SYLLABUS OF BIOLOGY
Dentistry - 1st year
academic year 2020/2021

LECTURES

Autumn semester – Biology I
Cell and Molecular Biology

1. **Introduction to the medical biology** *(I. Slaninová)*
The term medical biology; history of medically important biological discoveries; cell theory; the cell as an essential element of life; principles of structure and function of living systems; exceptions to the cellular concept – archaea; viruses. Model organisms. Application of knowledge and methods of medical biology to clinical medicine.

2. Chemical nature of life – chemical components of cells, protein structure and function *(I. Slaninová)*
Chemical composition of the human body and the cells. Basic molecules of life. Biopolymers. Lipids. Carbohydrates. Proteins. Basic types of chemical bonds. Peptide bond. Protein structure – primary structure; secondary structure; tertiary structure; quaternary structure. Protein functions – structural proteins; enzymes; membrane transporters and other transporter proteins; membrane receptors and signalling proteins. Adhesion proteins and glycoproteins. Examples of diseases related to protein dysfunction. Protein stability, protein degradation, proteasome. Prions.

3. Architecture and function of eukaryotic cell I – structure and function of biomembranes, organelles *(I. Slaninová)*
Eukaryotic cell, comparison with prokaryotic cell. Comparison of animal, plant and fungal cells. Cell membranes – function of membranes; membrane structure and their composition (phospholipids, sterols, membrane proteins, glycoproteins, glycolipids – their properties and functions); membrane fluidity. Membrane proteins – their types (receptors, adhesion proteins, membrane enzymes, surface antigens, membrane transporters) and their functions. Membrane transport – transport without the participation of transport proteins; membrane protein-mediated transport; ion channels; passive transport down the concentration gradient; active transport – against concentration gradient. Aquaporins. Osmosis. Exocytosis and endocytosis.
Organelles and their functions. Endoplasmic reticulum. Golgi apparatus. Lysosomes. Peroxisomes. Mitochondria. Secretory pathway and vesicular transport. Specifics and significance of organelle representation in different cell types. Pathology of organelles. Storage diseases.

4. Architecture and function of eukaryotic cell II – nucleus, cytoskeleton *(I. Slaninová)*
Nucleus and its organisation. Euchromatin and heterochromatin. Nuclear pores. Nuclear transport. Nucleolus. Nuclear receptors. Nuclear lamina. Diseases associated with nuclear pathology - laminopathies.

Cytoskeleton - properties of cytoskeleton, types of cytoskeletal fibres and their composition. Microtubules - polymerization and depolymerization; microtubule function in cell movement (kinocilia); microtubule function in intracellular transport and in chromosome separation. Centrosome. Mitotic spindle. Molecular motors. Mitotic poisons, their effect and use in anticancer therapy. Microfilaments (actin filaments) - polymerization and depolymerization. Microfilament function in cell shape maintaining and cell migration. Microvilli. Amoeboid movement. Phagocytosis. Muscle movement (actin and myosin). Cytokinesis. Deregulated cell migration and tumour metastasis. Intermediate filaments - types of proteins, use in tumour diagnostics; function in maintaining cell cohesion and resistance to mechanical damage. Membrane skeleton.

5. Genome organization - nucleic acids, chromosome structure, DNA replication
(I. Slaninová)
Types of nucleic acids and their functions - DNA, mRNA, rRNA, tRNA, other types of RNA. DNA structure - primary structure; secondary structure; nitrogen bases; principle of base complementarity; DNA double helix. Differences in DNA and RNA structure. Discovery of DNA structure. Watson and Crick. Structure of chromosome. Chromatin. Histones. Nucleosome. Chromosome condensation. Gene. DNA replication - DNA polymerase. Helicase. Primase. Primers. 3' and 5' ends. Leading and lagging strand. Okazaki fragments. Origin of replication. Replication fork. Replication bubble. Differences between the genetic information of prokaryotes and eukaryotes, differences in the mechanism of their DNA replication. Topoisomerases. Telomeres, telomerase. Experiments of Fred Griffith and Oswald Avery. Semiconservative DNA replication and Meselson-Stahl experiment. Nucleosome modifications. Genes and intergenic DNA. Mitochondrial genome. DNA replication as a target of antibiotic and anticancer treatment.

