Department:
DEPARTMENT OF CANCER GENETICS WITH CYTOGENETIC LABORATORY
Address: RADZIWILLOWSKA STREET 11 (COLLEGIUM MEDICUM BUILDING), 20-080 LUBLIN,
Course: MEDICAL GENETICS
Head of Department: PROF. AGATA FILIP
The course coordinator: DR. SZYMON ZMORZYŃSKI, **e-mail: szymonzmorzynski@umlub.pl**
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Course description:
1. The Medical Genetics course includes **10 hours of lectures** and **25 hours of classes** during one semester for EUROPEAN/International PROGRAM
2. The course consists of the following parts: Human genome, Point mutations and polymorphisms, Chromosomal aberrations, Pathomechanisms of genetic diseases, Chromosomes, Immunogenetics, Oncogenesis, Molecular methods.
3. During the course students write short quizzes.
4. The course ends with the **Final Test**.
5. All information are available on the website of the Department: **www.genetyka.umlub.pl bookmark English Division.**

Topics covered in the course

A) CLASSES – 25 hours

LAB 1

[2 hours]

SUBJECT: RULES AND REGULATIONS. INTRODUCTION TO GENETICS

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) Rules and regulations

II) Basic terms: genetics, nucleic acid, DNA and RNA, DNA replication, DNA polymerase, helicase, DNA ligase, gene, allele (dominant and recessive), codominant alleles, exon, intron, transcription, reverse transcription, RNA polymerase, translation, homozygous (dominant and recessive), heterozygous, hemizygous, chromatin, chromosome, genome, genotype, phenotype, haplotype, haploid cells, diploid cells, mitosis, meiosis, mutation, polymorphism, single nucleotide polymorphism (SNP), genetic anticipation.

III) Types of genetic diseases: chromosome disorders, single-gene disorders, multifactorial disorders, mitochondrial disorders

OBLIGATORY BOOK:

"Human genetics: from molecules to medicine" C.P. Schaaf, J. Zschocke, L. Potocki - Lippincott Williams & Wolters Kluwer business, 2012 (first edition). ISBN-13: 978-1-60831-671-7 and ISBN-10: 1-60831-671-8. CHAPTER: Glossary.

OR

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 1 and 2

LAB 2

[2 hours]

SUBJECT: HUMAN GENOME

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) DNA structure (nucleotides, base pairing, DNA as a double helix)

II) Nuclear genome:

-the structure of genes. Gene families. Protein coding genes, RNA-coding genes

-non-coding DNA: satellite DNA, minisatellite DNA, microsatellite DNA, transposons (SINEs, LINEs, LTR, DNA transposons). Use of microsatellite DNA in forensic genetics.

III) Mitochondrial genome:

-mitochondrial function

-protein coding genes, RNA-coding genes

-mutation rate

-mitochondrial inheritance

-examples of mitochondrial disorders – myoclonic epilepsy with ragged red fibers syndrome (MERRF), Leber's hereditary optic neuropathy (LHON), Kearns-Sayre syndrome (KS).

OBLIGATORY BOOK:

"Human genetics: from molecules to medicine" C.P. Schaaf, J. Zschocke, L. Potocki - Lippincott Williams & Wolters Kluwer business, 2012 (first edition). ISBN-13: 978-1-60831-671-7 and ISBN-10: 1-60831-671-8. CHAPTERS: 2.1 DNA, 2.2 Genes, 2.3. Repetitive sequences, 5.5 Mitochondrial inheritance.

OR

"GENETICS" Ronald W. Dudek – Lippincott Williams & Wolters Kluwer business, 2010. ISBN 978-0-7817-9994-2. CHAPTERS: 1. The human nuclear genome (I-General features; II-Protein-coding genes; III-RNA-coding genes; V-Non-coding DNA); 2. DNA packing (I-Biochemistry of nucleic acids; II-Double helix DNA) 3. Mitochondrial inheritance.

OR

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 2 and 5

LAB 3

[2 hours]

SUBJECT: FROM GENES TO PROTEINS

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) TERMS: promoter, enhancer, silencer, primary transcript, mature transcript, gene splicing, alternative splice sites, transcription factors, DNA-binding motifs, housekeeping genes, genetic code, codon and anticodon

II) Posttranslational modifications in the case of Osteogenesis imperfecta (an inherited collagen disorder and its genetic cause). The process of collagen fibril formation.

III) The concept of phenotype. Gene expression and mutations – classes of *CFTR* gene mutations in cystic fibrosis.

