Appendix No.3
to Resolution No. 2303
of Senate of Wroclaw Medical University
of 28 April 2021

Syllabus for academic year: 2021/2022 Training cycle: 2018/2019 – 2023/2024			
Description of the course			
Course	Clinical Genetics	Group of detailed education results Group code C	Group name **preclinical**
Faculty	Faculty of Medicine		
Major	medicine		
Level of studies	X uniform magister studies ☐ 1st degree studies ☐ 2nd degree studies ☐ 3rd degree studies ☐ postgraduate studies		
Form of studies	X full-time ☐ part-time		
Year of studies	IV	Semester:	X winter ☐ summer
Type of course	X obligatory ☐ limited choice ☐ free choice / optional		
Language of study	☐ Polish X English		

Number of hours Form of education	Lectures (L)	Seminars (SE)	Auditorium classes (AC)	Major Classes – not clinical (MC)	Clinical Classes (CC)	Laboratory Classes (LC)	Classes in Simulated Conditions (CSC)	Practical Classes with Patient (PCP)	Foreign language Course (FLC)	Physical Education (PE)	Vocational Practice (VP)	Directed Self-Study (DSS)	E-learning (EL)
Winter semester:													
Department of Genetics													
Direct (contact) education[1]				50									
Distance learning[2]	20												
Summer semester:													
Department of Genetics													
Direct (contact) education													
Distance learning													

[1] Education conducted with direct participation of university teachers or other academics
[2] Education with applied methods and techniques for distance learning

TOTAL per year: 70													
Department of Genetics													
Direct (contact) education				50									
Distance learning	20												

Educational objectives (max. 6 items)

C1. Understand molecular mechanism of human inheritance. Be familiar with the aetiology, symptomatology, and management of human genetic disorders, including hereditary and sporadic cancers, as well as personalised therapy in oncology.

C2. Know dysmorphologic nomenclature and understand principles of genetic testing methods, their applications and limitations and interpretation of results.

C3. Assessment of the indications for genetic testing in prenatal and posnatal clinical setting, including oncological management.

C4. Take relevant history, construct pedigrees, perform clinical examination and offer genetic counselling.

C5. Identify the legal, ethical and social implications of genetic testing, including predictive testing, carrier testing and prenatal diagnosis.

C6. Development of social competences needed to practice the medical profession, in accordance with graduate's profile.

Education result for course in relation to verification methods of the intended education result and the type of class:

Number of detailed education result	Student who completes the course knows/is able to	Methods of verification of intended education results	Form of didactic class **enter the abbreviation*
C.W1	the basic concepts of genetics		L, MC
C.W2	the phenomena of gene linkage and interactions		L, MC
C.W3	the proper human karyotype and the different types of sex determination		L, MC
C.W4	the chromosome structure and the molecular basis of mutagenesis		L, MC
C.W5	the principles of inheritance of different numbers of traits, inheritance of quantitative traits, independent inheritance of traits and inheritance of non-nuclear genetic information		L, MC
C.W6	the genetic determinants of human blood groups and serological conflict in the Rh system		L, MC
C.W7	the aberrations of autosomes and heterosomes that cause diseases, including oncogenesis and cancer		L, MC
C.W8	the factors influencing the primary and secondary genetic balance of the population		L, MC
C.W9	the basis for diagnosis of gene and chromosome mutations responsible for inherited and acquired		L, MC

	diseases, including cancer		
C.U1	analyze genetic crosses and pedigrees of human traits and diseases, and assess the risk of a child being born with chromosome aberrations		MC
C.U2	identify indications for performing prenatal tests		MC
C.U3	decide on the need for cytogenetic and molecular tests		MC
C.U4	perform morphometric measurements, analyse the morphogram and record disease karyotypes		MC
C.U5	estimate the risk of an offspring developing a particular disease based on family predisposition and the influence of environmental factors		MC

* L- lecture; SE- seminar; AC- auditorium classes; MC- major classes (non-clinical); CC- clinical classes; LC- laboratory classes; CSC- classes in simulated conditions; PCP- practical classes with patient; FLC- foreign language course; PE- physical education; VP- vocational practice; DSS- directed self-study; EL- E-learning