6. Genome stability and instability – DNA damage, mutations, DNA repair and defects in DNA repair *(I. Slaninová)*
Types of DNA damage; types of gene mutations - substitutions, additions, deletions; shift mutations. Somatic and germinal mutations; spontaneous mutations; replication errors; induced mutations - mutagens; principles of action of mutagens on DNA; UV radiation and the formation of thymine dimers; DNA repair mechanisms - base excision repair (BER); nucleotide excision repair (NER); mismatch repair (MR); translesion DNA synthesis; mechanisms for repairing single-stranded and double-stranded breaks in DNA; diseases associated with mutations in DNA repair genes (xeroderma pigmentosum, Fanconi anaemia, cancer). DNA damage sensors (ATM and ATR).

7. Gene expression I - central dogma of molecular biology, gene structure, transcription, genetic code, translation *(I. Slaninová)*
Genetic information - structure of prokaryotic and eukaryotic gene. Protein-coding genes. RNA-coding genes. Gene expression. Introns and exons. Transcription and RNA formation. Coding and template strand of DNA. RNA polymerases. RNA splicing. Polycistronic RNA, operon. Reverse transcription.
Translation - protein synthesis. The mechanism of translation. tRNA and aminoacyl-tRNA synthetase. Ribosome. Codon. Anticodon. Genetic code. Start codon, stop codons. Wobble

base pairing. Synthesis of proteins on free ribosomes and on ribosomes bound to the endoplasmic reticulum. Differences in prokaryotic and eukaryotic translation.

8. Gene expression II – regulation of gene expression, cell differentiation *(I. Slaninová)*
Molecular chaperones. Translation inhibitors as antibiotic therapy. Regulation of gene expression in prokaryotes. Positive and negative control of gene expression (synthesis strategy of adaptive proteins). The operon model and the lactose operon of *E. coli* (Jacob's and Monod's model) as a historical prototype of gene expression regulation. Tryptophan operon. Regulation of gene expression in eukaryotes - its levels and general characteristics. Regulation at the transcriptional level. Transcription factors: classification, types of DNA-binding domains, binding sites, promoters and enhancers. Regulation of the activity of transcription factors. Regulation of expression at the post-transcriptional level (alternative splicing and polyadenylation, non-coding RNA). Regulation at the chromatin level (epigenetic regulation). Cell differentiation and its control. Disorders of gene expression regulation as a cause of diseases (developmental defects, diabetes, cancer). Examples of diseases caused by disorders of transcription and translation. Ubiquitination and protein degradation.

9. Cellular communication - general principles of cell signalling, receptors, signalling pathways *(I. Slaninová)*
General principles of cell signalling. Signal transduction and forms of signals. Receptors; intracellular signalling pathways, molecular switches. Intracellular receptors (e.g. for steroid and thyroid hormones). Nitric oxide and direct activation of intracellular enzyme. Surface (membrane) receptors. Ion-channel-coupled receptors. G-protein-coupled receptors (second messenger, cyclic AMP pathway, phospholipase C pathway, calcium ions and calmodulin). Receptors with enzyme activity (tyrosine kinase receptors - activation and deactivation, adapter proteins, growth factors and MAPK and PI3K signalling pathways). Mutual interactions of signalling pathways (cross-talk). Disorders of cell signalling in human diseases (examples).

10. Cell cycle and principles of its regulation *(I. Slaninová)*
The importance of cell division for the human body; cell cycle phases - G1, S, G2, M; non-dividing cells and G0 phase. Cell cycle checkpoints and their importance. Cell cycle regulation – cyclin-dependent kinases (CDKs). Cyclins. Mitosis promoting factor (MPF). CDK inhibitors. Disorders of cell cycle regulation and associated diseases. The importance of CDK inhibitors in anticancer treatment. Cell cycle regulation - mitogenic signalling (growth factors and other stimuli). Positive cell cycle regulators (proto-oncogenes), negative cell cycle regulators (tumour suppressors) – examples and functions.