IV) Factors that affect expression of disease – new mutations in the case of achondroplasia, age dependent penetrance – in the case of Huntington disease, variable expression – in the case of neurofibromatosis (type I and II), *locus* heterogeneity and germline mosaicism (both) – in the case of osteogenesis imperfecta, pleiotropy – in Marfan syndrome

OBLIGATORY BOOK:

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 2, 3 and 4

LAB 4

[2 hours]

SUBJECT: POINT MUTATIONS AND POLYMORPHISMS

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) Terms: – point mutation, somatic mutation, germline mutation, constitutional mutation, missense mutation, nonsense mutation, splice mutation, frameshift mutation, null mutation, silent mutation, *de novo* mutation, copy number variation, gene amplification, gain of function, loss of function, haploinsufficiency

II) frameshift mutations – in the case of Duchenne muscular dystrophy; **in frame mutations** – in the case of Beckers muscular dystrophy

II) Location of mutations and their possible effects (location within different part of a gene: promoter region, introns, exons, regulatory regions).

III) Induced mutations - biological, chemical (base analogs, acridine dyes, nitrous acid) and physical factors (ionizing radiation and non-ionizing radiation, pyrimidine dimers). The effect of radiation on mutation rates.

IV) Spontaneous mutations – dynamic mutations, genetic anticipation, permutation status; genetic cause of fragile X syndrome and Huntington disease.

V) Mutation vs. polymorphism. Single nucleotide polymorphisms.

VI) Clinical consequences of mutation – the hemoglobin disorders: sickle cell anemia, thalassemia (α and β).

VII) DNA Repair (types and general overview). Xeroderma pigmentosum – a disease of faulty DNA repair.

OBLIGATORY BOOK:

"Human genetics: from molecules to medicine" C.P. Schaaf, J. Zschocke, L. Potocki - Lippincott Williams & Wolters Kluwer business, 2012 (first edition). ISBN-13: 978-1-60831-671-7 and ISBN-10: 1-60831-671-8. CHAPTERS: 1.2. Frequency of genetic diseases, 3.1. Mutation or polymorphism? 3.5. Gene mutations, 3.6 Dynamic mutations, trinucleotide repeats.

OR

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 3 and 5

LAB 5

[2 hours]

SUBJECT: PATHOMECHANISMS OF GENETIC DISEASES

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) Terms: pleiotropy, genetic heterogeneity, expressivity, variable expressivity, penetrance, epistasis, polyphenism, monogenic, digenic, polygenic, loss of heterozygosity

II) Semidominance (incomplete dominance) in the case of familial hypercholesterolemia and complete dominance – in the case of Huntington disease

III) Heterozygote advantage in the case of sickle cell anemia

IV) Codominance in the AB0 blood group system

V) Dominant negative effect in the case of osteogenesis imperfecta and Marfan syndrome

VI) DNA replication and aging effects – function of enzymes involved in DNA replication (DNA topoisomerase, helicase, DNA polymerase, DNA ligase), leading strand and lagging strand; telomeres and function of telomerase; telomere shortening, accumulation of mitochondrial mutations.

VII) Human progeria syndrome – Werner syndrome.

OBLIGATORY BOOK:

"Human genetics: from molecules to medicine" C.P. Schaaf, J. Zschocke, L. Potocki - Lippincott Williams & Wolters Kluwer business, 2012 (first edition). ISBN-13: 978-1-60831-671-7 and ISBN-10: 1-60831-671-8. CHAPTERS: 2.1. DNA – Replication of DNA, 4.1. From genotype to phenotype, 4.2. Dominant and recessive, 8. Aging and Genetics.

OR

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTER 4

LAB 6

[2 hours]

SUBJECT: IMMUNOGENETICS

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) The humoral and cellular immune systems

II) types of gene expression – biallelic and monoallelic expression, allelic exclusion

III) Immunoglobulin molecules and genes, the genetic basis of antibodies, structure and expression of immunoglobulin genes, synthesis of IgM and IgD in B-cells by alternate splicing, heavy chain class switching (another DNA rearrangement event), somatic mutation, random combinations of heavy and light chains

IV) T-cell receptor molecules and genes

V) The major histocompatibility complex

OBLIGATORY BOOK:

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTER 9

SOURCE of LEARNING:

-Lecture "immunogenetics" (Dr. Szymon Zmorzyński)

LAB 7

[2 hours]

SUBJECT: CHROMOSOMES AND THEIR ABERRATIONS

TEACHER: Prof. Agata Filip

TOPICS:

I) Chromosome structure and classification (depending on centromere localization).

II) Numerical chromosome abnormalities (aneuploidy, euploidy, meiotic nondisjunction, anaphase lag, mosaicism).

III) Structural chromosome abnormalities (deletions, duplications, inversions, translocations, isochromosome, Robertsonian translocation, balanced/unbalanced aberrations), **marker chromosomes**.

IV) Cytogenetic nomenclature.

