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 Comparison

# FACULTY OF MEDICINE

# **STUDY PROGRAM 0912.1 MEDICINE**

#### **CHAIR OF MOLECULAR BIOLOGY AND HUMAN GENETICS**

#### APPROVED

at the meeting of the Commission for Quality Assurance and Evaluation of the Curriculum

> faculty Minutes No. 6 of  $23 \cdot 64 \cdot 12$

Chairman, Associate professor, PhD Suman Serghei

APPROVED

at the Council meeting of the Faculty

Minutes No. 4 of 20. 0 3 (1)

Dean of Faculty Medicine 2, Associate professor, PhD

Betiu Mircea

a *Ba* 

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 HUMAN GENETICS

**Integrated studies** 

Type of course: Compulsory discipline

Chisinau, 2017



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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 Human 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 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. Human Genetics ensures the possibility of

• elucidation of pathogenic mechanisms of genetic diseases and genetic predisposition (cancers, coronary disease);

• genotypic diagnosis: pre-symptomatic or prenatal;

• genomic pharmacology - blocking the expression or replication of mutant genes;

• gene therapy - the introduction of normal genes into somatic cells of patients with mutant genes;

individualized disease prophylaxis;

• changing the doctor-patient relationship - "There are no sick people, but only families of sick people".

• Language (s) of the course: English.

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



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# II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		F.02.O.015		
Name of the discipline		Human Genetics		
Person(s) in charge of the discipline		Associate professor Igor Cemortan		
Year	Ι	Semester/Semesters	2	
Total number of hours, including:			150	
Lectures	34	Practical/laboratory hours	25	
Seminars	26	Self-training	65	
Clinical internship				
Form of assessment	E	Number of credits	5	

# III. TRAINING AIMS WITHIN THE DISCIPLINE

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

- at the level of knowledge and understanding:
- 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 cancerogenesis;
- 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:
  - twin method;
  - statistical population method.
  - 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.

#### PROVISIONAL TERMS AND CONDITIONS

Requirements for first 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 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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# IV. THEMES AND ESTIMATE ALLOCATION OF HOURS

#### A. Lectures

	Торіс	Hours
1.	Introduction into human genetics. Genetics – the science of heredity and variability. Human genetics – fundamental and applicative science. Human, heredity and environment. The role of Human Genetics in medicine.	2
2.	Morphology and structure of human chromosomes. Methods of the human chromosome analysis. Chromosome banding. Identification, classification and nomenclature of human chromosomes. Sexual chromosomes.	2
3.	Chromosome abnormalities. Abnormalities in chromosome number. Abnormalities in chromosome structure. Chromosomal formulas. Chromosomal syndromes.	2
4.	Inheritance of genetic information from cell to cell. Segregation of chromosomes during mitosis. Errors of distribution of genetic information during mitosis. Chromosomal mosaics.	2
5.	Transferring of genetic information from ascendant to offspring. Genetic events during meiosis. Errors of recombination and distribution of chromosomes during meiosis. Particularities of meiosis in men and women. Errors during fecundation.	2
6.	Human genes: structure, functions and location. Classical and modern concepts about gene's structure. Localization of genes. Locus. Allelic genes. Polyallelism. Gene linkage. Genetic recombination. Biological and practical role of the gene linkage and recombination.	2
7.	Isolation and cloning of genes. Molecular analysis of human genes	2
8.	Gene mutations. Classification of mutations. Gene mutations. Spontaneous and induced mutations. The rate of mutations. Molecular basis of mutations. Dynamic mutations. Phenotypic consequences of gene mutations.	2
9.	Gene functions and relation genotype-phenotype. Pleiotropic and polygenic characters. Genetic heterogeneity (allelic and locus). Gene's interactions: allelic, non-allelic and interaction between genes and environment. Gene interactions at the molecular level.	2
10.	Inheritance of monogenic characters. The Mendel's lows. Autosomal-dominant inheritance. Codominance. Incomplete dominance. Human blood types (AB0, Rh). Autosomal-recessive inheritance. Consanguinity. Sex-linked inheritance. X-linked and Y-linked traits. Expressivity. Penetration. Phenocopies.	2
11.	Non-mendelian transmission. Mitochondrial inheritance. Genomic imprinting. Uniparental disomy. Mosaics. Polygenic/multifactorial transmission. Polygenic inheritance. Predisposition for polygenic diseases.	2
12.	Genetics of population. Human populations. The Hardy-Weinberg principle. Factors influencing genic and genotypic frequency. Hardy-Weinberg low applications.	2
13.	Genetics of development. Genetic (molecular) control of embryogenesis. Inactivation of genes. Inactivation of X chromosome. Congenital abnormalities. Terratogenesis.	2
14.	Genetics of sex differentiation. The normal process of sexualization. Abnormalities of	2



