

# **SYLLABUS OF MEDICAL BIOLOGY**

## **General medicine - 1st year**

### **academic year 2023/2024**

## **LECTURES**

### ***Cell and Molecular Biology (Autumn semester)***

#### **1. Introduction to the medical biology (*O. Slabý*)**

Milestones in the history of cell and molecular biology and genetics - from cell theory, Darwin and Mendel to the Human Genome Project, preimplantation genetic diagnostics and gene therapy. Medical biology (definition). Application of knowledge and methods of medical biology to clinical medicine = molecular medicine (definitions, examples of applications). Precision medicine concept. Molecular case studies.

#### **2. Fundamental chemistry of life – chemical components of cells, protein structure and function (*O. Slabý*)**

Chemical composition of the cell and the human body. Basic types of chemical bonds in biomolecules. Small chemicals and macromolecules in the human body and their functions (lipids, polysaccharides). Proteins. Protein structure. Primary structure of proteins - amino acids (types) and peptide bond. Secondary ( $\alpha$ - and  $\beta$ -conformation) and tertiary structure of proteins (importance of spatial arrangement for protein functions and for specificity of their interactions). Quaternary structure (protein subunits). Stability of proteins and their degradation. Functions of proteins. Structural, enzymatic and signalling functions. Antibodies and their production and use in medicine. Basic methods of studying proteins.

#### **3. Architecture and function of eukaryotic cell - membrane system and organelles, cytoskeletal system (*O. Slabý*)**

Tree of Life. Prokaryotic cell structure. Archea. General structure of a eukaryotic cell. Differences between prokaryotic and eukaryotic cells. Differences between animal and plant cells. Membrane principle of cell organization. Molecular structure of biomembranes. Chemical components of biomembranes (phospholipids, membrane proteins, glycoproteins, glycolipids - their properties and functions). Arrangement of molecules in biomembranes (asymmetry of biomembranes, fluid-mosaic model). Differences in the composition of biomembranes of different organelles. Cytoplasmic membrane. Cytoplasmic membrane structure. Membrane transport. Endocytosis and exocytosis. Membrane proteins - types and functions (ion channels, receptors, transport proteins, surface antigens - indicators of cell identity). Types of cell organelles, their structure, function and their mutual communication. Nucleus, nuclear membrane and nuclear transport. Rough and smooth endoplasmic reticulum. Synthesis of proteins, lipids and compartmentation of calcium ions. Golgi apparatus. Metabolic functions and secretory pathway. Lysosomes. Peroxisomes. Mitochondria - structure and metabolic function - ATP synthesis. Cytoskeletal principle of cell organization. Properties of the cytoskeleton, types of cytoskeletal fibres and their

composition. Microtubules (molecular motion, molecular motors, dividing spindle). Microfilaments (cell shape and migration, muscle movement, cytokinesis). Intermediate filaments. Examples of diseases associated with functional disorders of particular organelles and components of the cytoskeleton.

#### **4. Genome organization - nucleic acids, chromosome structure, DNA replication (O. Slabý)**

Primary structure of nucleic acids. Nucleotides. Polynucleotide chain structure. Principle of complementarity. Secondary structure (double helix) and tertiary structure of DNA (supercoiled winding). Conformations of DNA molecule (A-, B- and Z-DNA). DNA as a carrier of hereditary information (experiments of Fred Griffith and Oswald Avery). Prokaryotic and eukaryotic genome (properties and differences). Prokaryotic genome. Nucleoid and plasmids. Intracellular transmission of genetic information. Organization of the human genome. The structure of the human chromosome. Histones, nucleosomes and chromatin condensation. Nucleosome modifications. Genes and intergenic DNA. Mitochondrial genome. Semiconservative DNA replication (Meselson-Stahl experiment). Importance of DNA replication for cell division. Replication initiation and replication origins. Asymmetric replication fork. Reason and mechanism of continuous and discontinuous DNA synthesis. Protein apparatus performing DNA replication. Telomeres and telomerase. Comparison of replication in prokaryotes and eukaryotes and the logic of their differences. DNA replication as a target of antibiotic and anticancer treatment.