Student's amount of work (balance of ECTS points):

Student's workload (class participation, activity, preparation, etc.)	Student Workload
1. Number of hours of direct contact:	50
2. Number of hours of distance learning:	20
3. Number of hours of student's own work:	109
4. Number of hours of directed self-study	n/a
Total student's workload	179
ECTS points for course	5

Content of classes: (please enter topic words of specific classes divided into their didactic form and remember how it is translated to intended educational effects)

Lectures

Lectures

1. Introduction to cancer genetics. Theory of carcinogenesis. High, moderate, and low penetrance genes.
2. Chromosome instability syndromes.
3. Genetic basis of breast/ovarian cancer susceptibility syndromes. Diagnosis, management, and genetic counselling.
4. Genetic basis of colorectal cancer susceptibility syndromes. Diagnosis, management, and genetic counselling.
5. Genetic basis of neurofibromatosis (NF1 and NF2). Diagnosis, management, and genetic counselling.
6. Li-Fraumeni syndrome, von Hippel Lindau syndrome and multiple endocrine neoplasia. Diagnosis, management, and genetic counselling.
7. Genetic basis of childhood cancers.
8. Genetics of sporadic cancers. Mutagenesis, carcinogenesis, teratogenesis.
9. Introduction to personalized therapy in oncology.
10. Personalised therapy in the management for breast and ovarian cancer patients. Genetic alterations in tumour cells informing treatment, prognosis, and clinical course of the disease.
11. Personalised therapy in the management for colorectal cancer patients. Genetic alterations in tumour cells informing treatment, prognosis, and clinical course of the disease.
12. Personalised therapy in the management for melanoma patients. Genetic alterations in tumour cells informing treatment, prognosis, and clinical course of the disease.
13. Personalised therapy in the management for lung cancer patients. Genetic alterations in tumour cells informing treatment, prognosis, and clinical course of the disease.

14. Personalised therapy in the management for brain tumour patients. Genetic alterations in tumour cells informing treatment, prognosis, and clinical course of the disease.
15. Ethics and personalised therapy in oncology.

Seminars

Classes

MC1. Organization of classes. Rules for passing the subject. Definition of clinical genetics as a medical specialty and the definition of genetics as a basic science. Cooperation between clinical geneticist and laboratory diagnostician. Principles of genetic counseling. Definition of "rare disorders" and relationship with genetically determined diseases. Examples of genetic conditions in particular medical specialties. Objectives and tasks of genetic counseling. Registry of congenital defects. Genetic counseling: workup for suspected genetic disorders in prenatal and postnatal setting. Indications for referring a patient for genetic counseling. Prenatal screening. Basic methods for prenatal diagnosis. Invasive and non-invasive methods for prenatal diagnostics. The scope of activity of clinical geneticists: dysmorphic syndromes and congenital malformations syndromes, neurogenetics (neuromuscular diseases, genetic ataxias, genetic syndromes with psychomotor developmental delay, hypotonia, intellectual disability, autism spectrum disorders, genetics of epilepsy, chanallopathies, leukodystrophies and other genetic degenerative diseases of the nervous system, genetics of dementia, skin disorders), metabolic and mitochondrial diseases (screening in Poland, aminoacid transformation, organic acidosis, hyperammonemia, urea cycle anomalies, storage diseases, hemochromatosis, Wilson disease), skeletal dysplasia, connective tissue disorders, preconception counseling (including infertility and recurrent miscarriages, preimplantation and prenatal diagnosis), sex differentiation disorders, oncogenetics, childhood syndromes cancer predispositions, somatic mutations and personalized therapy. Elements of clinical evaluation in genetic counseling: family history, pedigree construction and symbols, medical history: prenatal, perinatal, early childhood, additional testing: eg. biochemical, imaging, endoscopic, EMG/ENG/EEG, microbiological, immunological, semen analysis etc.; physical examination: methods of assessing dysmorphic features (subjective and objective - including anthropometric measurements and centile charts), photographic documentation (examples of photos: en face, profile, silhouette, hands, feet), differential diagnosis, databases (OMIM, Genereviews, Face2Gene, LMD), making diagnostic decisions (cytogenetic/molecular - resolution of tests). Genetic counseling: diagnosis (confirmed molecularly/cytogenetically or on the basis of clinical criteria or clinical features), prognosis and natural history of the disorder (lethal or non-lethal, influence on life expectancy, influence on intellectual and physical abilities), legal possibilities for ending/continuing pregnancy/methods prenatal treatment, prevention options (diet, preventive operations, prophylactic imaging and endoscopic examinations, targeted treatment in oncology), causative and symptomatic treatment options, developmental support and rehabilitation, tips for specialist doctors, disease inheritance and risk of reoccurrence in the family, a possible indication for genetic testing of relatives. How to inform the patient and family members about the results of genetic testing. Basic ethical and moral dilemmas of genetic counseling. The principle of non-directiveness of genetic counseling.