OBLIGATORY BOOK:

"Human genetics: from molecules to medicine" C.P. Schaaf, J. Zschocke, L. Potocki - Lippincott Williams & Wolters Kluwer business, 2012 (first edition). ISBN-13: 978-1-60831-671-7 and ISBN-10: 1-60831-671-8. CHAPTERS: 2.7. Chromosomes, 3.2. Types of mutations, 3.3. Numerical chromosome abnormalities, 3.4. Structural chromosome abnormalities, 4.4 Mosaicism

OR

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 2 and 6

LAB 8

[2 hours]

SUBJECT: CHROMOSOME ANALYSIS

TEACHER: Prof. Agata Filip

TOPICS:

I) Methods of chromosome analysis

II) Source of cells for chromosome analysis

III) Cell cultures

IV) Classical cytogenetics (G-banding, R-banding)

V) Molecular cytogenetics – FISH and its variants, CGH and array CGH.

OBLIGATORY BOOK:

"Human genetics: from molecules to medicine" C.P. Schaaf, J. Zschocke, L. Potocki - Lippincott Williams & Wolters Kluwer business, 2012 (first edition). ISBN-13: 978-1-60831-671-7 and ISBN-10: 1-60831-671-8. CHAPTERS: 15.1. Cytogenetics, 15.2. Molecular cytogenetics.

OR

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 2 and 6

SOURCE of LEARNING:

Material from lecture (prof. Agata Filip)

LAB 9

[2 hours]

SUBJECT: Molecular methods

TEACHER: Dr. Szymon Zmorzyński

TOPICS:

I) Examples of biological material for nucleic acid isolation

II) Restriction enzymes:

-names, types I-IV, blunt ends, sticky ends (5'-overhang and 3'-overhang)

-examples: AluI, SmaI, BamHI, EcoRI, PstI, TaqI

III) Detecting variation at DNA level: Southern blotting and restriction fragment analysis, tandem repeats polymorphisms, single nucleotide polymorphisms, copy number variants.

IV) DNA sequencing technique, next generation sequencing (high-throughput DNA sequencing) – diagnostics of colagenopathies – osteogenesis imperfecta and Ehlers-Danlos syndrome

V) PCR METHOD (general procedure and stages), **PCR multiplex, reverse transcription PCR, real time PCR, PCR-RFLP** -diagnostics of sickle cell anemia.

VI) Genetic testing – heterozygote screening, direct mutation analysis. Limitations of genetic testing.

OBLIGATORY BOOK:

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTERS 3 and 13

SOURCE of LEARNING:

-Lecture "molecular methods" (Dr. Szymon Zmorzyński)

LAB 10

[2 hours]

SUBJECT: ONCOGENESIS – PART I

TEACHER: Prof. Agata Filip

TOPICS:

I) Oncogenic transformation – definition, stages of transformation and their characteristics.

II) Cancer cell characteristics.

III) Tumor classification with respect to biology and histology.

IV) Benign and malignant tumors – differences.

V) Apoptosis and necrosis

VI) Molecular pathway of tumor development: oncogenes – types, mechanisms of activation, examples.

VII) Molecular pathway of tumor development: tumor suppressor genes – types, mechanisms of activation, examples.

VIII) microRNA – definition, structure and role in oncogenesis.

XIX) Role of angiogenesis in tumor development, pro- and antiangiogenic factors.

X) Metastases – stages of development, sites.

OBLIGATORY BOOK:

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTER 11

LAB 11

[2 hours]

SUBJECT: ONCOGENESIS – PART II

TEACHER: Prof. Agata Filip

TOPICS:

I) Two-hit hypothesis for tumorgenesis

II) Cancer predisposition – role of germline mutations

III) Familial cancer – Lynch syndrome, retinoblastoma, breast cancer, familial adenomatous polyposis of colon, hereditary diffuse gastric cancer, Li-Fraumeni syndrome

IV) molecular tests in cancer predisposition (germline mutations)

V) molecular lesions as prognostic and predictive factors

VI) targeted treatment

OBLIGATORY BOOK:

"Medical genetics" L.B. Jorde, J.C. Carey, M.J. Bamshad (fifth edition), ELSEVIER, ISBN 978-0-323-188835-7 CHAPTER 11

LAB 12/13

[2 hours/1hour]

SUBJECT: Written quiz/Points calculation (before the final test).

TEACHER: Dr. Szymon Zmorzyński

According to RULES and REGULATIONS a Student is obliged to take a written quiz

(**material from the whole semester**),

if the total score from the classes is less than 60% (**60 points**), but more than 40% (**40points**).

[100% = 100 points]

B) LECTURES – 10 hours

1. Chromosome analysis – meiosis and mitosis, cell cultures, classical cytogenetics (banding techniques), molecular cytogenetics – FISH, CGH, array CGH; PROF. AGATA FILIP
2. Types of RNA. Role of non-coding RNA. MicroRNAs – their biogenesis and function, miRNAs as prognostic and predictive factors; PROF. AGATA FILIP
3. Prenatal diagnostics – aims, indications, noninvasive and invasive testing techniques, preimplantation testing; PROF. AGATA FILIP
4. Molecular methods in medical genetics. DR. SZYMON ZMORZYŃSKI
5. Immunogenetics. DR. SZYMON ZMORZYŃSKI