# REQUIREMENTS

**Semmelweis University, Faculty of Dentistry**
**Name(s) of the Institute(s) teaching the subject:**
Department of Genetics, Cell- and Immunobiology

**Name of the subject:** Genetics and Genomics

**Credits:** 2

**Total number of hours:** 42 **lectures:** 28 **practices:** 14 **seminars:** -

**Type of the course (mandatory/elective):** mandatory

**Academic year:** 2019/2020

**Code of the course[1]:**

**Course director (tutor): Prof. Edit Buzás**

**Contact details:** Semmelweis University, Department of Genetics, Cell- and Immunobiology

**Position:** Professor and Chairman

**Date of habilitation and reference number: 2009. június 2. #273**

**Aim of the subject and its place in the curriculum:**
Introductory course in classical and molecular genetics and functional genomics, as well as basic course for the clinical module. It addresses the types, general laws of human inheritance, characteristics, organization and structure of the human genome, and the most important methods and / or their application in theoretical and clinical medicine, according to the needs of medical students, and evaluates the results (in practice). It presents the forms of genetic and epigenetic variability, their mechanisms and their consequences for human health. Through selected examples, the pathway from gene to disease is analyzed using a systems biology approach.

**Location of the course (lecture hall, practice room, etc.):** Semmelweis University, Department of Genetics, Cell- and Immunobiology, H-1089 Budapest, Nagyvárad tér 4. Hungary

**Competencies gained upon the successful completion of the subject:**
Basics of cytogenetics. Setting up and interpreting pedigrees. Basic knowledge of human genetics and human genomics. Background of monogenic and multifactorial diseases. Basics of prenatal diagnosis, detection of monogenic diseases by molecular genetic methods. Basic knowledge of oncogenetics, epigenetics, population genetics, nutrigenetics, evolutionary genetics, pharmacogenetics with biomedical approach. Role of gene-gene and gene-environment interactions in various diseases. Basic knowledge of bioinformatics and systems biology related to medical genetics and genomics. Basics of gene therapy.

**Prerequisite(s) for admission to the subject:** Cell Science, Medical Biochemistry II.

**Minimum and maximum number of students registering for the course:** According to Study and Exam Policy
**Student selection method in case of oversubscription:** According to the Study and Exam Policy

**How to register for the course:** in Neptun system

**Detailed thematic of the course[2]:**

***Lectures (2 hours per week)*:***
1. Introduction to human genetics, the human genome (E. Buzás)
2. Genetic variations (Cs. Szalai)
3. Mutation and polymorphisms (Cs. Szalai)
4. Chromosomal aberrations (M. Holub)
5. Epigenetics (S. Toth)
6. Monogenic inheritance (Autosomal inheritance) (E. Pap)
7. Role of sex in inheritance (S. Toth)
8. Genetics of biological processes (S. Toth)
9. Introduction to genomics (Cs. Szalai)
10. Methods in genomics (Cs. Szalai)
11. Genomic approach of complex inheritance (Cs. Szalai)
12. Genome and environment, Population and evolution genetics and genomics (Cs. Szalai)
13. Pharmaco- and nutrigenomics (Cs. Szalai)
14. Systems Biology. Ethical, legal and social aspects of human genetics (Ea .: Cs. Szalai)

* The order of the lectures and the date of the midterm may vary (depending on holidays and workday transfers). Colleagues with senior teaching status may also act as lecturers, if the lecturer on schedule is prevented.

