UNIWERSYTET MEDYCZNY
IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

Appendix 5
to Resolution No. 15630
of Senate of Wroclaw Medical University
of 30 March 2016

Syllabus 2019/2020														
Description of the course														
Module/Course	**CLINICAL GENETICS**										**Group of detailed education results**			
											Group code C	**Group name Preclinical Sciences**		
Faculty	Medicine													
Major	medicine													
Specialties	Not applicable													
Level of studies	Uniform magister studies **X** * 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 / elective													
Course	☐ major **X** basic													
Language of instruction	☐ Polish **X** English ☐ other													
* mark ☐ with an **X**														
Number of hours														
Form of education														
Unit teaching the course	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)	Specialist Classes – magister studies (SCM)	Foreign language Course (FLC)	Physical Education obligatory (PE)	Vocational Practice (VP)	Self-Study (Student's own work)	E-learning (EL)
Winter Semester														
Department of Genetics	**20**			**50**										
Summer Semester														
TOTAL per year: 70														
Department of Genetics	**20**			**50**										

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Educational objectives (max. 6 items)

C1. Understand molecular mechanism of human inheritance. Be familiar with the aetiology, symptomatology and management of human genetic disorders.

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.

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. Make diagnosis of genetic conditions/syndromes and perform genetic counselling.

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

Number of course education result	Number of major education result	Student who completes the module/course knows/is able to	Methods of verification of intended education results (forming and summarising)	Form of didactic class ***enter the abbreviation*
W01	**CW1**	understands basic concepts of genetics	test, oral response, colloquium, written examination	L MC
W02	**CW2**	describes genetic linkage and gene-gene interactions	test, oral response, colloquium, written examination	L MC
W03	**CW3**	describes a normal human karyotype and different types of sex determination	test, oral response, colloquium, written examination	L MC
W04	**CW4**	is familiar with chromosome and molecular basis of mutagenesis	test, oral response, colloquium, written examination	L MC
W05	**CW5**	is familiar with inheritance of a variety of traits, quantitative traits, mendelian inheritance and non-nuclear inheritance	test, oral response, colloquium, written examination	L MC
W06	**CW7**	describes autosome and heterosome aberrations in the context of their pathogenicity including oncogenesis	test, oral response, colloquium, written examination	L MC
W07	**CW8**	is familiar with primary and	test, oral response,	L

		secondary factors influencing genetic equilibrium of the population	colloquium, written examination	MC
W08	**CW9**	is familiar with basic diagnostic methods of chromosome aberrations and gene mutations responsible for hereditary and acquired disorders, including tumours	test, oral response, colloquium, written examination	L MC
U 01	**CU1**	analysis transmission of traits and pedigrees with traits and disorders as well as assesses risk of having offspring affected by chromosomal aberrations	test, oral response, colloquium, written examination	MC
U02	**CU2**	identifies indications for prenatal diagnosis	test, oral response, colloquium, written examination	MC
U03	**CU3**	makes decisions about cytogenetic and molecular testing	test, oral response, colloquium, written examination	MC
U04	**CU4**	makes morphologic measurements, analysis morphograms and describes karyotypes	test, oral response, colloquium, written examination	MC
U05	**CU5**	assesses risk of affected offspring by analysing familial predispositions and environmental factors	test, oral response, colloquium, written examination	MC

** L - lecture; SE - seminar; AC – auditorium classes; MC – major classes (non-clinical); CC – clinical classes; LC – laboratory classes; SCM – specialist classes (magister studies); CSC – classes in simulated conditions; FLC – foreign language course; PCP practical classes with patient; PE – physical education (obligatory); VP – vocational practice; SS – self-study, EL – E-learning .

Please mark on scale 1-5 how the above effects place your classes in the following categories:
communication of knowledge, skills or forming attitudes:
Knowledge: +++
Skills: +++

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

Student's workload (class participation, activity, preparation, etc.)	**Student Workload (h)**
1. Contact hours:	70
2. Student's own work (self-study):	109
Total student's workload	179
ECTS points for module/course	**5,5**
Comments	

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)