#### **5. Genome stability and instability – DNA damage, mutations, DNA repair and defects in DNA repair (O. Slabý)**

Types of DNA damage. Spontaneous mutations in DNA - replication errors. Induced mutations in DNA - physical and chemical mutagens. Principles of action of mutagens on DNA. Barriers protecting genome stability. DNA damage sensors (ATM and ATR). Tumour suppressor p53. DNA repair mechanisms. Base mismatch repair and microsatellite instability. Nucleotide excision repair. Base excision repair. Repair of double-stranded DNA breaks. Homologous recombination. Non-homologous ends joining. Chromosomal instability and aneuploidy. Diseases associated with DNA repair disorders (xeroderma pigmentosum, Fanconi anaemia, cancer). DNA repair as a target of anticancer treatment.

#### **6. Gene expression I - central dogma of molecular biology, gene structure, transcription and RNA modification (O. Slabý)**

Central dogma of molecular biology. Structure of prokaryotic and eukaryotic gene. Types of RNA. General principles of transcription - coding and template strand of DNA, speed and error rate of replication. Prokaryotic transcription. Eukaryotic transcription and RNA processing. Types of RNA polymerases. Post-transcriptional modifications of pre-rRNA and pre-tRNA. Posttranscriptional modifications of hnRNA (cap formation, polyadenylation, splicing). Intron structure and splicing mechanism (snRNP, snRNA and spliceosome). Alternative splicing and biological significance of introns. Examples of diseases caused by RNA splicing defects (spinal muscular atrophy, tauopathies, cancer). mRNA nuclear export and mRNA degradation. RNA editing. Reverse transcription.

### **7. Gene expression II - translation, genetic code, post-translational modifications (O. Slabý)**

Genetic code and its deciphering. tRNAs and aminoacyl-tRNA synthetases. Codon-anticodon interactions, wobble base pairing. Ribosome structure. The process of translation (initiation, elongation, termination). Basic comparison of translation in prokaryotes and eukaryotes. Maturation and fate of proteins. Signal sequences of polypeptides. Free ribosomes and bound ribosomes and protein transport. Molecular chaperones. Co- and post-translational modifications of proteins. Protein degradation. Ubiquitin-proteasome pathway. Translation inhibitors as antibiotic therapy. Examples of diseases caused by translational disorders (Diamond-Blackfan anemia, cancer, proteinopathies and protein degradation disorders).

### **8. Regulation of gene expression (O. Slabý)**

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).

### **9. Cellular communication - general principles of cell signalling, receptors, signalling pathways (O. Slabý)**

General principles of cell signalling. Transduction and forms of signals. Receptors and intracellular signalling pathways, molecular switches. Intracellular receptors (e.g. for steroid and thyroid hormones). Nitric oxide and direct activation of intracellular enzyme. Surface 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 (S. Uldrijan)**

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) and cyclins. Mitosis promoting factor (MPF). CDK inhibitors. Disorders of cell cycle regulation and associated diseases. The importance of CDK inhibitors in anti-cancer therapies.

### **11. Cell division – mitosis and meiosis (V. Rotrekl)**

The importance of mitotic division for the human body - formation of two genetically identical cells. Growth and regeneration. The course of the M-phase of mitotic division - prophase, prometaphase, metaphase, anaphase, telophase. Mitotic apparatus (centrosomes and mitotic spindle). Chromosome centromeres and kinetochores. Checkpoint between metaphase and anaphase of mitosis and its significance. Mitotic kinase Cdk1, cyclin B, anaphase promoting complex (APC). Mechanism of sister chromatid separation during anaphase. Importance of cohesins, securin and separase for cohesion and separation of sister chromatids. Ubiquitination of securin. Cytokinesis. Importance of sister chromatid separation for proper distribution of replicated genetic material. Errors in mitosis and their impact - mitotic nondisjunctions, chromosome mosaics. Numerical chromosome aberrations in tumour cells. Importance of meiotic division for the formation of haploid cells - gametes. Individual phases and course of meiosis. Chromatin condensation, pairing and separation of chromosomes during meiosis. Homologous recombination (crossing-over). Errors in meiosis (uneven crossing-over, incorrect chromosome segregation - nondisjunctions) and their impact on gametes. Gametogenesis. Differences in gametogenesis in women and men. Differences in the impact of meiotic errors in women and men.