11. Cell division – mitosis and meiosis *(I. Slaninová)*
Mitosis and its significance. Phases of mitosis - prophase; prometaphase; metaphase; anaphase; telophase. Mitotic apparatus. Centromeres and kinetochores of chromosomes. Mitosis checkpoint. Mitotic kinase Cdk1, cyclin B, anaphase promoting complex (APC). Mechanism of sister chromatid separation during anaphase. Importance of cohesins, securin and separase. Cytokinesis. Errors in mitosis and their consequences - mitotic nondisjunctions, chromosome mosaics; numerical aberrations of chromosomes in tumour cells.
Meiosis and its significance. Phases of meiosis; pairing and separation of chromosomes during meiosis. Homologous recombination. Crossing-over. Gametogenesis. Differences in

gametogenesis in women and men. Genetic consequences of meiosis. Meiotic errors and their impact on gametes.

12. Cell death *(I. Slaninová)*
Basic types of cell death (programmed cell death, apoptosis, autophagy, necrosis); stages and typical features of apoptosis; regulation of apoptosis; Proteins of BCL2 family; caspase function. The intrinsic pathway of apoptosis and inducing signals. The extrinsic pathway of apoptosis and inducing signals. Death ligands. Death receptors. The role of mitochondria in apoptosis. Physiological significance of apoptosis. Difference between apoptosis and necrosis. *Caenorhabditis elegans* as a model for the study of apoptosis. Disorders of programmed cell death regulation in diseases - cancer, neurodegenerative and autoimmune diseases. Importance and use of pro-apoptotic drugs in the treatment of cancer.

13. Cells and tissue - cell junctions, adhesive molecules and extracellular matrix *(I. Slaninová)*
Principle of tissue arrangement of cells (cytoskeleton and extracellular matrix). Tissue types and their features, structure-function relationship (connection of tissue properties and the content and composition of the extracellular matrix). Connective tissues and extracellular matrix. Organization, structure and production of collagen. Elastins. Molecular connection of extracellular matrix and cytoskeleton (fibronectin, integrins). Proteoglycan aggregate. Epithelia and intercellular junctions. Polarization of epithelia and basement membrane. Types of intercellular junctions (tight, adhesion and gap junctions, desmosomes and hemi-desmosomes) and adhesion molecules involved in these junctions (cadherins, integrins, immunoglobulins, selectins). Transient intercellular interactions. Diseases associated with impaired intercellular interactions and interactions of cells with the extracellular matrix.

Spring semester – Biology II
Genetics, Genomics and Molecular Medicine

14. Introduction to genetics I – role of genetics in medicine, Mendelian Inheritance, autosomal and gonosomal inheritance, chromosome abnormalities *(I. Slaninová)*
Gene - significance and function. Gene locus. Allele. Genotype. Phenotype. Trait. Mendel's laws. Johan Gregor Mendel. Genealogy. Principles of pedigree construction. Relationship between alleles – recessivity, dominance, codominance; intermediate inheritance. Monohybridism. Dihybridism. Interactions of non-allelic genes. Homozygote; heterozygote. Monogenic inheritance. Autosomal inheritance. Gonosomal inheritance – X-linked genes. Y-linked genes. Hemizygote. Baar body – X chromosome condensation in women. Penetration and expressivity. Uniparental isodisomy. Genome imprinting. Chromosomal disorders. Chromosomal aneuploidy (Down syndrome, Edwards syndrome, Patau syndrome, Klinefelter syndrome and Turner syndrome). Structural aberrations of chromosomes. Gene dose.

15. Introduction to genetics II – multifactorial inheritance, genetic linkage, population genetics *(I. Slaninová)*
Multifactorial inheritance. Multifactorial trait determination. Quantitative traits and polygenic inheritance. Heritability. Twin method. Threshold effect model. Examples of multifactorial diseases. Gene linkage. Gene mapping. Association analysis. LOD score. Population genetics. Allele frequency theory (Hardy-Weinberg equilibrium). Natural selection. Mutation-selection balance. Inbreeding. Panmixia (random mating). Factors disturbing the genetic balance of populations - selection, mutations. Random genetic shift (drift). Assortative mating. Migration. Geographical differences in allele distribution. Examples of diseases.

