COURSE UNIT (MODULE) DESCRIPTION

Course unit (module) title	Code
CLINICAL GENETICS AND BIOINFORMATICS	

Academic staff	Core academic unit(s)
Coordinating: Aušra Matulevičienė, Associate Professor, MD, PhD **Other(s) (clinical genetics):** Eglė Preikšaitienė, Professor, MD, PhD Algirdas Utkus, Professor, MD, PhD Birutė Burnytė, Associate Professor, MD, PhD Natalija Krasovskaja, Lecturer, MD Karolis Baronas, Junior Assistant Deimantė Braždžiūnaitė, Junior Assistant, MD Evelina Vaitėnienė, Junior Assistant, MD **Other(s) (bioinformatics):** Monika Mozerė, Associate Professor, PhD Kamilė Šiaurytė, Junior Assistant, MD	Faculty of Medicine Institute of Biomedical Sciences Department of Human and Medical Genetics

Study cycle	Type of the course unit
Integrated	Compulsory

Mode of delivery	Semester or period when it is delivered	Language of instruction
Lecturers, tutorials and self-study	9th semester	English

Requisites	
Prerequisites: Pre-course: basic knowledge of natural sciences gained during general secondary education. Earlier university level medical modules in basic and human biology, basic and human genetics, medical ethics, and clinical modules, human health, research methodology and biostatistics, and clinical modules. Students are required to demonstrate knowledge of Lithuanian at B1 level or higher for clinical subjects.	**Co-requisites (if relevant):** Not applicable.

Number of ECTS credits allocated	Student's workload (total)	Contact hours	Individual work
5	**133**	**66**	**67**

Purpose of the course unit
Core competencies as described in the Description of Study Program of Medicine. Professional competencies: assessment of genetic factors in human health and pathology, assessment of indications for clinical genetic consultation, annotation and analysis of genetic data.

Learning outcomes of the course unit	Teaching and learning methods	Assessment methods
Basic terminology of human and medical genetics	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to collect family/disease history, draw pedigree, recognize patterns of inheritance, and apply these skills in provision of health care services to patients and families	Lectures, tutorials, consultations	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to assess the impact of genetic factors in human health and pathology (including multifactorial diseases) and indications for genetic counselling	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to use medical literature and web-based resources when assessing genetic influences of genetic factors on health and disease and considering indications for genetic counseling	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Basics of genetic disease diagnostics, including core competencies in the interpretation of genetic tests	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to assess ethical, social and legal aspects, related to genetic information relevant to the individual, family and society, and to apply bioethical and legal requirements, related to collection, storage and provision of genetic information	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to participate in the activities of a multidisciplinary team and to organize and provide multidisciplinary health care (including diagnostics, management and long-term follow-up, social adaptation) for the patients with genetic diseases	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to apply core genetic competencies in daily medical practice, when considering ever increasing knowledge in the field of human and medical genetics and considering indications for genetic counseling	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to recognize clinical signs and symptoms and to assess laboratory and instrumental test results, suggesting possible inborn errors of metabolism	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to recognize the atypical signs of human morphology suggesting diagnosis of syndrome(s), evaluate patient ‘s phenotype according to the Human Malformation Terminology and identify the suspected diagnosis	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to recognize clinical signs and symptoms and to assess laboratory and instrumental test results of selected monogenic disorders and chromosomal aberrations	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to assess indications for prenatal genetic counseling and interpret core prenatal diagnostic test results	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to assess impact of teratogenic factors and to consider indications for genetic counseling	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial
Ability to annotate genetic data using bioinformatics tools and to perform search for information using databases	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial

Ability to perform analysis of basic genetic data	Lectures, tutorials	Individual assessment for participation in the tutorials, a test/quiz during the tutorial