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Lectures

1. Introduction to genetic aspects of sporadic, familial and hereditary cancers. Genetic basis of carcinogenesis.
2. Major groups of genes involved in carcinogenesis. High (oncogenes, tumour suppressor and mutator genes), moderate and low penetrance genes.
3. Autosomal dominant cancer susceptibility syndromes. Clinical characteristics, clinical and pedigree criteria for diagnosis, diagnostic methods, genetic counselling. Part I: retinoblastoma, Li-Fraumeni syndrome, Wilms syndrome.
4. Autosomal dominant cancer susceptibility syndromes. Clinical characteristics, clinical and pedigree criteria for diagnosis, diagnostic methods, genetic counselling. Part II: familial adenomatous polyposis, hereditary non-polyposis colorectal cancer.
5. Autosomal dominant cancer susceptibility syndromes. Clinical characteristics, clinical and pedigree criteria for diagnosis, diagnostic methods, genetic counselling. Part III: neurofibromatosis type I and II, hereditary melanoma, MEN1 and MEN2.
6. Autosomal recessive chromosomal instability syndromes.
7. The mechanism of metastasis. Clinical implications.
8. Molecular basis of mutagenesis, carcinogenesis and teratogenesis. Similarities and contrasts.
9. Personalised medicine as a new paradigm of patient management in the XXI century. Part I: significance of personalised medicine in oncology: in diagnosis, prognosis and treatment of breast, ovarian and colorectal cancers.
10. Personalised medicine as a new paradigm of patient management in the XXI century. Part II: significance of personalised medicine in diagnosis, prognosis and treatment of gastric cancer, brain tumours and malignant melanoma.
11. Personalised medicine in cardiology as a new paradigm of patient management in the XXI century.
12. Personalised medicine in endocrinology as a new paradigm of patient management in the XXi century; examples: diabetes and cystic fibrosis treatment.
13. Homeotic genes. Teratogy.
14. Genetic aspects of dementias.
15. Genetic and clinical aspects of mitochondrial disorders.

Seminars

Practical classes - 50 hours

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. 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). 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. 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. 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. 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.

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. The role of the X and Y chromosome in the process of sex determination. DSD - disorders of sexual development. 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. 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. Algorithm of diagnostic procedure in case of 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

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etc. ...

Basic literature (list according to importance, no more than 3 items)

1. Medical Genetics (fourth edition) – LB Jorde, JC Carrey, MJ Bamshad
2. Essential Medical Genetics – M Connor, M Ferguson-Smith
3. Molecular Diagnosis of Genetic Diseases – R Elles

Additional literature and other materials (no more than 3 items)

1. Practical Genetic Counselling – PS Harper
2. A Practical Guide to Human Cancer Genetics – SV Hodgson, WD Foulkes, C Eng, ER Maher
3. Oxford Desk Reference Clinical Genetics – HV Firth, JA Hurst

Didactic resources requirements (e.g. laboratory, multimedia projector, other...)
Multimedia projector, laptops, blackboard or whiteboard, chalk or markers

Preliminary conditions (minimum requirements to be met by the student before starting the module/course)
Knowledge of the genetic and molecular basis of disorders and inheritance.

Conditions to receive credit for the course (specify the form, criteria and conditions of receiving credit for classes included in the module/course, admission terms to final theoretical or practical examination, its form and requirements to be med by the student to pass it and criteria for specific grades).
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 course
Very Good (5.0)	grade from final test or the average of oral exams on individual exercises
Good Plus (4.5)	grade from final test or the average of oral exams on individual exercises
Good (4.0)	grade from final test or the average of oral exams on individual exercises
Satisfactory Plus (3.5)	grade from final test or the average of oral exams on individual exercises
Satisfactory (3.0)	grade from final test or the average of oral exams on individual exercises

Grade:	Criteria for exam (if applicable)
Very Good (5.0)	>93% correct answers on the MCQ test
Good Plus (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

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Name of unit teaching course:	**Department of Genetics, Wroclaw Medical University**
Address	ul. Marcinkowskiego 1, 50-368 Wrocław
Phone	717841256
E-mail	ryszard.slezak@umed.wroc.pl

Person responsible for course:	Prof. dr hab. Maria Sąsiadek
Phone	717841255
E-mail	maria.sasiadek@umed.wroc.pl

List of persons conducting specific classes:	*degree/scientific or professional title*	*Discipline*	*Performer profession*	*Form of classes*
Maria Sąsiadek	professor	clinical genetics	clinical geneticist	lectures
Anna Doraczyńska-Kowalik	instructor	clinical genetics	clinical geneticist	classes
Błażej Misiak	tutor	clinical genetics	psychiatrist	classes
Izabela Łaczmańska	tutor	clinical genetics	clinical geneticist	classes
Paweł Karpiński	tutor	clinical genetics	clinical geneticist	classes
Justyna Gil	tutor	clinical genetics	clinical geneticist	classes
Karolina Pesz	tutor	clinical genetics	clinical geneticist	classes

Date of Syllabus development

11.06.2019

Syllabus developed by

... Dr Ryszard Ślęzak ...

Signature of Head of teaching unit

Uniwersytet Medyczny we Wrocławiu
KATEDRA I ZAKŁAD GENETYKI
kierownik
prof. dr hab. Maria M. Sąsiadek

Signature of Faculty Dean

Wroclaw Medical University
FACULTY OF MEDICINE I
VICE-DEAN FOR STUDIES IN ENGLISH

Prof. Andrzej Hendrich, PhD