16. Human genome and methods of its study *(I. Slaninová)*
History of the human genome project. Information content of the human genome (genome size, size of genomes of other organisms, number of genes). Human genome architecture (coding and non-coding sequences, repetitive sequences). Encyclopaedia of DNA Elements (ENCODE). Dynamic genome: mobile genetic elements. Regulatory architecture of the human genome (topologically associated domains). Mitochondrial human genome. Genome variability (polymorphisms and gene variants). Methods of human genome studying. Targeted identification of gene variants. PCR-based methods. Capillary sequencing. DNA arrays. Comparative genomic hybridization. Restriction enzymes. Electrophoretic methods. Hybridization methods. DNA amplification (PCR). Methods of mutation identification. Classification of variants. Molecular case studies.

17. Epigenetics - interactions of genes and environment *(S. Uldrijan)*
Epigenetics - basic regulatory mechanisms of gene expression at the cellular level. Mechanism of DNA methylation - methyltransferases. Impact of DNA methylation and histone acetylation on gene expression intensity. Post-translational modifications of histones. Genomic imprinting and silencing of the maternal or paternal allele of a gene. Examples of diseases related to genomic imprinting disorders. Influencing of gene expression by RNA interference. Epigenetic inactivation of the X chromosome in women. Prions.

18. Immunogenetics *(O. Slabý)*
Specific and non-specific immunity. Components of the immune system (lymphatic organs, lymphocytes, T- and B-cells, cellular and humoral response). Immunoglobulins. Origins of antibodies variety. Organization of immunoglobulin loci in the human genome. Rearrangements of immunoglobulin gene segments in differentiation of B-cells. T-cell receptor (TCR). TCR structure and interactions with the major histocompatibility complex (MHC). Genomic organization of the MHC complex. Genetic disorders of the immune system (immunodeficiencies - absence of B-cell (humoral) immunity, absence of T-cell immunity, complete absence of B- and T-cell immunity, autoimmune diseases).

19. Cancer biology I - carcinogenesis, hallmarks of cancer *(I. Slaninová)*
Classification of tumours. Benign and malignant tumours. Primary tumour. Metastasis. Carcinogens. Clonal origin of tumours. Properties of a malignant tumour cell. Tumour genome variability. Signalling pathways and their activation. Typical features of a tumour cell. Growth and inhibition signals. Senescence. Contact inhibition. Telomeres and telomerase. Apoptosis. Hypoxia. Deregulation of energy metabolism. Growth factors. Angiogenesis. Formation of metastases. EMT (epithelial-mesenchymal transition). Tumour as a complex tissue. Tumour stem cell model. Tumour stem cells. Cell clone. Tumours and differentiation; differentiation therapy. Evasion from the immune system. Genetic predisposition to cancer. Familial and hereditary tumours, Li-Fraumeni syndrome, hereditary non-polyposis colorectal cancer, familial adenomatous polyposis, retinoblastoma.

20. Cancer biology II - oncogenes and tumour suppressors, oncogenic viruses *(I. Slaninová)*
Proto-oncogene, oncogene. Tumour suppressor gene. Receptor tyrosine kinases; receptor activation; non-receptor tyrosine kinases. Functions of the Ras protein. Functions of the Ras protein. B-Raf and malignant melanoma. Transcription factors. Amplification of the myc gene. Rb protein; phosphorylation of Rb. Sporadic and familial retinoblastoma; two-hit hypothesis; p53 protein; p53 and cellular stress response. Restriction point; p53-induced cell cycle arrest; p53 and Mdm2; p53 and apoptosis; p53 loss of function mechanisms in the tumour cell, Li-Fraumeni syndrome. Oncogenic retroviruses; Rous sarcoma virus (RSV); oncogenic DNA viruses.