Content	Contact hours							Individual work: time and assignments	
	Lectures	Tutorials	Seminars	Workshops	Laboratory work	Internship	**Contact hours, total**	**Individual work**	**Tasks for individual work**
1. PRENATAL DIAGNOSTICS (PD): Definition, indications for PD, methods. Ultrasound markers of chromosomal anomalies in the 1st and 2nd trimesters. Biochemical markers of chromosomal abnormalities and neural tube defects in the 1st and 2nd trimesters. Invasive procedures: chorionic villus sampling, amniocentesis, cordocentesis. Other methods of PD: fetoscopy, MRI, cell-free fetal DNA in maternal blood. Preimplantation genetic diagnostics. Indications and methods of fetal treatment.	2	-	-	-	-	-	**2**	**3**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for the interim assessment on a specific topic. Interim assessment will be included in the topic 3 assessment.
2. GENETIC COUNSELING: GENEALOGY ANALYSIS (structure, principles). **EVALUATION OF PHENOTYPE.** Evaluation of head, face, ear, periorbital, nose and oral regions, hands and feet. Databases for differential diagnostics in clinical genetics. Autosomal trisomies. Sex chromosomal aberrations. Uniparental disomy and imprinting disorders. Chromosomal instability syndromes Clinical features, diagnostic points and follow-up.	2	5	-	-	-	-	**7**	**7**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for the interim assessment on a specific topic. Topic 1st will be included in the interim assessment of this topic.
3. CLINICAL SYNDROMOLOGY. DYSMORPHOLOGY. Congenital anomalies (CA), types of CA. Syndromes of chromosomal aberrations. Syndromes mostly affecting face; skin and mucosa; bones and connective tissue. Overgrowth and short stature syndromes. RAS'opathies. Clinical features. Diagnostics and follow-up. Inheritance. Differential diagnostics.	2	5	-	-	-	-	**7**	**7**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for

									the interim assessment on a specific topic. Topic 1st will be included in the interim assessment of this topic.
4. INBORN ERRORS OF METABOLISM (IEM). Classification. Clinical expression of IEM. Diagnostics. Newborn screening programs for IEM. Phenylketonuria (PKU). Mucopolysaccharidoses. Clinical features. Diagnostics. Principals of follow-up.	2	5	-	-	-	-	**7**	**7**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for the interim assessment on a specific topic.
5. RARE DISEASES (Neurofibromatosis, I type; Wilson disease. Congenital hypothyroidism. Adrenogenital syndrome. Cystic fibrosis). TERATOGENIC EFFECTS OF ALCOHOL (fetal alcohol spectrum disorders). Etiology of the diseases. Clinical features. Diagnostics and follow-up. Genetic counselling.	2	5	-	-	-	-	**7**	**7**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for the interim assessment on a specific topic.
6. NEUROGENETICS. Etiology, clinical symptoms, diagnostics, treatment, follow-up, genetic counseling.	2	5	-	-			**7**	**7**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for the interim assessment on a specific topic.
7. CYTOGENETIC METHODS. Karyotyping. Fluorescence in situ hybridization (FISH) and SNP comparative genomic hybridization (SNP-CGH) methods. ISCN nomenclature. **MOLECULAR GENOME ANALYSIS METHODS.** Practical application of methods based on genome amplification. Polymerase Chain Reaction. Practical applications of electrophoresis. Application of restriction endonucleases for genetic testing. Capillary electrophoresis. Multiple ligation probe amplification (MLPA). Application of fragment length determination methods to test	2	5	-	-	-	-	**7**	**7**	Preparation for the tutorials. Learning the lecture content uploaded to VLE. Analysis of scientific literature on a specific topic. Preparation for the interim assessment on a specific topic.