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	sexualisation. Male and female pseudo hermaphrodites.	
15.	Immunogenetics. The genetics of immune response. The HLA system. Immune deficiencies.	2
16.	Genetic nature of cancer. The cancer and chromosomes. Oncogenes and protooncogenes. Tumor suppressor genes. Mechanisms of cancer induction. Genetic predisposition to cancer.	2
17.	General information about genetic pathology. Genetic diseases. Classification and frequency of diseases. General characterization of genetic diseases. Methods of studying and diagnostic of genetic diseases. Genetic counselling. Prevention of the genetic diseases. Prenatal diagnostic.	2
	Total	34

# V. THEMES AND ESTIMATE ALLOCATION OF HOURS

#### **B.** Lectures

#### C. Practical hours/seminars and self-training

No.		Number of hours		
d/o	THEME		Practical hours	Self- training
1.	Genetic apparatus of human cell. Nuclear and mitochondrial genome.		1	3
2.	Morphology and structure of human chromosomes. Chromosomal nomenclature. Sexual chromosomes. Normal human karyotype.	2	1	4
3.	Methods of studying of human chromosomes. Techniques of chromosome banding. Sexual chromatin. Barr test, F test: indications and limits. Molecular-cytogenetic methods: FISH, SKY.	1	2	4
4.	Numeric and structural chromosome abnormalities.	2	1	4
5.	Dynamics of chromosomes during mitosis. Errors of distribution of genetic information during mitosis. Chromosomal mosaics		2	4
6.	Genetic events during meiosis. Transferring of genetic information from ascendant to offspring. Errors of meiosis and their consequences.		1	4
7.	Evaluation of the normal and pathological human karyotypes	1	2	4
8.	Human genes: structure, functions and location.	2	1	4
9.	Methods of direct and indirect gene analysis.	1	2	4
10.	Gene mutations. Classification of mutations. Point mutations. Phenotypic consequences of gene mutations.	2	1	4
11.	Normal monogenic human traits (I). Human blood types (AB0, Rh).	1	2	4
12.	Normal monogenic human traits (II). Inheritance of the systems: MNS, Hp, Xg, HLA.	1	2	3
13.	Polygenic inheritance. Dermatoglyphs and their applications.	2	1	4



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No.		Number of hours		
d/o			Practical hours	Self- training
14.	Study of human hereditary traits. Hardy-Weinberg low. Twins studies. Applications of the populational-statistic method and twins studies.	2	1	4
15.	Human pathological monogenic traits. Types of inheritance. Criteria for the recognition of dominant and recessive, autosomal and X-linked inheritance.	1	2	4
16.	Inheritance of human pathological traits with incomplete penetrance, variable expression, genetic heterogeneity.	1	2	4
17.	Genetic counselling. Prenatal diagnosis.	1	2	3
	Total	26	25	65

# VI. REFERENCE OBJECTIVES OF CONTENT UNITS



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Objectives	Content units
Theme (chapter) 2. Human genes	
<ul> <li>To define gene, gene expression, genotype, homozygote, heterozygote, hemizigot, phenotype</li> <li>to know the particularities of organization, properties and functions of different genes;</li> <li>to know and understand the causes, mechanisms and nomenclature of gene mutations;</li> <li>to know the consequences of mutations of coding, regulatory and modulating regions of human genes;</li> <li>to demonstrate the dominant, codominant or recessive effect of molecular mutations at the molecular, cellular and organism levels.</li> <li>to understand the principles, stages and components needed for different gene analysis techniques;</li> <li>to model PCR technique, Southern blot technique, dideoxy sequencing;</li> <li>to apply the knowledge gained to other disciplines</li> </ul>	<ol> <li>Human genes: structure, functions and location.</li> <li>Methods of direct and indirect gene analysis.</li> <li>Gene mutations. Point mutations. Phenotypic consequences of gene mutations.</li> <li>Normal monogenic human traits (I). Human blood types (AB0, Rh).</li> <li>Normal monogenic human traits (II). Inheritance of the systems: MNS, Hp, Xg, HLA.</li> <li>Polygenic inheritance. Dermatoglyphs and their applications.</li> </ol>
Theme (chapter) 3. Study of the human hereditary	
<ul> <li>To define gene pool, MZT concordance, DZT concordance, AD, AR, XD, XR gene transmission;</li> <li>To now the methods of confirming the genetic nature of a normal or pathological trait;</li> <li>To build and analyze genealogical trees with the study of heredity of different phenotypes;</li> <li>To understand the genetic phenomena that may occur in the manifestation and transmission of traits: incomplete penetrance, variable expression, allelic / non-allelic heterogeneity, anticipation;</li> <li>to apply the population-statistical method in calculating the frequency of pathological genes and carriers in the RM population;</li> <li>to apply the twin method in calculating the share of genetic and environmental factors in the manifestation of normal or pathological traits;</li> </ul>	<ol> <li>Study of human hereditary traits. Hardy Weinberg low. Twins studies. Applications of the populational-statistic method and twins studies.</li> <li>Human pathological monogenic traits. Type of inheritance. Criteria for the recognition o dominant and recessive, autosomal and X-linked inheritance.</li> <li>Inheritance of human pathological traits with incomplete penetrance, variable expression genetic heterogeneity.</li> <li>Genetic counselling. Prenatal diagnosis.</li> </ol>