***Practices (1.5 hours per week)*:***
1. Atypical mitosis, typical and atypical meiosis
2. Cytogenetics I.
3. Cytogenetics II.
4. Introduction to pedigree analysis
5. Molecular genetic methods and applications in human genetics I.
6. Molecular genetic methods and applications in human genetics II.
7. Pedigree analysis: Autosomal inheritance
8. Pedigree analysis: Autosomal recessive inheritance
9. Pedigree analysis: Sex-linked inheritance
10. Midterm
11. Complex inheritance
12. Gene therapy
13. Gametogenesis, prenatal genetic testing
14. From genes to bedside

* The order of the practises and the date of the midterm may vary (depending on holidays and workday transfers). Practice instructors: Colleagues with teaching status at the Institute of Genetics, Cell and Immunobiology

**Potential overlap(s) with other subjects:**
Understanding of Genetics and Genomics is based on the knowledge of molecular biology and molecular genetic techniques studied at Medical Biochemistry I-II. Elective subjects taught by our institute (Sex Genetics, Epigenetics, Genomics) elaborate on some of the subchapters of "Genetics and Genomics", with overlaps needed for understanding, focusing on topics not covered in the main subject.

**Special training activities required[3]: -**

**Policy regarding the attendance and making up absences:**
Completion of prerequisite subject.
Practices can only be attended to in an appropriate mental and health condition. Practical absence can be remedied during the current training week, in parallel courses, after prior consultation with the practice instructors.

**Means of assessing the students' progress during the semester[4]:**
Written midterm from the topics of taught lectures and practices. We provide an opportunity to retake the midterm, only for students who have proven absence.

**Requirement for acknowledging the semester (signature):**
According to the Study and Exam Policy the students must visit at least 75% of the lectures and practices.

**Type of the examination**: written (lectures and practices)

**Exam requirements[5]:**

***Exam topics:***

1.) **Introduction to human genetics and genomics.** Basic genetic terms, e.g.: genome, genetics, genomics, homologous chromosomes, gene, locus, allele, wild type allele, genotype, phenotype, homozygote, heterozygote, hemizygote, dominant, recessive, cytogenetics; Mendel's laws, Model organisms in genetics; DNA: structure, function, amount, organization (chromatin, chromosome). Replication, transcription, mRNA maturation (splicing, alternative splicing), types of RNA-s, features of genetic code. Translation and posttranslational modifications. Human genome: nuclear and mitochondrial. Structure of eukaryotic gene. Intergenic DNA; Specific sequences of nuclear genome. Repetitive sequences. Human Genome Project, ENCODE Project

2.) **Transmission of genetic information from cell to cell in an organism.** Main features and concept of multicellular cell cycle (phases, checkpoints). M-phase: activation and activity of MPF. Features of mitotic phases. Functional parts of chromosomes (telomere, centromere, kinetochore, sister chromatids, additional protein complex: cohesin and condensin and their role). Structure and role of centrosome, the centrosome cycle. Structure of mitotic spindle. Activity of APC. Cytokinesis. Changes of DNA amount and chromosome number during cell cycle. Types, causes and consequences of atypical mitosis. Light microscopic slide: 52

3.) **Transmission of genetic information from generation to generation.** Significance and source of genetic variability. Significance of meiosis. Stages of meiosis: meiosis I. and II. Features of phases of first prophase (leptotene, zygotene, pachytene, diplotene, diakinesis; synapsis, crossing over, chiazma). Random alignment and assortment of homologous chromosomes in meiosis I anaphase. Atypical meiotic process: non-disjunction. Change of DNA amount and chromosome number during meiotic process.

4.) **Pedigree analysis** Mendelian or monogenic inheritance, Construction of pedigree: main symbols that are used in pedigrees. Pedigree analysis (characteristics pedigree patterns of monogenic inheritances: AD, AR, XD, XR, Y-linked, mitochondrial). Disease examples for monogenic inheritances (AD, AR, XD, XR, mitochondrial); ***Important terms****:* gene, genome, locus, allele, multiple allelism, wild type (normal) allele, genotype: homozygote, heterozygote, complex heterozygote, hemizygote, phenotype: dominant, codominant, recessive.