dynamic mutations. Sanger sequencing method and interpretation of results. HGVS nomenclature.									
CLINICAL GENETICS	**14**	**30**	**-**	**-**	**-**	**-**	**44**	**45**	
BIOINFORMATICS									
1. INTRODUCTION TO BIOINFORMATICS. Structure of the human genome: coding and non-coding sequences, structure of the gene, functional sequences of non-coding genome, chromatin configuration. Visualization and interpretation of the structure of human genome with different genome browsers, such as UCSC Genome Browser, IGV, GTEx Portal). Understanding different types of genomic variants: point variants (missense, nonsense, frameshift, synonymous), deletions, insertions, structural variants. Visualization and interpretation of different types of genomic variants using different genomic browsers and datasets (*dbSNP, ClinVar, IGV*). Next-generation sequencing (NGS): methodology and application, analysis using UCSC Genome Browser. VCF (Variant Calling Format) interpretation.	2	5	-	-	-	-	**7**	**7**	Listening to online lectures and reading the workbook assigned for this practical session within Virtual Learning Environment (VLE). Analysis of scientific literature using online sources by topic. An overview of the given genetic case study through access to various databases such as Clinical Genomic Database (NIH), *GnomAD, GeneReviews, OMIM, ClinVar, dbSNP, GTEx* Portal. Preparation for a test which will consist of a short assignment based on the material covered that day.
2. ANALYSIS METHODS OF SINGLE-GENE DISORDERS. Short read sequencing vs long-read sequencing, methodology and applications. A specific monogenic disorder case: NGS output filtering, annotation, and analysis using in silico bioinformatics tools such as *wANNOVAR* and *eEnsembl*. Using in silico tools for genetic variant annotation: impact of single amino acid change upon protein structure, the importance of allele frequencies, using SIFT and PolyPhen to predict possible impact of an amino acid substitution on the structure and function of a protein, importance of genetic conservation scores. OMIM (Mendelian Inheritance in Man) database and its importance for rare genetic disease diagnosis. Strategic planning of follow-up laboratory experiments to assess the pathogenicity of variants of uncertain clinical significance.	**-**	5	-	-	-	-	**5**	**5**	Listening to online lectures and reading the workbook assigned for this practical session within Virtual Learning Environment (VLE). Analysis of scientific literature using online sources by topic. An overview of the given genetic case study through access to various

									databases such as Clinical Genomic Database (NIH), *GnomAD, GeneReviews, OMIM, ClinVar, dbSNP, GTEx* Portal. Preparation for a test which will consist of a short assignment based on the material covered that day.
3. MULTIVARIATE GENOTYPE - PHENOTYPE ANALYSIS FOR GENOME - WIDE ASSOCIATION STUDIES (GWAS). Understanding the genetic principles of complex genetic disorders. Applying SNP-chip genotyping and GWAS methodologies for complex genetic disorders. Understanding outputs and interpreting Manhattan plots. Conducting clinical case analysis using UCSC *Genome Browser.* Prioritisation disease-causing variants with in silico tools like *CADD, ClinVar, db*SNP, GTEx.	**-**	5	-	-	-	-	**5**	**5**	Listening to online lectures and reading the workbook assigned for this practical session within Virtual Learning Environment (VLE). Analysis of the given genetic case study through access to scientific literature. Time predominately spent on the usage of UCSC Genome Browser while analyzing genetic case studies. Preparation for the interim assessment on a specific topic.
4. INTEGRATED ANNOTATION, FILTERING AND ANALYSIS OF GENETIC VARIANTS OBTAINED FROM NGS STUDIES. Using databases like *NCBI, Ensembl, UCSC Genome Browser, dbSNP, GTEx Portal (for eQTL), wANOVVAR*, and *ClinVa*r, to analyse distinct genetic cases. The goal is to identify disease-causing variants, applying skills from practical sessions 1-3 for effective interpretation and understanding.	**-**	5	-	-	-	-	**5**	**5**	Online lecture listening and learning under the VLE. Testing of various bioinformatic tools while solving the given genetic case study. Preparation for the interim assessment on a specific topic.
BIOINFORMATICS	**2**	**20**	**-**	**-**	**-**	**-**	**22**	**22**	