MC2. Dysmorphology.

Definitions: dysmorphic trait, nomenclature of dysmorphic traits, malformation, deformation, disruption, dysplasia, syndrome, sequence, association, lethal defect, field defect, neuromuscular disorders, ataxia, hypotonia, leukodystrophy, skin-nervous disorders (phakomatosis), metabolic diseases, mitochondrial diseases, storage diseases, enzyme replacement therapy (ERT), bone dysplasia, connective tissue disorders, preconceptive, preimplantation, prenatal diagnostics, infertility, disorders of sex development (DSD), hereditary predisposition to cancer. Diseases: amniotic band syndrome, caudal regression complex, Pierre Robin sequence, Potter sequence (oligohydramnios), VACTERL association, CHARGE syndrome, FAS, neural tube defects, cleft lip and palate, Poland association. Classical cytogenetics: principles of sampling, transport and storage of material for cytogenetic tests. Cytogenetic analyses. Classical methods of chromosome staining (G, C, R, Ag-NOR). Other tissues, except peripheral blood lymphocytes (fibroblasts, trophoblast cells, amniocytes). Chromosomal polymorphisms, structural aberrations of chromosomes, balanced and unbalanced aberrations. Basics of dysmorphology: dysmorphic features, mechanism and

etiology of developmental malformations, diagnosis of congenital malformations, genetic and environmental causes of congenital malformations. "Facial gestalt" - examples, fetus/child with atypical dysmorphic features. Diagnostic algorithms - examples of when to apply individual techniques of genetic testing. Concepts: disruption, malformation, deformation, dysplasia. Sequences (Potter and Pierre Robin). Syndromes. Field defects. Associations (examples).

MC3. The most frequent autosomal aberrations (trisomy 13, 18, 21).

Concepts: trisomy, partial trisomy, nondisjunction, monosomy, aneuploidy, polyploidy, translocation trisomy, mosaicism, chimerism. Cytogenetic basis, notation, genotype-phenotype correlation, clinical course. Genetic counseling in diseases caused by numerical chromosomal aberrations. Theoretical and empirical risk. Genetic counseling - principles of further diagnostic procedures, assessment of the risk of the disease being repeated in the proband's mother and other family members. Prenatal diagnosis - general rules of management. Mosaicism - examples (Palistister-Kilian syndrome, hypomelanosis of Ito). Polyploid - triploidy (prenatal diagnosis, prognosis, risk of reoccurrence). Prenatal diagnosis of numerical chromosomal abnormalities. Molecular cytogenetics. Fluorescent in situ hybridization. Types of probes. Comparative genomic hybridization. Microarray. MLPA as a molecular technique used in the diagnosis of chromosomal aberrations. QF-PCR in the diagnosis of chromosomal aneuploidy. Types of structural aberrations (deletion, inversion, insertion, isochromosome, duplication, balanced and unbalanced translocations). Microaberration, genome imprinting, DNA methylation. Diagnostic possibilities - cytogenetic analysis, molecular cytogenetics (FISH), molecular tests (methylation test), direct examination of gene mutations.