5.) **Cytogenetics** Structure and types of eukaryotic chromosome. Karyotyping (chromosome preparation, principle, significance and types of banding techniques, principle and significance of multicolor-FISH, and M-banding); kariogram, idiogam; X inactivation. Study of sex chromosomes in interphase. Characteristics of human karyotype. Mutagenicity tests: micronucleus and sister chromatid exchange. Chromosome territories. Light microscopic slides: 54, 60, 64

6.) **Structural chromosome mutations** Structural chromosome aberrations. Types of structural aberrations: deletion (terminal, interstitial), duplication, translocation (reciprocal, Robertsonian), inversion (paracentric, pericentric), ring chromosome, isochromosome. Balanced and unbalanced mutations. Chromosomal translocations in leukemia. Consequence of structural aberrations.

7.) **Numerical chromosome mutations** Numerical chromosome aberrations: euploidy, polyploidy, aneuploidy, mixoploidy (mosaicism, chimerism). Possible cause of aneuploidy (non-disjunction in meiosis I and II). Autosomal (Patau, Edwards and Down syndromes) trisomies. Numerical aberrations of sex chromosomes (Klinefelter, XYY, triplo X, Turner syndromes). Uniparental disomy (UDP). Cause and consequence of of polyploidy and mixoploidy (mosaicism and chimerism).

8.) **Mutations and polymorphisms** Different meanings of mutation and polymorphism. Significance of mutation. Classification of mutations: by cause (spontaneous, induced, different DNA repair mechanisms, consequence of their failure), by site (in the organism: somatic, germline, in the gene), by function (loss-of-function, gain-of-function, dominant negative, lethal, back), by fitness (neutral, beneficial, harmful), by size (genome, chromosome, gene: insertions, deletions, substitutions). Repetitive insertions, triplet repeat: polyglutamine and polyalanine disorders. inDel mutations: frame shift and in frame mutations. Nucleotide substitutions: transition, transversion, sense (synonymous) missense and nonsense (non-synonymous) mutations. Types, size and significance of genetic polymorphism.

9.) **Epigenetics** Meaning of epigenetics. Relationship of genome, epigenome and phenotype. Epigenetic mechanisms: transcriptional (DNA methylation, histone modifications), posttranscriptional (RNAi, miR). X chromosome inactivation, role of XIST. Autoimmunity and X inactivation. Genomic imprinting, evidences of nonequivalence of parental genome. Mechanism of genomic imprinting. Causes of Prader Willi and Angelman syndromes. Possible role of genomic imprinting. Relationship between genomic imprinting and cancer. Position effect. Epigenetic changes caused by aging and by in vitro fertilization. Transgenerational effects.

10.) **Introduction to genomics. Methods in genomics** Genomics, Human Genome , DNA sequencing, Participants in the Human Genome Project, Some results of the HGP, Variations in the human genome, Some novel data about gene expression and genetic variability, Junk DNA in the human genome, Comparative genomics, ENCODE project, Genetic markers, GWAS, Principle of molecular genetic methods: hybridization, restriction enzymes, DNA isolation, Visualization of genomial DNA, Southern blot: separation of DNA fragments by gelelectrophoresis , capillary gelelectrophoresis), non-specific staining of DNA (EtBr), Allele-Specific Oligonucleotide (ASO) test, RFLP, Southern-RFLP, microarray, PCR, PCR- RFLP, Multiplex PCR, MLPA, nested PCR, Significance of real time-PCR. Significance and detection of VNTR. VNTR and trinucleotid diseases. Significance of polymorphism detection in forensic medicine. DNA fingerprint. Foreign DNA (bacterial, viral) detection. Sequencing in genotyping. NGS. Study of gene expression: Northern blot, RT(reverse transcriptase)-PCR.

11.) ***Complex inheritance.*** Features of complex inheritance. Environmental factors. Heritability of the complex diseases. Disease examples

12.) **Pharmacogenomics** Pharmacogenetics and pharmacogenomics. Pharmacokinetics, -dimamics, Drug development Adverse drug response, Genomic background of adverse effects, CYP (cytochrom P-450) gene family, Warfarin, Mercaptopurine, Genes influencing pharmacodynamics, Examples of pharmacogenetic studies, Pharmacogenetics of statins, Clopidogrel, Pharmacotherapy of asthma, MODY, Succinylcholine sensitivity, Thiopurin methyltransferase variations, Role of membrane receptors in drug effects.

