1. COURSE DECRIPTION – GENERAL INFORMATION			
1.1. Course teacher	Associate Professor Gordana Maravić Vlahoviček, PhD Professor Gordan Lauc, PhD	1.6. Year of study	3rd
1.2. Name of the course	**Molecular Biology and Genetic Engineering**	1.7. Credit value (ECTS)	6
1.3. Associate teachers	Professor Jerka Dumić, PhD Associate Professor Sanja Dabelić, PhD Assistant Professor Sandra Šupraha Goreta, PhD Assistant Professor Olga Gornik, PhD Toma Keser, MPharm	1.8. Type of instruction (number of hours L+E+S+e-learning)	30+30+15+0 (e-learning - is not included in standard hours, but is used in teaching)
1.4. Study programme (undergraduate, graduate, integrated)	Integrated study of Medical biochemistry	1.9. Expected enrolment in the course	25
1.5. Status of the course	Compulsory	1.10. Level of use of e-learning (1, 2, 3 level), percentage of instruction in the course on line (20% maximum)	2nd
2. COURSE DESCRIPTION			
2.1. Course objectives	To acquire the basic knowledge on organisation and maintenance of the genome and on control of gene expression; to understand the processes that govern cell cycle and control mechanisms of cell death and renewal; to recognise the scheme of the cell-cell interactions and cell signalling; to relate the irregularities in the genome and basic cell processes to the development of cancer; to acquire the principles and practical applications of the basic methods in molecular biology and genetic engineering.		
2.2. Enrolment requirements and required entry competences for the course	Enrolment requirement: passed exam of the Biological Chemistry course Entry competences: to apply the basic knowledge of cell biology, microbiology, genetics and biochemistry; to describe and understand the basic principles, theories and mechanisms of DNA replication, transcription and translation.		
2.3. Learning outcomes at the level of the study programme to which the course contributes	• Applying fundamental knowledge in biochemistry and molecular biology for the laboratory diagnosis, in defining, analysing and proposing actions related to the research, production and quality assurance and implementation of		

	new laboratory methods for the detection and monitoring of diseases and the effect of therapy. • Assessing the clinical significance of biochemical and molecular biological indicators, detecting variability of laboratory analysis. • Optimizing and performance of laboratory analyses in different areas of health care. • Critical assessment and application of scientific knowledge and available information in order to improve the profession, problem solving, application of new technologies and improving the existing ones.
2.4. Expected learning outcomes at the level of the course (4-10 learning outcomes)	Upon completion of the course and passed exam, the student will be able: 1. To analyse and compare the organisation of the genome in different organisms, to explain the processes of genome maintenance and rearrangements and to describe the means of analysis of entire genomes, proteomes and transcriptomes; 2. To describe the correlation between DNA damage and repair and cell death and renewal; 3. To describe different levels of regulation of gene expression, to identify the purpose and examples of molecular analysis of gene expression, to recognise the ways of gene expression modulation in experimental conditions; 4. To explain the molecular structure of extracellular matrix and ways of cell-cell interactions; 5. To describe the basic principles of cell signalling, with special emphasis on signal transduction, amplification and specificity, to give examples of integration of signalling pathways; 6. To relate the effect of extracellular signals to molecular mechanisms that control and regulate cell division and cell cycle; 7. To explain how cell defects on different levels change the properties of normal cells and lead to development of cancer cells; 8. To exemplify and differentiate the application of genetic analysis and genetic engineering in scientific research, diagnostics and treatment of disease and drug development; 9. To conduct and interpret simple experiments that involve basic methods of molecular biology, including methods of genetic analysis and recombinant DNA methods.
2.5. Course content broken down in detail by weekly class	LECTURES: • Introductory lecture – Molecular biology in development of new drugs: Molecular biology as a foundation of