Disorders: Wolf-Hirschhorn syndrome, Prader-Willi syndrome, Miller-Dieker syndrome, cri-du-chat syndrome, Angelman syndrome, DiGeorge syndrome, William's syndrome, Beckwith-Wiedemann syndrome, Silver-Russell syndrome, Smith-Magenis syndrome. Genetic counseling in disorders caused by structural chromosomal aberrations. Counseling and prenatal diagnosis in the case of structural chromosome disorders.

Genetic counseling in disorders caused by numerical aberrations of sex chromosomes. Disorders caused by chromosome aberrations (Turner syndrome, Klinefelter syndrome). Other aberrations (XX men, XYY, XXX women). Concepts of hypergonadotropic and hypogonadotropic hypogonadism. Short stature - differential diagnosis and diagnostic algorithm.

MC4. Infertility. Preimplantation diagnosis.

The role of post-mortem examinations and material from spontaneous abortions. Male infertility. Semen analysis. Y chromosome deletion map. Cytogenetic studies, *CFTR* mutations, factor II and V (Leiden mutation). Counseling and prenatal diagnosis in the case of sex chromosome aberrations. Molecular genetic diagnosis - possibilities and limitations. PCR and its variants, fragment analysis, QF-PCR, real-time-PCR, PCR-RFLP (restriction enzymes), ASA-PCR, gel and capillary electrophoresis, Southern blotting. Methylation test. Sequencing. Minisequencing (SNaPshot). Next generation sequencing (NGS). Interpretation of molecular results.

MC5. Types of inheritance AD, AR, XR, XD, mitochondrial, multifactorial. Somatic variants and germinal variants. Epigenetic changes. Variants: pathogenic, probably pathogenic, unknown significance, probably benign, benign, polymorphism. Genetic variation in the population and its causes. Population differences - Tay-Sachs disease, sickle cell anemia, phenylketonuria, cystic fibrosis. Concepts: expression, penetration, pleiotropism, somatic and germinal mosaics, homozygoticism, heterozygotism. Meaning of allelic and non-allelic heterogeneity. Genetic counseling - assessment of the risk of disease in another child in the family. Dynamic mutations. The phenomenon of anticipation. Presymptomatic testing. Achondroplasia, Marfan syndrome, osteogenesis imperfecta, neurofibromatosis, familial hypercholesterolemia, Huntington's disease, polycystic kidney syndrome, bone dysplasia (tanatophoric, campomelic). Genetic counseling in autosomal recessive disorders: Inheritance of autosomal recessive traits. Carriers. Founder effect. Genetic counseling - calculating the risk of disease recurrence in the family. Prenatal diagnosis. Diseases: cystic fibrosis, metabolic diseases (phenylketonuria, albinism, alkaptonuria), cystic fibrosis, spinal muscular atrophy, hemochromatosis, Wilson's disease, mucopolysaccharidosis (I, II, III, VI), SLO (Smith, Lemli and Opitz syndrome). Counseling and prenatal diagnosis in the event of suspicion of a monogenic disease in the fetus.