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Objectives	Content units
<ul> <li>the type of transmission and calculating the risk of recurrence of monogenic, Mendelian diseases;</li> <li>to understand the role and place of genetic counseling in addressing the patient, the couple, healthy people;</li> <li>to understand the indications and limits of prenatal diagnosis.</li> </ul> Theme (chapter) 4. Basics of genetics of development.	t immunogenetics and cancer genetics
<ul> <li>To know the major stages of development and genetic control mechanisms;</li> <li>To understand the role of genomic imprinting in the development control;</li> <li>To define MUD and PUD, chromosomal mosaicism and their consequences on development</li> <li>To know the role of HOX genes in development and the consequences of their mutations;</li> <li>To define congenital malformations, deformations, disruptions and dysplasia, assessment of recurrence risks;</li> <li>To know the stages of sexualization and the major responsible genes;</li> <li>To differentiate hermaphroditism from pseudohermafroditism and the role of genetic counseling in sexuality disorders;</li> <li>To know the genetic mechanisms of IG diversity</li> </ul>	<ul> <li>genetic mechanisms and phenomena.</li> <li>2. Genetics of sex differentiation – steps of male development and the involved genes, steps of female development and the involved genes, sexual determinism. Abnormalities of sexualisation. Male and female pseudo hermaphrodites.</li> <li>3. Immunogenetics. The genetics of immune response. Ig and TcR genes families. The HLA system. Somatic recombinations and antibodies diversity. Immune deficiencies.</li> <li>4. Genetic nature of cancer. The cancer and chromosomes. Oncogenes and protooncogenes. Tumor suppressor genes. Mechanisms of cancer induction. Genetic predisposition to cancer.</li> </ul>
<ul> <li>To know the genetic mechanisms of rocurversity and TcR involved in the humoral or cellular immune response;</li> <li>To understand somatic recombination and role in T- or B-lymphocyte specialization.</li> <li>To know the proto-oncogenic and GST characteristics in cell cycle control;</li> <li>To define the stages of transition of a normal cell into the malignant cell and the compromised molecular processes;</li> <li>To understand the clonal and multistage origin of carcinogenesis caused by dominant or recessive somatic, inherited or acquired mutations.</li> <li>Assess the risk of recurrence of different tumors in affected families.</li> </ul>	



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**Objectives** 

**Content units** 

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

#### ✓ Professional (specific) (SC) competences

SC1. Knowledge, understanding and use of language specific to human genetics, genetic medicine; SC 2. Knowledge and understanding of the organization of the human genome, chromosomes and genes;

SC 3. Knowledge of human karyotype and principles of cytogenetic techniques.

SC4. Explanation and interpretation of karyograms.

SC5. Knowledge of the gene mutation nomenclature.

SC6. Solving the situation problems and formulating the conclusions.

SC7. Classification of different genetic elements - chromosomes, genes, genetic methods, types of human traits transmission.

SC8. Comparing the results obtained by different cytogenetic and molecular techniques.

SC9. Analysis and interpretation of various genetic tests.

#### Transversal competences (TC)

- TC1. Improving the capacity of decisional autonomy;
- TC2. Formation of personal attitude;
- TC3. Ability to social interaction, group work with different roles;
- TC4. participating in interdisciplinary projects, extracurricular activities;
- TC5. Improving digital skills;

TC6. Developing different learning techniques;

TC7. Selection of digital materials, critical analysis and conclusions;

TC8. Presentation of individual scientific projects.

#### ✓ Study outcomes

- to determine normal and abnormal karyotype;
- to determine the nature of the chromosomal anomaly mitotic error, meiotic error;
- to know the principles and practical applications of cytogenetic techniques;
- to apply the heredity laws for normal and pathological monogenic characters;
- to know the nomenclature of chromosomal and gene mutations;
- to know the indications and limits of the PCR, Southern blot and Sanger techniques;
- to analyze the genealogical transmission of normal or pathological traits and determine the type of inheritance, genotype and calculate the risk of recurrence of a genetic disease;
- to apply the methods studied in determining the genetic nature of different traits.



