Катедра по медицинска генетика, Медицински Факултет, Медицински Университет-София, ул. Здраве 2, 1431 София, medgenetics@medfac.mu-sofia.bg

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Syllabus for theoretical semester exam for Medical students

2020/2021

1. Gene structure and function. DNA replication, transcription and translation. Organization of the human genome.
2. Molecular mechanisms of gene expression regulation.
3. Changes in chromatin structure as a mode of genomic modification. Genomic modification - reorganization of the immunoglobulin genes. Epigenetics.
4. Biology and genetics of mitochondria.
5. Chromosome morphology. Structure and function of chromosomes. Normal human karyotype. Chromosomal heteromorphism.
6. Chromosome mutations – numerical and structural. Marker chromosomes. Chromosomal fragile sites.
7. Etiology of inherited disorders. Mutagenesis. Definition and classification of gene mutations. Phenotypic effect of mutations. Germ-line and somatic mutations.
8. DNA damage and repair systems. Direct reversal of DNA damage. DNA repair of one-strand damage (BER, NER, Mismatch repair systems). DNA repair of double-strand breaks.
9. Clinical genealogy method. Types of monogenic inheritance – autosomal dominant and autosomal recessive type of inheritance.
10. Clinical genealogy method. Types of monogenic inheritance – sex-linked type of inheritance.
11. Non-mendelian inheritance. Inheritance of chromosomal aberrations.
12. Molecular genetic methods – PCR, Sanger sequencing, Next generation sequencing, SSCP, DGGE.
13. Next generation sequencing (NGS). Array comparative genomic hybridization (aCGH).
14. Molecular genetic methods – RFLP, ASO, allele specific PCR.
15. MLPA. Microarray methods for genomic analysis.
16. Genetic methods for diagnosis of chromosomal diseases – cytogenetic, molecular-cytogenetic methods (FISH).
17. Genetic anemias – thalassemia syndromes.
18. Genetic anemias - abnormal hemoglobins.
19. Genetic anemias – anemia caused by membrane defects, by enzymatic defects, hypoplastic anemias – Fanconi anemia.
20. Coagulation disorders – Haemophilia A and B. Von Willebrand disease.
21. Inborn errors of metabolism of amino acids – PKU, tyrosinemia, homocysteinuria
22. Inborn errors of metabolism of carbohydrates – galactosemia.
23. Inborn errors of metabolism of lipoproteins – familial hypercholesterolemia.
24. Lysosomal storage diseases – mucopolysaccharidoses: Hurler disease, Hunter disease, Sanfilippo disease; sphingolypidoses: Tay-Sachs disease, Sandhoff disease, Fabry disease, Gaucher disease, Farber disease, Nieman-Pick disease.
25. Connective tissue disorders - Osteogenesis imperfecta.
26. Connective tissue disorders - Ehlers-Danlos syndrome.

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27. Connective tissue disorders - Marfan syndrome.
28. Primary immunodeficiency syndromes – general features and classification.
29. Neuromuscular disorders. Spinal muscular atrophy.
30. Neuromuscular disorders. Hereditary motor sensory neuropathy (HMSN).
31. Neuromuscular disorders. Muscular dystrophies – dystrophinopathies, limb-girdle muscular dystrophies.
32. Monogenic disease affecting the respiratory system – cystic fibrosis.
33. Monogenic disease affecting the respiratory system - α1-antitrypsin deficiency.
34. Syndromic and nonsyndromic hearing loss and deafness
35. Trinucleotide repeat expansion disorders – Huntington's disease.
36. Trinucleotide repeat expansion disorders - Myotonic dystrophy.
37. Trinucleotide repeat expansion disorders - Fragile X syndrome.
38. Mitochondrial diseases – general characteristics. LHON, MERRF, MELAS, NARP, Leigh disease, Kearns-Sayre syndrome.
39. Diseases due to sex chromosome abnormalities. Turner syndrome.
40. Diseases due to sex chromosome abnormalities. Klinefelter syndrome. Fraccaro syndrome (49,XXXXY).
41. Diseases due to sex chromosome abnormalities. Polysomy X. Polysomy Y
42. Autosomal aneuploidy diseases – Trisomy 21.
43. Autosomal aneuploidy diseases – Trisomy 18. Trisomy 13.
44. Diseases caused by structural chromosomal aberrations. Crie-du-chat syndrome. Wolf-Hirschhorn syndrome.
45. Diseases caused by structural chromosomal aberrations. Rethore syndrome. De Grouchy syndrome, ring chromosome.
46. Contiguous gene syndromes – Prader-Willi syndrome, Angelman syndrome.
47. Genetic disorders of sex development.
48. Contiguous gene syndromes - DiGeorge syndrome, Williams-Beuren syndrome.
49. Multifactorial diseases. Genetic epidemiology. Family, twin, adoption studies. Genetic polymorphisms -RFLP, VNTRs, SSRs, SNPs.
50. Genetic mechanisms underlying the predisposition to heart disease – coronary artery disease, arterial hypertension. Genetic mechanisms in predisposition to gastrointestinal disease. Genetic mechanisms in predisposition to endocrine disease – diabetes type I and type II, MODY diabetes, polycystic ovary syndrome. Genetic mechanisms in predisposition to psychiatric disease – schizophrenia, affective disorders.
51. Cancer genetics. Proto-oncogenes. Tumor-suppressor genes.
52. Familial adenomatous polyposis (FAP).
53. Hereditary nonpolyposis colorectal cancer (HNPCC).
54. Hereditary breast and ovarian cancer. Multiple endocrine neoplasia (MEN1, MEN2).
55. Genetic markers in leukemia – chronic myelogenous leukemia (CML).
56. Dysmorphology and Teratology.
57. Genetic mechanisms in global developmental delay. Genetics of autism spectrum disorder (ASD).
58. Reproductive genetics. Female infertility. Male infertility. Genetics of miscarriages. Genetic testing options for infertility.
59. Preimplantation genetic diagnosis (PGD). Preconception genetic testing.
60. Prenatal diagnosis of monogenic diseases.

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61. Prenatal diagnosis of chromosomal diseases. Noninvasive prenatal test (NIPT).
62. Screening programs. Aneuploidy screening in pregnancy – first and second trimester.
63. Screening programs. Massive and selective newborn screening. Selective metabolic screening in children. Population heterozygote screening programs.
64. Medical genetic counselling. Principles, aims, indications, risk assessment. Challenges in risk assessment.
65. Pharmacogenetics. G6PD deficiency. TPMT.
66. Pharmacogenomics. CYP2D6. CYP2C9.
67. Conventional treatment options for genetic disorders. Orphan drugs.
68. Targeted therapy. Targeted therapy for breast cancer. Targeted therapy for colorectal cancer. Targeted therapy for lung cancer. Targeted therapy for chronic myelogenous leukemia.
69. Gene therapy – principles, capabilities, application. CRISPR gene-editing.

TEXTBOOKS:

1. Genomic medicine, 2016, Sofia, Toncheva, D., Ganev V. ISBN 978-619-183-043-5
2. Medical genetics. Practical course for medical students, Toncheva, D., Hadjidekova S.,2020, Pusblisher: Apco
3. Emery's Elements of Medical genetics,14th ed. ISBN: 978-0702066856
4. Genetics home reference - https://ghr.nlm.nih.gov/

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HEAD OF THE DEPARTMENT OF MEDICAL GENETICS
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