### **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. Functions of caspases - proteases that cleave structural and functional proteins in the cell and mediate controlled breakdown of the cell. Intrinsic pathway of apoptosis - signals from the internal environment of the cell (DNA damage, disorders of cell cycle regulation, disorders of mitochondria and metabolic stress). Extrinsic pathway of apoptosis - signals from the external environment of the cell (death ligands and death receptors). 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 (O. Slabý)**

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 hemidesmosomes) 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.

## **Genetics, Genomics and Molecular Medicine (spring semester)**

### **14. Introduction to genetics I – genetics in medicine, Mendelian Inheritance, autosomal and gonosomal Inheritance, chromosome abnormalities (O. Slabý)**

Basic genetic terminology. Principle of dominance and recessivity. Mendelian inheritance. Monohybridism. Dihybridism. Interactions of non-allelic genes. Monogenic diseases. Autosomal recessive diseases (phenylketonuria, cystic fibrosis, sickle cell anaemia). Autosomal dominant disease (polycystic kidney disease, Huntington's disease). Gonosomal recessive diseases (haemophilia type A and B, Duchenne muscular dystrophy). Gonosomal dominant diseases (rickets). Intermediate inheritance (dominance and codominance, penetrance and expressivity, uniparental isodisomy, genomic imprinting). Chromosomal disorders. Chromosomal aneuploidy (numerical chromosomal aberrations) – Down syndrome, Edwards syndrome, Patau syndrome, Klinefelter syndrome and Turner syndrome. Structural aberrations of chromosomes.

*Recommended reading:*

*Alberts B., Essential Cell Biology (5th edition, 2019):*

*Chapter 19: Sexual Reproduction and Genetics (p. 664 - 672)*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 3: Mendelism (p. 40–48; 52–57)*

*Chapter 4: Extensions of Mendelism (p. 63–76)*

*Chapter 5: The Chromosomal Basis of Mendelism (p. 89–91; 98–102; 104–105)*

### **15. Introduction to genetics II – multifactorial inheritance, genetic linkage, population genetics (I. Slaninová)**

Multifactorial inheritance. Multifactorial trait determination. Heritability. Twin method. Threshold effect model. Examples of multifactorial inheritance disorders. Gene linkage. Gene mapping. Association analysis. LOD score. Population genetics. Allele frequency theory (Hardy-Weinberg equilibrium). Natural selection. Mutation-selection balance. Inbreeding. Random genetic shift (drift). Assortative mating. Migration. Geographical differences in allele distribution. Clinical case (cystic fibrosis, comparison of population genetics and molecular genetics approach).

*Recommended reading:*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 4: Extensions of Mendelism (p. 76–78)*

*Chapter 7: Linkage, Crossing Over, and Chromosome Mapping (p. 135–138; 141–153)*

*Chapter 16: Applications of Molecular Genetics (cystic fibrosis - p. 445–448)*

*Chapter 22: Inheritance of Complex Traits (p. 607–611)*

*Chapter 23: Population Genetics (p. 634–651)*

### **16. Human genome (O. Slabý)**

History of the human genome project. Information content of the human genome (genome size, size of genomes related to human genome, 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).

*Recommended reading:*

*Alberts B., Essential Cell Biology (5th edition, 2019):*

*Chapter 9: How Genes and Genomes evolve (p. 306 – 315; 320 - 329)*

*Chapter 10: Analyzing the Structure and Function of Genes (p. 346 - 349)*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 15: Genomics (p. 397–431)*

*Chapter 16: Applications of Molecular Genetics (p. 455–461)*

*Chapter 17: Transposable Genetic Elements (p. 477–479; 494–496)*

### **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.

*Recommended reading:*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 19: Regulation of Gene Expression in Eukaryotes (p. 547–552)*

### **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).

*Recommended reading:*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 20: The Genetic Control of Animal Development (p. 675–678)*

### **19. Cancer biology I - carcinogenesis, hallmarks of cancer (O. Slabý)**

Tumour classification (benign and malignant tumours, primary tumour and metastasis).