13.) **Nutrigenomics** Genetic variations and food, food and gene expression.

14.) **Gene therapy** Gene therapy types (real, gene expression modification) and forms (in vivo, ex vivo). Nucleic acids applied in gene therapy: DNA, RNA. Forms of introduction of nucleic acids into target cells. Vectors applied in gene therapy: adenovirus, adeno associated virus, retrovirus, lentivirus, nonviral integrating vectors. Comparison of viral vectors. Examples of succesful gene therapy trial.

15.) **Population genetics** Types of sample collection, prospective and retrospective studies. Selection of populations for genetic studies. Hardy Weinberg equilibrium. Linkage, haplotype, linkage disequilibrium. Founder populations. Association studies, population stratification, population admixture. Risk calculation, odds ratio and relative risk, p-value.

16.) **Evolution genetics**: Gene environmental interactions and the human genome. Natural selection. Role of infections in formation of the genome. Genetic drift, bottleneck effect. Why are some lethal mutations frequent? Examples for effects forming the genome.

17.) **Genome and environment:** Penetrance of the genetic variants; Interactions between highly and low penetrant variations and the environment; smoking-genome interaction, gene-environmental interactions;

18.) **Gametogenesis, prenatal genetic testing:** Comparison of spermatogenesis and oogenesis; Genetic aspects of infertility; Genetic aspects of assisted reproduction techniques; CGH; aCGH prenatal genetic testing; Non-invasive prenatal testing

19.) **Genetics of biological processes:** Genetics of development: development potentials (totipotent, pluripotent, multipotent, unipotent), cell differentiation, significance of stem cells. Role of morphogens and their concentration gradient (Sonic hedgehog), homeotic genes. Genetics of sex: sex determination, male sex determination. Causes of maldevelopment. Oncogenetics: oncogenes and tumor suppressor and mutator genes. Activation mechanisms of oncogenes. Tumor suppressor genes, LOH. Immunogenetics: somatic gene rearrangement, role of epigenetics, genetic background of antibody diversity.

**Type and method of grading[6]:** Based on the result of the exam.

**How to register for the exam:** In the Neptun system, according to current university and faculty settings, or in the case of a post-holiday exam, you can apply for the exam until the morning of the last working day before the public holiday.

**Opportunities to retake the exam:** According to the Study and Exam Policy

**Literature, i.e. printed, electronic and online notes, textbooks, tutorials (URL for online material):**
Cs. Szalai (Editor): Medical Genetics and Genomics e-.book, 2018
Power Point presentations of the lectures and practices; The e-book and presentations available at the homepage: **http://gsi.semmelweis.hu/index.php/en/education/**

**Signature of the tutor:**

**Signature(s) of the head(s) of the Institute(s):**

**Date:** 2019.09.27

**Credit Transfer Committee's opinion:**

**Comment of the Dean's Office:**

**Signature of the Dean:**

[1] Dékáni Hivatal tölti ki, jóváhagyást követően.
[2] Az elméleti és gyakorlati oktatást órákra (hetekre) lebontva, sorszámozva külön-külön kell megadni, az előadók és a gyakorlati oktatók nevének feltüntetésével. Mellékletben nem csatolható!
[3] Pl. terepgyakorlat, kórlapelemzés, felmérés készítése stb.
[4] Pl. házi feladat, beszámoló, zárthelyi stb. témaköre és időpontja, pótlásuk és javításuk lehetősége.
[5] Elméleti vizsga esetén kérjük a tételsor megadását, gyakorlati vizsga esetén a vizsgáztatás témakörét és módját.
[6] Az elméleti és gyakorlati vizsga beszámításának módja. Az évközi számonkérések eredményeink beszámítási módja.