CLINICAL GENETICS AND BIOINFORMATICS. Analysis of clinical cases. Attending the consultations and practically evaluating clinical cases. Annotation and analysis of genetic data.									
CLINICAL GENETICS AND BIOINFORMATICS **TOTAL (133 hours)**	**16**	**50**	**0**	**0**	**0**	**0**	**66**	**67**	

Assessment strategy	Weight (%)	Deadline	Assessment criteria
TUTORIALS	100% (10% for each topic)	During each tutorial (1-7 topics of "Clinical genetics" part and 1-4 topics of "Bioinformatics" part)	**ATTENDANCE REQUIREMENTS:** No more than 2 tutorials missed to pass the subject. **COMMENT:** if a tutorial is missed, the student will receive 0 for the missed tutorial. A student is allowed to miss a maximum of 2 tutorials. In such case, the maximum mark a student can receive will be 80%. If more than 2 tutorials are missed, the students will not be allowed to pass the subject. The student can be assessed for a missed tutorial during the next available session with another group, provided the total student number remains suitable for the session based on the judgement of the seminar leader. The assessment must be coordinated and arranged with both the tutorial lecturer and the module coordinator. If student misses a tutorial without medical grounds (i.e. does not provide a valid doctor's note) and wants to make up for the assessment, the maximum mark for a tutorial they can receive is 80% of the available mark for missed topic (i.e. 20% deduction). If the total mark received is lower than the pass mark, the retake assessment will include questions from all tutorial topics. Only one retake attempt is allowed. 10: Excellent. 95-100 % 9: Very good. 85-94 % 8: Good. 75-84% 7: Moderate. 65-74% 6: Satisfactory. 55-64% 5: Poor. 45-54% 4: Unsatisfactory. 40-49% 3: Unsatisfactory. 30-39% 2: Unsatisfactory. 20-29% 1: Unsatisfactory. Less 20% Any requests to change timetabled sessions or attendance of the timetabled sessions must be first requested and approved by the Study Department of the Faculty. **TUTORIAL REQUIREMENTS:** all participating students have to be extensively prepared for the tutorial topic in advance. Have to actively participate in the discussion of clinical situations and cases, know how to analyze the cases and provide arguments for suspected diagnosis, showing their existing clinical knowledge and skills. Work in a team. Answer lecturer's questions in the tutorial. **FINAL ASSESSMENT:** the final assessment which is equated to the exam assessment consists of the sum of the

			evaluations received over the 10 tutorials. Each of the topics represents 10 percent or 1 point. Assessment for the topic takes place at the end of the tutorial of that day. The test on VLE takes up to 15 minutes. The test may consist of open and multiple-choice questions. Each question may be worth a different number of points, based on the difficulty and the required answer length of the question.
FINAL ASSESSMENT - CUMULATIVE ASSESSMENT (at the end of courses)	100% (10% for each topic)	During each tutorial (1-7 topics of "Clinical genetics" part and 1-4 topics of "Bioinformatics" part)	The final assessment which is equated to the exam assessment consists the cumulative assessment over the 10 tutorials. Each of the topics represents 10 percent or 1 point. The final result is rounded to whole mark, i.e. 9.5 is 10 and 9.4 is 9. Assessment for the topic takes place at the end of the tutorial of that day. The test on VLE takes up to 15 minutes. The test according to the day topic may consist of open and multiple-choice questions. Each question may be worth a different number of points, based on the difficulty and the required answer length of the question. Any suspicion of academic misconduct or reliable information about cases of students' dishonesty must be provided by academic staff to Core Academic Unit of the University for assessment on case-by-case basis. The student will not receive a mark and be allowed to pass the subject while the decision from the Core Academic Unit of the University is pending.