MC6. Molecular testing in cancer.
Genetic instability. Tests: SCE, CA, MN (Fanconi anemia, Bloom syndrome, Nijmegen syndrome, ataxia-teleangiectasia). Tumor studies: chromosomal instability (CIN), MSI microsatellite instability, LOH, methylation/epigenetic instability. Gene studies: *BRCA1, BRCA2, MSH2, MLH1, KRAS, BRAF, HER2, NF1, Rb1, APC, NBN* and others. Genetic basis of tumors (oncogenes, suppressor and mutator genes). Family history, pedigree - sporadic, hereditary and familial cancers. Classification criteria. Indications for genetic tests. Diagnostic possibilities. Interpretation of molecular testing results. Ethical and legal aspects of DNA testing. Cancer prevention and recommendations for patients with cancer and mutation, for patients with but without cancerous mutation, for patients without mutations and for neoplastic changes in families with tumor aggregation. Breast and ovarian cancer. Breast cancer. HNPCC. MEN. Retinoblastoma. Other rare hereditary cancers: ataxia - telangiectasia. Familial adenomatous polyposis - FAP. Li-Fraumeni syndrome. Neurofibromatosis type I (von Recklinghausen disease) and type II. Retinoblastoma, Wilms tumor. Von Hippel-Lindau syndrome. Hereditary stomach cancer. Hereditary pancreatic cancer. Chronic myelogenous leukemia. Sporadic neoplasms. Pedigree and clinical analysis in families with tumor burden.
MC7. X-linked inheritance.
Genetic counseling - assessment of the risk of disease in the next offspring and carrier in women in the family. Prenatal diagnosis. Disorders: hemophilia A and B, fragile X chromosome syndrome, hypophosphatemia, muscular dystrophy of Duchenne and Becker, Rett syndrome, color blindness.
MC8. DSD - disorders of sexual development.
The role of the X and Y chromosome in the process of sex determination. Ambiguous genitalia. The importance of early diagnosis and subsequent stages of the diagnostic procedure and treatment of disorder of sex development. Primary/secondary amenorrhea, lack of secondary sexual characteristics during puberty distribution of fat tissue, hypoplasia of external sex organs, assessment of gonads and structures derived from Muller and Wolff ducts with USG/MRI imaging. Pure gonadal dysgenesis, Turner and Klinefelter syndrome, androgen insensitivity syndrome and 5-alpha reductase deficiency, Kalmann syndrome. Diagnosis of dysfunctions of the reproductive system in the pubertal and post-pubertal period. The course of sex determination and sex differentiation. Role of the *SRY, SOX*, testosterone, estrogen, 5-alpha reductase and AMH. Knowledge of the elements of pituitary-ovarian/adrenal axis - the ability to interpret the results of pituitary, gonadal and adrenal hormone tests. Nondisjunction as the cause of Turner, Klinefelter, 47, XXX and 47, XYY syndromes. Patterns of behavior in disorders of sex determination.
MC9. Teratogenesis. The threshold model for multifactorial inheritance. Types and mechanisms of birth defects. Teratogenesis: infectious agents (rubella, toxoplasmosis, syphilis, cytomegaly, herpes), chemical agents (drugs, alcohol), physical factors (ionizing radiation, temperature). Metabolic disorders in the mother (diabetes, phenylketonuria, androgen excess). Congenital heart defects, cleft lip and palate, mental illness, diabetes, congenital dislocation of the hip joints, clubfoot. Purpose of prenatal diagnosis. Evaluation of the relationship: embryo - patient, fetus - patient. Embryology - when defects of individual systems and organs arise. Time of appearance of symptoms. Prenatal screening tests/diagnostic prenatal tests - difference. Screening tests: ultrasound + biochemical test (first trimester screening test), free fetal DNA, other tests - possibilities and limitations, principles. Diagnostic tests - possibilities, limitations, various methods of material collection for testing (chorionic villi sampling, amniocentesis, cordocentesis), complications. Prenatal testing program - management method, stages, possibilities, limitations. Intrauterine death is at different stages of pregnancy - genetic tests, pathomorphological evaluation, postnatal assessment (babygram and dysmorphological assessment). Descriptions of behavioral patterns (suspicion of chromosomal aberrations, fetal oedema, suspicion of skeletal dysplasia, multiple anomalies - suspicion of the syndrome, numerous non-characteristic defects). Indications for invasive prenatal testing. Prenatal counseling (the principle of non-directiveness). Standards of care in cases of continuation of pregnancy with diagnosed fetal pathology. Termination of pregnancy. In vitro fertilization. Preimplantation diagnosis. Ethical issues in genetics. Practice algorithms: additional tests used in the diagnosis of dysmorphology (X-ray, babygram, MRI, CT, laboratory tests). Methods of securing material and data on congenital defects/dysmorphic features in fetuses, children and adults. Physical development assessment tools: milestones of child development, percentiles, proportions, biological age and its components, Tanner's scale. **MC10. Algorithms of diagnostic procedures.**

