, MN, Xg). Genetics of HDNB. 5. Normal hereditary characters with polygenic determinism. 6. Mendelian monogenic diseases (AD, AR, XD, XR). Non-Mendelian monogenic diseases (mitochondrial, imprinted). 7. Gene interactions and genetic phenomena in the determinism and



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Objectives	Content units
<p>expressiveness, allelic / non-allelic heterogeneity, anticipation;</p> <ul style="list-style-type: none"> to understand the principles, stages and components needed for different gene analysis techniques; to model PCR technique, Southern blot technique, dideoxy sequencing; to interpret the results of gene analysis in various techniques; to apply the knowledge gained to other disciplines 	<p>expression of normal and pathological genes.</p>

Objectives	Content units
Chapter 3. Study of the normal and pathological hereditary traits	
<ul style="list-style-type: none"> to define gene pool, MZT concordance, DZT concordance, AD, AR, XD, XR gene transmission; To know the methods of confirming the genetic nature of a normal or pathological trait; To build and analyze genealogical trees with the study of heredity of different phenotypes; to apply the population-statistical method in calculating the frequency of pathological genes and carriers in the RM population; to apply the twin method in calculating the share of genetic and environmental factors in the manifestation of normal or pathological traits; to apply the genealogical method in determining the type of transmission and calculating the risk of recurrence of monogenic, Mendelian diseases; to understand the role and place of genetic counseling in addressing the patient, the couple, healthy people; to understand the indications and limits of prenatal diagnosis. 	<ol style="list-style-type: none"> Study of hereditary traits. Practical applications of the population statistical, genealogical and twins studies. Transmission of abnormal monogenic traits. Criteria for recognition of dominant and recessive, autosomal and X-linked inheritance. Inheritance of human pathological traits with incomplete penetrance, variable expression, genetic heterogeneity, anticipation. Genetic counselling. Prenatal genetic diagnosis. Principles of pharmacogenomics Gene therapies - applications and limitations.
Chapter 4. Basics of genetics of development, immunogenetics and cancer genetics	
<ul style="list-style-type: none"> to know the major stages of development and genetic control mechanisms; to understand the role of genomic imprinting in the development control; to define MUD and PUD, chromosomal mosaicism and their consequences on development 	<ol style="list-style-type: none"> Genetics of development- - main steps, genetic mechanisms and phenomena. Sex genetics - stages of masculinization and genes involved, stages of feminization and genes involved, sexual determinism and hermaphroditism, sexual differentiation and pseudohermaphroditism.



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Objectives	Content units
<ul style="list-style-type: none">• to know the role of HOX genes in development and the consequences of their mutations;• to define congenital malformations, deformations, disruptions and dysplasia, assessment of recurrence risks;• to know the stages of sexualization and the major responsible genes;• to differentiate hermaphroditism from pseudohermafroditism and the role of genetic counseling in sexuality disorders;• to know the genetic mechanisms of IG and TcR diversity involved in the humoral or cellular immune response;• to understand somatic recombination and role in T- or B-lymphocyte specialization.• to know the proto-oncogenic and GST characteristics in cell cycle control;• to define the stages of transition of a normal cell into the malignant cell and the compromised molecular processes;• to understand the clonal and multistage origin of carcinogenesis caused by dominant or recessive somatic, inherited or acquired mutations.• to assess the risk of recurrence of different tumors in affected families.	<ol style="list-style-type: none">3. Immunogenetics - proteins and genes responsible for the immune response, Ig and TcR gene superfamilies, somatic recombination and antibody diversity, genetic causes of immunodeficiencies.4. Cancer genetics - evidence of genetic origin of cancer, proto-oncogenes, GST and somatic mutations, stages of tumorigenesis, molecular characteristics, mutations and oncogenes.



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

✓ **Professional competences (SC):**

- ✓ PCI. 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 2.
- ✓ PC3. Resolving clinical situations by developing a plan for diagnosis, treatment and rehabilitation in various pathological situations and selecting appropriate therapeutic procedures for them, including providing emergency medical care 4.
- ✓ PC4. Promoting a healthy lifestyle, applying prevention and self-care measures 5.
- ✓ PC5. Interdisciplinary integration of the doctor's activity in a team with efficient use of all resources 6.
- ✓ PC6. Carrying out scientific research in the field of health and other branches of science 7.

✓ **Transversal competences (TC):**

- ✓ TC1. Autonomy and responsibility in the activity.

✓ **Study finalities**

- to understand the relationship between genome and environment in the determinism of normal and pathological traits;
- to determine the normal and abnormal karyotype;
- to establish the nature of the chromosomal abnormality - mitotic error, meiotic error;
- to know the principles and practical applications of cytogenetic techniques;
- to apply the laws of heredity for normal and pathological monogenic traits;
- to know the nomenclature of chromosomal and gene mutations;
- to understand the role of gene, chromosomal and genomic mutations in the etiology and pathogenesis of different human diseases;
- to know the indications and limitations of the PCR, Southern-blot and Sanger technique;
- to analyze the genealogical inheritance of some normal or pathological traits and to determine the type of inheritance, the genotype and to calculate the risk of recurrence of a genetic disease;
- to apply the studied methods in establishing the genetic nature of different human diseases.



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VIII. STUDENT'S SELF-TRAINING

Nr.	Expected product	Implementation strategies	Assessment criteria	Implementation terms
1	Working with information sources:	<p>Reading the lecture or the material from the textbook on the topic carefully.</p> <p>Reading questions on the topic, which require a reflection on the subject.</p> <p>To get acquainted with the list of additional information sources on the topic. Select the source of additional information for the topic.</p> <p>Reading the text entirely, carefully and writing the main content.</p> <p>Writing generalizations and conclusions regarding the importance of the topic / subject.</p>	Ability to extract the main information; interpretative skills; the volume of work	During semester the
2	Working with the Workbook:	<p>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.</p> <p>Formulate conclusions at the end of each lesson. Verifying the final conclusions of the lesson and appreciating their fulfilment.</p> <p>Selection of additional information, using electronic addresses and additional bibliography.</p>	Workload, problem solving, ability to formulate conclusions	During semester the
3	<i>Working with online materials</i>	Online self-assessment, study of online materials on Moodle, expressing own opinions on forum and chat	Number and duration of Moodle entries, self-evaluation results	During semester the
4	<i>Preparing and presenting presentations / portfolios</i>	<p>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</p>	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 semester the



IX. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

✓ *Teaching and learning methods used*

In teaching Medical Genetics 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,



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- (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%).

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 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.

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 failed exams.



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X. RECOMMENDED LITERATURE

- A. Compulsory

1. Lecture materials on www.biologiemoleculara.usmf.md
2. Reading materials in medical genetics on www.biologiemoleculara.usmf.md
3. Medical Genetics. Guide for practical lessons Capcelea S., Perciuleac L., Cemortan I. 2021
4. Genetica medicală Covic M., Ștefanescu D., Sandovici I. 2004, 2011
5. Genetica medicală Covic M., Ștefanescu D., Sandovici I., Gorduza E.V. 2017
6. <https://ghr.nlm.nih.gov>

- B. Additional

1. 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
2. Curs de biologie moleculară Cemortan I., Capcelea S., 2000 Țaranov L., Amoașii D.
3. Medicina genomică și bolile comune ale adultului. Covic A., Gorduza V.E., Covic M. 2020
4. <http://www.genecards.org/>
5. <https://www.malacards.org/>
6. <https://www.ncbi.nlm.nih.gov/pubmed/>
7. <https://genome.cshlp.org/>
8. Biologie moleculaire en biologie clinique V.2. M. Bogart 2005