МЕДИЦИНСКИ УНИВЕРСИТЕТ – СОФИЯ
Medical University - Sofia
МЕДИЦИНСКИ ФАКУЛТЕТ
Faculty of Medicine – Dean's Office

MEDICAL GENETICS CURRICULUM

The curriculum has been adopted at the meeting of the Faculty Council № 41/08.07.2020

Annotation of the academic discipline

Medical genetics is one of the fastest growing fields in medicine. The aim of the theoretical and practical training in Medical genetics is for students to acquire an up-to-date knowledge of human hereditary pathology. The course covers the basic principles of human genetic pathology - etiology, pathogenesis, inheritance, modern approaches to diagnostics, prevention and treatment. A major focal point of the lecture and practical course are congenital anomalies and the role of teratogenic factors in their etiology. The course also emphasizes on the problems of pharmacogenetics and pharmacogenomics - genetic determinants of therapeutic response and adverse drug reactions. Students acquire working knowledge of genetic testing's place in personalized and precision therapy of oncological and other common diseases; of current approaches to pharmacotherapy for rare genetic diseases with emphasis on orphan drugs and options and conditions for gene therapy. The course also covers the basic aspects of genetic prevention - medical genetic counseling, prenatal diagnostics, and genetic screening programs.

Lectures

1. Subject, tasks and aspects of Medical genetics. Heredity – structures, composition and organization of DNA. Organization of hereditary information.
2. Mutagenesis. Medicines as mutagens. Types of mutations. Classification of genetic diseases.
3. Birth defects. Genetic and non-geentic causes. Teratogenic effect of drugs.
4. Pharmacogenetic defects (PhGDs).General characteristics. Classification. Monogenic PhGDs.
5. Pharmacogenetic defects. Liver cytochrome P450 monooxygenase polymorphisms. PhGDs in genetic diseases.
6. Genetic regulation of cell proliferation, cell differentiation and apoptosis. Carcinogenesis.
7. Treatment of genetic diseases. Conventional therapy and gene therapy. Current trends.

Seminars

1. Structure of the human genome. Humangenome variability. Genetic methods. Types of ihteritance

1. Chromosomal mutations. Clastogenic effect of drugs
2. Precision medicine and pharmacogenetic defects (PhGDs)
   Pprecision therapy based on *CYP2D6, CYP2C9, CYP2C19,* and *HLA* genetic variants
3. Monogenic diseases and orphan drugs.
4. Oncogenetics and targeted therapy
5. Dysmorphology and teratology

Ongoing assessment

- Oral examination at the beginning of every seminar

- Oral presentations

Syllabus for practical semester exam

1. Building a pedigree
2. Determination of the type of inheritance in monogenic diseases
3. Diagnosis and treatment of beta-thalassemia major and beta-thalassemia minor
4. Diagnosis and treatment of cystic fibrosis
5. Diagnosis, treatment and prevention of PKU
6. Diagnosis and treatment of Duchenne/Becker type muscular dystrophy
7. Diagnosis and treatment of hypercholesterolemia
8. Teratogenic effect of anti-epileptic agents
9. Teratogenic effect of cytostatics (methotrexate)
10. Diagnosis, treatment and prevention of malignant hyperthermia
11. Adverse drug reactions due to polymorphisms in *TPMT*
12. Adverse drug reactions due to polymorphisms in *CYP2C9*
13. Adverse drug reactions due to typical response to polymorphisms in *CYP2D6*
14. Adverse drug reactions due to polymorphisms in *CYP2C19*
15. Adverse drug reactions due to polymorphisms in *HLA*
16. Diagnosis, treatment and prevention of Down Syndrome. Cytogenetic forms.
17. Diagnosis, treatment and prevention of Patau syndrome. Cytogenetic forms.
18. Diagnosis, treatment and prevention of Edwards syndrome
19. Diagnosis and treatment of Turner syndrome and its variants
20. Diagnosis and treatment of Klinefelter syndrome
21. Genetic markers for targeted therapy in breast cancer
22. Genetic markers for targeted therapy at the NSCLC
23. Genetic markers for targeted therapy in CRC
24. Genetic markers for targeted therapy in CML