Abnormal physical development: lack of weight gain, excessive body mass, microcephaly/macrocephaly, short stature/excessive height, abnormal gait, accelerated/delayed puberty. An algorithm for testing for intellectual disability and autism.
Other --------
Basic literature (list according to importance, no more than 3 items) 1. Medical Genetics, 6th Edition, 2020 – LB Jorde, JC Carrey, MJ Bamshad 2. Essential Medical Genetics, 6th Edition, 2011 – M Connor, M Ferguson-Smith 3. Molecular Diagnosis of Genetic Diseases, 2nd edition, 2010 – R Elles **Additional literature and other materials** (no more than 3 items) 1. Practical Genetic Counselling, 8th edition, 2019 – PS Harper 2. A Practical Guide to Human Cancer Genetics, 4th edition, 2013 – SV Hodgson, WD Foulkes, C Eng, ER Maher 3. Oxford Desk Reference Clinical Genetics, 2nd edition, 2017 – HV Firth, JA Hurst
Preliminary conditions: (minimum requirements to be met by the student before starting the course) Knowledge of the genetic and molecular basis of disorders and inheritance.
Conditions to receive credit for the course: (specify the form and conditions of receiving credit for classes included in the course, admission terms to final theoretical or practical examination, its form and requirements to be met by the student to pass it and criteria for specific grades) Assessment of the learning outcomes may be conducted in contact with an academic teacher or online. Form of receiving credit: written tests, oral responses, short tests/structured questions, problem-based tasks, case-based analysis, MCQs. Conditions for receiving credit: gaining credit for classes, presence in 100% of classes. There is a possibility of making up for the absences if no more than 30% of classes were missed. **Each absence must be made up, including rector's days or dean's hours.**

Grade:	Criteria for courses ending with a grade[3]
Very Good (5.0)	Grade average: 4,6-5,0
Good Above (4.5)	Grade average: 4,3-4,5
Good (4.0)	Grade average: 3,8-4,2
Satisfactory Plus (3.5)	Grade average: 3,2-3,7
Satisfactory (3.0)	Grade average: 3,0-3,2
	Criteria for courses ending with a credit[3]
Credit	---

Grade:	Criteria for exam[3]
Very Good (5.0)	>93% correct answers on the MCQ test
Good Above (4.5)	85-92% correct answers on the MCQ test
Good (4.0)	77-84% correct answers on the MCQ test
Satisfactory Plus (3.5)	69-76% correct answers on the MCQ test
Satisfactory (3.0)	62-68% correct answers on the MCQ test

Department in charge of the course:	**Department of Genetics, Wroclaw Medical University**
Department address:	ul. Marcinkowskiego 1, 50-368 Wrocław

[3] The verification must cover all education results, which are realize in all form of classes within the course

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Person in charge for the course:	Prof. dr hab. Maria Sąsiadek
Telephone:	717841255
E-Mail:	maria.sasiadek@umed.wroc.pl

List of persons conducting specific classes:

Name and surname	Degree/scientific or professional title	Discipline	Performed profession	Form of classes
Maria Sąsiadek	professor	Medical science	clinical geneticist	lecture
Karolina Pesz	PhD	Medical science	clinical geneticist	classes
Stanisław Supplitt	physician	Medical science	resident	classes
Izabela Łaczmańska	associate professor	Medical science	genetic diagnostitian	classes
Paweł Karpiński	PhD	Medical science	genetic diagnostitian	classes
Anna Doraczyńska – Kowalik	physician	Medical science	clinical geneticist	classes
Gabriela Janus-Szymańska	physician	Medical science	clinical geneticist	classes

Date of Syllabus development
29.06.2021
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Syllabus developed by
.....

Signature of Head(s) of teaching unit(s)
.....
Uniwersytet Medyczny we Wrocławiu
KATEDRA I ZAKŁAD GENETYKI
kierownik
prof. dr hab. Maria M. Sąsiadek

Dean's signature
.....
Wroclaw Medical University
Faculty of Medicine
Vice-Dean for Medical Studies
prof. Beata Sobieszczańska, PhD