Author (-s)	Publishing year	Title	Issue of a periodical or volume of a publication	Publishing house or web link
Required reading				
Allanson JE, Cunniff C, Hoyme HE and ect.	2009	Elements of Morphology (Human Malformation Terminology)	Am J Med Genet A. 2009 Jan; 149A (1).	https://www.ncbi.nlm.nih.gov/pubmed/19125436
J.C. Carey, A.Battaglia, D.Viskochil, S.B.Cassidy, Allanson J.E.	2020	Management of Genetic Syndromes	4th Edition; ISBN-10: 1119432677	Wiley-Blackwell
J. Zschocke, G.F. Hoffmann	2020	Vademecum Metabolicum (Diagnosis and Treatment of Inherited Metabolic Disorders)	5th Edition, ISBN 978-3-13-243551-3	LEGO S.p.A. Vicenza (Italy)
Kenneth Lyons Jones, Marilyn Crandall Jones, Miguel del Campo	2013	Smith‘s Recognizable Patterns of Human Malformations	7th Edition; ISBN 9781455738113	Elsevier Saunders
G. Bradley Schaefer, James N., Thompson, Jr	2014	Medical Genetics: An Integrated Approach		https://accessmedicine.mhmedical.com/book.aspx?bookid=2247
Dario Paladini, Paolo Volpe	2014	Ultrasound of Congenital Fetal Anomalies: Differential Diagnosis and Prognostic Indicators	2nd edition	CRC Press
Ed. A. Milunsky and Jeff. M. Milunsky	2015	Genetic Disorders and the Fetus: Diagnosis, Prevention, and Treatment	ISBN:978-1-118-98152-8	Wiley-Blackwell
Richards S. and et al.	2015	Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology	Genetics in Medicine. 2015, 17(5), p. 405-24. PMID 25741868	

J. Zschocke, G.F.Hoffmann	2016	Vademecum Metabolicum (Diagnosis and Treatment of Inborn Errors of Metabolism), electronic version for iPhone		https://evm.health2media.com/#/start; https://apps.apple.com/nl/app/evm-vademecum-metabolicum/id1123172322
Peter D Turnpenny, Sian Ellard	2017	Emery's elements of medical genetics	15th Edition ISBN-9780702066856	Churchill Livingstone Elsevier, Philadelphia
Helen V. Firth, Jane A. Hurst	2017	Oxford Desk Reference Clinical Genetics and Genomics	2nd edition ISBN 978-0-19-955750-9	Oxford University Press
Recommended reading				
Database: *Orphanet*				www.orpha.net
Database: *GeneReviews*				http://www.ncbi.nlm.nih.gov/books/NBK1116
An Online Catalog of Human Genes and Genetic Disorders (OMIM)				https://www.omim.org/
Elements of Morphology				https://elementsofmorphology.nih.gov/
UCSC *Genome Browser*				https://genome.ucsc.edu/training/
Ensembl Genomes project				https://www.ensembl.org/info/docs/tools/vep/index.html
Phenotype Based Gene Analyzer (*Phenolyzer*)				http://phenolyzer.wglab.org
National Center for Biotechnology Information				https://www.ncbi.nlm.nih.gov
The Database of Genomic Variants				http://dgv.tcag.ca/dgv/app/home
DECIPHER (**D**atabas**E** of genomi**C** var**I**ation and **P**henotype in **H**umans using **E**nsembl **R**esources)				https://www.deciphergenomics.org/
Sequence Variant Nomenclature				https://varnomen.hgvs.org/
				https://cran.r-project.org/
Databases of Faculty of Medicine of Vilnius University				
https://5minuteconsult.com/				
https://accessmedicine.mhmedical.com/index.aspx				
https://hstalks.com/biosci/				
https://www.clinicalkey.com/#!/				
https://www.clinicalkey.com/student/login?target=%2Fstudent				
https://www.amboss.com/int/wb/lt/vilnius/vu/0421?hp=1&utm_source=road&utm_medium=web&utm_campaign=wb-lt_vilnius_vu-0421&utm_2=comm&utm_3=faculty&utm_market=rs&utm_lng=en				