schedule (syllabus)	biomedical sciences; the importance of molecular biology and genetic engineering for pharmacy. Understanding the processes on molecular level as a prerequisite for disease treatment and diagnostics. HIV and AIDS. Role of viruses in development of cancer. Viroids. Prions. Recombinant proteins as drugs. • Molecular biology methods: Types of DNA analysis; nucleotide sequence analysis and analysis of gene expression. Hybridisation. Southern blot. Northern blot. Polymerase chain reaction (PCR). Multiplex PCR. Real-time PCR. Single strand conformation polymorphism (SSCP). DNA sequencing. DNA microarray technology. • Gene cloning and production of recombinant proteins: Basic principle of cloning. Enzymes for molecular cloning. Restriction endonucleases, polymerases, DNA ligase. Host cells: *Escherichia coli*, yeasts, plant cells, animal cells. Selection markers. Types of vectors. Plasmid vectors. α-complementation. Bacteriophages as vectors. Hybrid vectors. Shuttle vectors. Expression systems. Host cells and expression vectors. Fusion proteins and affinity tags. Factors that influence protein expression. Expression systemT7. • Transgenic plants and animals: Definition of terms: transgene, transgenic organism, genetically modified organism. Production of transgenic plant. Ti plasmid. Plants resistant to insects, herbicides, viruses. Edible vaccines. Golden rice. Advantages and disadvantages of transgenic plants. Production of transgenic animals. Ways of transgene transfer. Integration of transgene into genome. Transgenic animals as disease models. Examples of transgenic animals. • The organisation and sequences of cellular genomes: Whole genome sequencing. Coding and non-coding DNA. Repetitive DNA. SINE, LINE, retrotransposons, pseudogenes. Comparison of genomes between different organisms. • Maintenance and rearrangements of the genomic DNA: Maintenance of genome integrity by DNA repair. Direct reversal of DNA damage. Excision repair. Translesion DNA synthesis. Repair of double strand breaks. Homologous recombination: models and enzymes. DNA rearrangements. Site-specific recombination. Transposition via DNA and RNA intermediates. Gene amplification. Rearrangements of immunoglobulin genes. • Regulation of gene expression (epigenetics and small RNAs): Differential gene expression in different tissues. Nuclear receptors. Eukaryotic promoters and transcription factors. Chromatin modelling. Epigenetics. Small RNAs. • Functional genomics, bioinformatics and system biology: What is bioinformatics? Biological sequences. Biological databases. Primary and secondary databases. Literature databases. Sequence similarity. Multiple sequence alignment. Evolutionary analysis. Structure modelling. Functional genomics: prediction of properties and function of a gene product. Individual variations and genome medicine. • Posttranslational modifications in regulation of cellular processes: Glycosylation. Origins of variations of oligosaccharide structures. Glycosyltransferases. Oligosaccharide structures and blood groups. O-linked and N-linked glycoproteins. Synthesis of oligosaccharide precursor in endoplasmic reticulum. Synthesis of glycoprotein in Golgi apparatus. Control of glycoprotein folding: calnexin and calreticulin. Congenital disorders of glycosylation. Addition of N-acetylglucosamine as a regulatory modification. Lectins and their role in cell-cell interactions: fertilisation, inflammation, interaction with viruses and bacteria. • Cellular membrane, extracellular matrix and cell-cell interactions: Role of cellular membrane in homeostasis. Disorders – cystic fibrosis, hypercholesterolemia. Matrix structural proteins, polysaccharides and matrix adhesion proteins. Cell-matrix interactions. Adhesion junctions, gap junctions, tight junctions and plasmodesmata. Gap junction diseases.

	• Cell signalling: Signal molecules and their receptors. Steroid hormones. NO i CO. Neurotransmitters. Peptide hormones and growth factors. Eicosanoids. Plant hormones. G-protein coupled receptors. Receptor protein-tyrosine kinases. Cytokine receptors and non-receptor protein tyrosine kinases. Receptors coupled with other enzyme activities. Intracellular signalling pathways. Second messengers and protein phosphorylation. cGMP pathway and its role in seeing process. Calcium mobilisation. Transduction of electrical signal into chemical signal. Muscle contraction. Regulation of cell growth and proliferation – Ras, Raf, MAP kinase. Signal pathways in inflammatory response. Signal transduction and cytoskeleton. Signalling in development and differentiation. • Cell cycle: Phases of cell cycle. Cell cycle checkpoints. DNA repair. Cyclins and other regulatory proteins. P53, MPF. Mitosis. Molecular mechanisms of mitosis. Meiosis. • Cell death and cell renewal: Programmed cell death. Caspases. Regulators of apoptosis. Regulation of programmed cell death. Stem cells and the maintenance of adult tissues. Medical application of adult stem cells. Embryonic stem cells, therapeutic cloning, induced pluripotent stem cells. • Cancer: Development and causes of cancer. Types of cancer. Tumour classification. Stages of tumour development. Properties of cancer cells. Transformation of cells in culture. Tumour viruses. Oncogenes and proto-oncogenes. Tumour suppressor genes. Molecular approaches to cancer prevention and treatment. • Gene therapy: Gene therapy in vivo and ex vivo. Methods of therapeutic DNA transfer. DNA-vaccine for malaria. Gene therapy of muscular dystrophy. Liposomes and gene therapy of cystic fibrosis. Viruses as vectors for gene therapy. Examples of retroviral gene therapy. Adenoviral gene therapy. Killer genes. Gene therapy coupled with stem cell therapy. Tissue engineering. SEMINARS: • Introductory seminar: content and procedures of laboratory exercises. • Applications of methods for gene analysis: DNA fingerprint. Identification by amplified fragment length polymorphism (AFLP). CODIS loci. Paternity testing. Identification of homeland war victims. Prenatal diagnostics. DNA labelling. Problems. • Cultivation of microbial and cell cultures: Microbial cultures. Types of media. Growth curve of bacterial cells. Growth in fermenter. Viral hosts. Bacteriophages – lytic and lysogenic cycles. Animal cell culture. Primary culture. Cell lines. Growth conditions and types of growth media. Sterilisation. Problems. • Methods of DNA transfer: Bacterial transformation. Yeast transformation. Animal cell transfection. Electroporation. Problems (generation time, transformation efficiency). • Artificial chromosomes and gene libraries: Artificial chromosomes: PAC, PAC, YAC. Gene libraries: genomic libraries, cDNA libraries, expression libraries. Gene library screening. Chromosome walking. Problems (gene library size). • Mutagenesis and strategies of cloning: Random and site-directed mutagenesis. PCR mutagenesis. Gene inactivation. Linkers and adaptors. Directed cloning. Serial cloning. Reporter genes. Yeast two hybrid system. Analysis of important gene regions. Problems. • Application of genetic engineering in biomedicine and industry: Commercial products made by recombinant microorganisms. Indigo synthesis. Production of biological therapeutics. Protein expression in yeast (*Saccharomyces cerevisiae, Pichia pastoris*). Baculovirus system. Protein expression in mammalian cell culture. Interferon, growth