21. Bacterial and viral genomics *(D. Šmajs)*
The term genome, transcriptome and proteome. Overview of modern methods of whole genome sequencing. Phylogenetic relationship of organisms. Mutations, their fixation, mutation rate. Negative, neutral and positive selection. Plasticity of genomes. Reduction of bacterial genomes during adaptation to the host. Genetic diversity of genomes. Mechanisms of genetic recombination. Regulation of alternative genome transcription. Variation of antigens in the proteome. Structure, reproduction and recombination of viruses (DNA viruses, RNA viruses, bacteriophages). Viroids and prions. The spread of viruses in nature. Phylogenesis and basic classification of viruses. Virus replication and pathogenesis. Transduction. Development of viral vectors for gene and tumour therapy. Mechanisms of interferon response to viral infection. Retroviruses. Viruses as a tool for studying cells.

22. Use of knowledge of molecular biology and genetics in medicine *(I. Slaninová)*
Basic principles of pharmacological anticancer treatment (chemotherapy, targeted treatment). Monoclonal antibodies. Recombinant vaccines; recombinant proteins. Kinase inhibitors. Small bioactive molecules. Rational design of inhibitors. Molecular classification of tumours and therapy personalisation. Personalized medicine. Pharmacogenetics, targeted therapy - examples. Precision medicine concept.
Pre-implantation diagnostics and therapy. Animal models (*in vivo*, transgenic organisms - knockin, knockout, animal models of diseases).

23. Gene therapy *(I. Slaninová)*
The term gene therapy. Candidate diseases of gene therapy. Ups and downs in gene therapy history. Types of gene therapy (germ vs. somatic cells, *in vivo* vs. *ex vivo* gene therapy). Basic strategies of gene therapy (gene augmentation, gene silencing, correction of a target gene – editing). Methods of DNA delivery to target tissues. Gene transport systems. Viral vectors (retroviruses, lentiviruses, adenoviruses, adeno-associated viruses, comparisons, advantages and disadvantages). Ideal vector. Gene therapy with suicide genes. Gene surgery. Examples of approved gene therapy products (Glybera, Strimvelis, T-lymphocytes with chimeric antigen receptor).

24. Human microbiome *(D. Šmajs)*
Microbiome; symbiosis of the human body with microorganisms – the number of microorganisms in human body, organs populated by microorganisms; the importance of microbiome composition for human health and metabolism; formation of human microbiome in the first years of life, changes of microbiome during life; microbiome alterations and connection with diseases - bacterial vaginosis, diseases of the digestive system, Crohn's disease, skin diseases; The Human Microbiome Project - whole genome shotgun sequencing (WGS) methods; 16S rRNA sequencing; principles and methods of classification of prokaryotic organisms based on genome and ribosomal RNA; microbial communities

25. Stem cells and tissue engineering *(V. Rotrekl)*
Basic characteristics of stem cells; mechanism of stem cell self-renewal by division; basic stem cells types according to the ability to differentiate - totipotent, pluripotent, multipotent, oligopotent, unipotent stem cells and their properties; stem cell types by source - embryonic, foetal and adult (tissue, organ) stem cells; relationship between normal and tumour stem cells; progenitor cells; symmetric and asymmetric cell division; determination of differentiation directions of stem cells; structure and function of the stem cells "niche"; stem cells and cell therapy; ethics and legislation in stem cell research; perspectives in research and the use of stem cells in therapy; cell dedifferentiation and transdifferentiation - induced pluripotent stem cells (iPS cells); principles and methods of tissue engineering; synthetic and biological cell scaffolds; applications and perspectives of tissue engineering in medicine.

26. Evolutionary Biology *(I. Slaninová)*
Evolutionary biology - what it is and what it is not. The origin of life on Earth. Evolutionary mechanisms (natural selection, sexual selection, mutations, genetic drift, migration). Species and speciation. Evolution of genes. Evolution of the Y chromosome. Human evolution.

Phylogenesis of primates. From apes to humans. The emergence of modern man. Australopithecus. Development of the genus Homo.

COMPULSORY LITERATURE:

- ALBERTS, Bruce, Karen HOPKIN, Alexander JOHNSON, David Owen MORGAN, Martin C. RAFF, Keith ROBERTS a Peter WALTER. ***Essential cell biology***. Fifth edition. New York: W.W Norton, 2019. xxxii, 734. ISBN 9780393680393.

- SNUSTAD, D. Peter a Michael J. SIMMONS. ***Principles of genetics***. Seventh edition. Wiley, 2015. ISBN 9781118875896.

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