Syllabus for theoretical semester exam

1. Cellular and molecular basis of inheritance. Organization of the human genome. Nuclear and mitochondrial DNA.
2. Hereditary information. Gene structure and function. Regulation of gene function.
3. Chromosomal organization of the hereditary material. Human karyotype. Chromosomal aberrations.
4. Chromosomal diseases – Down syndrome, Edwards syndrome, Patau syndrome, Klinefelter syndrome, Turner syndrome.
5. Patterns of inheritance. Criteria of autosomal – dominant inheritance. Osteogenesis imperfect. Marfan syndrome. Familial hypercholesterolemia.
6. Patterns of inheritance. Criteria of autosomal – recessive inheritance. Cystic fibrosis. Beta-thalassemia. Phenylketonuria.
7. Patterns of inheritance. Criteria of sex-linked inheritance. Haemophilia A and

B. Muscular dystrophy type Duchenne/Becker.

8. Mutations and mutagenesis. Mutational potential of drugs.
9. Types of gene mutations. Role of mutagensesis in the etiology of human pathology.
10. Methods for genetic analysis.
11. Genetic regulation of the cell cycle.
12. Protooncogenes - normal function and mechanisms of activation.
13. Tumor-suppressor genes - normal function and mechanisms of inactivation and their role in familial cancer.
14. Apoptosis – mechanisms and factors of the programmed cell death.
15. Congenital anomalies and dysmorphic syndromes. Teratogenic factors. Teratogenic potential of

drugs.

16. Pharmacogenetics. Definition. Pharmacogenetic defects. Principal pathogenetic mechanisms of adverse drug reactions.
17. Pharmacogenetic defects. Adverse drug reactions, caused by glucose-6- phospate dehydrogenase deficiency.
18. Pharmacogenetic defects. Adverse drug reactions, caused by atypical butyrilcholinesterase. Malignant hyperthermia.
19. Pharmacogenetic defects. Adverse drug reactions, caused by defects of enzymes, involved in glutathion synthesis, methemoglobinreductase defect, abnormal hemoglobins, catalase deficiency.
20. Polymorphic pharmacogenetic defects. Genetic variations of alcoholdehydrogenase, aldehyddehydrogenase and N-acetyltransferase (NAT2).TPMT.
21. Genetic polymorphism of cytochrome P450 monooxygenases and drug metabolism. CYP2C9, CYP2D6, CYP3A4, CYP2C19.
22. Genetic polymorphismand individual sensitivity to carcinogens and environmental pollutants. Genetic variations in ALDH2, GST, NAT2, NQO1.
23. Conventional therapy for genetic diseases.
24. Gene therapy for monogenic diseases – principles, possibilities, application.
25. Antisense gene therapy and tumor-suppressor gene therapy - principals, possibilities, application.
26. Gene therapy by immune system stimulation - principles, possibilities, application. Gene therapy by inducing drug sensitivity in cancer cells.
27. Orphan drugs in medicine.
28. Target therapy for oncological diseases- principles, possibilities, application.
29. Target therapy for breast cancer.
30. Target therapy for lung cancer.
31. Target therapy for colon cancer
32. Target therapy for chronic myelogenic leukemia.
33. Medical-genetic counseling – organization, goals, indications. Genetic risk and genetic prognosis.
34. Prevention of hereditary diseases – prenatal diagnosis – indications, approaches, methods.
35. Prevention of hereditary diseases – general and selective screening – principles and methods.

Academic literature:

1. Genomic medicine, 2016, Sofia, Toncheva, D., Ganev V. ISBN 978-619-183-043-5
2. Medical genetics workbook for students in pharmacy, Toncheva, D., Hadhidekova S., Simel Pres, 2018, ISBN:978-619-183-065-7
3. Emery's Elements of Medical genetics,14th ed. ISBN: 978-0702066856
4. Genetics home reference - https://ghr.nlm.nih.gov/
5. Gene Reviews®- http://www.ncbi.nlm.nih.gov/books/NBK1116/