<table>
<tr><td></td><td colspan="6">hormone, insulin, enzymes, monoclonal antibodies, nucleic acids, vaccines. Problems.
• Overview of the course chapters – additional clarification of certain problems, concepts or terms based on student queries.
EXERCISES:
• Immunochemical determination of hCG in urine (Pregnancy test) - ELISA, dot-blot.
• PCR as a diagnostic method; DNA sequencing
• Isolation of E. coli genomic DNA and restriction enzyme digestion; Ames test
• Cell culture, isolation of genomic DNA from animal cells, apoptosis; Gene cloning into plasmid vector (Part 1)
• Gene cloning into plasmid vector (Part 2); Recombinant protein expression
• Biological databases: database search, scientific literature search, restriction mapping.</td></tr>
<tr><td rowspan="2">2.6. Type of instruction</td><td colspan="2" rowspan="2"><u>lectures</u>
<u>seminars</u> and workshops
<u>exercises</u>
online in entirety
<u>mixed e-learning</u>
field work</td><td colspan="2" rowspan="2">independent study
multimedia and the internet
<u>laboratory</u>
work with the mentor
(other)</td><td>2.7. Comments:</td></tr>
<tr><td>e-learning - is not included in standard hours, but is used in teaching and contains links to different pages, video and audio materials, etc.</td></tr>
<tr><td>2.8. Student responsibilities</td><td colspan="6">Students are required to attend the lectures, seminars and laboratory exercises. The students are required to prepare for laboratory exercises by studying the principles and protocols provided in the educational text (G. Maravić Vlahoviček i sur. – Molekularna biologija s genetičkim inženjerstvom – Praktikum). Upon completion of laboratory exercises students are required to fill in the laboratory work sheets. To achieve the credits and grades, students are required to take and successfully pass the written and oral exam.</td></tr>
<tr><td rowspan="6">2.9. Screening of student's work (specify the proportion of ECTS credits for each activity so that the total number of CTS credits is equal to the credit value of the course)</td><td>Class attendance</td><td>1.5</td><td>Research</td><td></td><td>Practical training</td><td></td></tr>
<tr><td>Experimental work</td><td>1</td><td>Report</td><td></td><td></td><td></td></tr>
<tr><td>Essay</td><td></td><td>Seminar essay</td><td></td><td>(Other--describe)</td><td></td></tr>
<tr><td>Tests</td><td>0.5</td><td>Oral exam</td><td>2</td><td>(Other—describe)</td><td></td></tr>
<tr><td>Written exam</td><td>1</td><td>Project</td><td></td><td>(Other—describe)</td><td></td></tr>
<tr><td colspan="6"></td></tr>
<tr><td>2.10. Grading and evaluation of student work over the course of instruction and at a final exam</td><td colspan="6">Oral exams before the start of laboratory exercises as a prerequisite to enter the laboratory; final exam that consists of a written exam that includes questions with multiple choice answers (passing the written exam is a prerequisite for taking the oral exam, except in the case of the committee examination; 30%) and of oral exam (70%). On the final exam students are required to demonstrate the knowledge of all areas covered by the course program, at the level of skilled information management and synthesis.</td></tr>
<tr><td>2.11. Required literature (available at the library and via other media)</td><td colspan="6">Title
G. Maravić Vlahoviček i sur. – Molekularna biologija s genetičkim inženjerstvom – Praktikum, Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu, Zagreb, 2010., ISBN 978-953-6256-59-4.
Geoffrey M. Cooper, Robert E. Hausman – Stanica: Molekularni pristup, 5. Izdanje; Medicinska naklada, Zagreb, 2010.
Desmond N. T. Nicholl – An introduction to genetic engineering, 3rd edition, Cambridge University Press, 2008.</td></tr>
</table>

	Maravić Vlahoviček, Lauc: Molecular biology and genetic engineering – PowerPoint presentations
2.12. Optional literature	Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff: Molecular Biology of the Cell, 5th edition, Garland Science, 2007. or newer editions James D. Watson, Richard M. Myers, Amy A. Caudy, Jan A. Witkowski: Recombinant DNA: Genes and Genomes - A Short Course, 3rd Edition, W. H. Freeman, 2006. or newer editions Sandy B. Primrose, Richard M. Twyman, Robert W. Old: Principles of gene manipulation, 6th edition, Wiley-Blackwell, 2006. or newer editions
2.13. Methods of monitoring quality that ensure acquisition of exit competences	Outcomes 1-9 are checked by written and oral exam.