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# STUDENT'S SELF-TRAINING

No.	Expected product	Implementation strategies	Assessment criteria	Implementation terms
1	Working with information sources:	Reading the lecture or the material from the textbook on the topic carefully. Reading questions on the topic, which require a reflection on the subject. To get acquainted with the list of additional information sources on the topic. Select the source of additional information for the topic. Reading the text entirely, carefully and writing the main content. Writing generalizations and conclusions regarding the importance of the topic / subject.	Ability to extract the main information; interpretative skills; the volume of work	During the semester
2	Working with the Workbook:	Before solving the tasks in the workbook to analyze the information and images from the respective subject in the lecture and textbook. Solving consecutive tasks. Formulate conclusions at the end of each lesson. Verifying the final conclusions of the lesson and appreciating their fulfilment. Selection of additional information, using electronic addresses and additional bibliography.	Workload, problem solving, ability to formulate conclusions	During the semester
3	Working with online materials	Online self-assessment, study of online materials on the Chair site, expressing own opinions on forum and chat	Number and duration of chair site entries, self- evaluation results	During the semester
4	Preparing and presenting presentations / portfolios	Selection of the research topic, establishing the research plan, setting the terms of realization. Establishing the components of the project / PowerPoint presentation - topic, goal, results, conclusions, practical applications, bibliography. Peer reviews. Teacher reviews	The volume of work, the degree of understanding of the essence of the project topic, the level of scientific argumentation, the quality of the conclusions, the elements of creativity, the personal attitude, the coherence of the exposure and the	During the semester



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scientific correctness, the way of presenting

### VIII. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

#### • Teaching methods used

In teaching Human 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.

#### Learning methods used

- **Observation** Identification of elements characteristic to some structures or biological phenomena, describing these elements or phenomena.
- Analysis Imaginary decomposition of the whole into component parts. Highlighting the essential elements. Studying each element as part of the whole.
- **Diagram / picture analysis** Selection of required information. Recognition based on knowledge and selected information of the structures indicated in the diagram, drawing. Analysis of the functions / role of recognized structures.
- Comparison Analysis of the first object / process in a group and determining its main features. Analysis of the second object / process and determining its main features. Comparing objects / processes and highlighting common features. Comparing objects / processes and determining differences. Establishing distinguishing criteria. Formulating conclusions.
- **Classification** Identification of the structures / processes to be classified. Determining the criteria on which classification is to be made. Distribution of structures / processes by groups according to established criteria.
- Scheme drawing Selection of elements, which must be included in the scheme. Showing the selected elements through different symbols / colors and showing their relationships. Formulating an appropriate title and legend for the symbols used.
- Modeling Identifying and selecting the elements needed for modeling the phenomenon. Imaging (graphically, schematically) the phenomenon studied. Realizing the phenomenon using the developed model. Formulating conclusions, deduced from arguments or findings.
- **Experiment** Formulating a hypothesis, based on known facts, on the process / phenomenon studied. Verifying the hypothesis by performing the processes / phenomena studied under laboratory conditions. Formulation of conclusions, deduced from arguments or findings.
- Applied teaching strategies / technologies (specific to the discipline)



**√** 

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

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

- **Current**: frontal and / or individual control through
- (a) applying docimological tests,
- (b) solving problems / exercises,
- (c) analysis of case studies
- (d) performing role-plays on the topics discussed.
- (e) tests

Final: exam.

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

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

Intermediate marks scale (annual average,	National Assessment	ECTS
marks from the examination stages)	System	Equivalent
1,00-3,00	2	F
3,01-4,99	4	FX
5,00	5	
5,01-5,50	5,5	Ε
5,51-6,0	6	
6,01-6,50	6,5	D
6,51-7,00	7	D
7,01-7,50	7,5	С
7,51-8,00	8	C
8,01-8,50	D	
8,51-8,00	9	В
9,01-9,50	9,5	•
9,51-10,0	10	Α

#### Method of mark rounding at different assessment stages



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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.

#### **IX. RECOMMENDED LITERATURE:**

#### A. Compulsory:

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

#### B. Additional

- 1. Information about the Human Genome Project. www.ornl.gov
- 2. Free online books www.freebooks4doctors.com
- 3. Online scientific journals www.pubmed.com
- 4. Online scientific journals www.freemedicaljournals.com
- 5. www.nature.com
- 6. www.genome.org
- 7. http://www.genecards.org/
- 8. Genes B.Lewin, 2017
- 9. Genetics (4 volumes), Robinson R., 2003
- 10. Human Molecular Genetics, Strachan T., Read A., 2001