Tumour as a complex tissue. The process of carcinogenesis (chemical, physical and biological) and malignant transformation. Tumour suppressors and oncogenes. Traits determining tumour formation. Genomic instability. Hereditary and sporadic tumours. Clonal model of tumour development. Sequential model of carcinogenesis (Vogelstein's model).

Tumour-associated inflammation. Hallmarks of malignant tumour (Weinberg's and

Hanahan's model). Self-sufficiency in the production of growth signals, insensitivity to negative regulators of the cell cycle, impaired apoptosis, unlimited replication potential (telomerase activation), neoangiogenesis, formation of metastases, deregulation of energy metabolism, evasion of the immune system.

*Recommended reading:*

*Alberts B., Essential Cell Biology (5th edition, 2019):*

*Chapter 20: Cell Communities: Tissues, Stem Cells and Cancer (p. 718 - 726)*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 21: The Genetic Basis of Cancer (p. 581–603)*

## **20. Cancer biology II - application of cancer biology into cancer diagnostics and therapy (O. Slabý)**

Basic principles of pharmacologic anti-cancer treatment (chemotherapy, targeted therapy). Monoclonal antibodies and small tyrosine kinase inhibitors. Molecular classification of tumours and personalized therapy. Example of lung and colorectal cancer. Precision oncology concept. Cancer genome. Classification of variants in the cancer genome. Cancer genome variability. Molecular Tumour Boards and an example from Paediatric Oncology Clinic. Molecular case studies.

*Recommended reading:*

*Alberts B., Essential Cell Biology (5th edition, 2019):*

*Chapter 20: Cell Communities: Tissues, Stem Cells and Cancer (p. 726 - 732)*

## **21. Gene therapy (O. Slabý)**

What is 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. Viral vectors (retroviruses, lentiviruses, adenoviruses, adeno-associated viruses, comparisons, advantages and disadvantages). Ideal vector. Preparation of medicinal gene therapy products (laboratory, industry). How is gene therapy different from conventional drugs? Examples of approved gene therapy products (Glybera, Strimvelis, T-lymphocytes with chimeric antigen receptor).

*Recommended reading:*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 16: Applications of Molecular Genetics (p.450–455)*

## **22. Bacterial and viral Genomics (D. Šmajš)**

The term genome, transcript 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.

*Recommended reading:*

*Alberts B., Essential Cell Biology (5th edition, 2019):*

*Chapter 9: How Genes and Genomes evolve (p. 315 - 320)*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 8: The Genetics of Bacteria and Their Viruses (p. 163–172)*

*Chapter 24: Evolutionary Genetics (p. 656–672)*

### **23. Human microbiome (D. Šmajš)**

Microbiome. Symbiosis of the human body with microorganisms – the number of microorganisms, and organs populated by microorganisms. Importance of microbiome composition for human health and metabolism. Formation of the human microbiome in the first years of life, changes of the microbiome during life. Disruption of the microbiome and its 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 their genome and ribosomal RNA. Microbial communities.

### **24. Stem cells and tissue engineering (V. Rotrekl)**

Basic characteristics of stem cells. Mechanism of stem cell self-renewal by division. Basic stem cell 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 regulations in stem cell research. Perspectives in research and 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.

*Recommended reading:*

*Alberts B., Essential Cell Biology (5th edition, 2019):*

*Chapter 20: Cell Communities: Tissues, Stem Cells and Cancer (p. 709 - 718)*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 20: The Genetic Control of Animal Development (p. 558; 573–575)*

### **25. Introduction to human ontogeny (pre- and postnatal development) (V. Rotrekl)**

Basic stages of intrauterine development in mammals; basic principles and mechanisms regulating the development in mammals – genetic and non-genetic mechanisms; epigenetic changes in DNA after fertilization and parental genetic imprinting; embryonic genome



activation – degradation of transcripts in the oocyte and activating the expression of embryonic genes; timing and molecular mechanisms of embryonic genome activation; polarization of developing embryos – morphologic and functional differentiation of dividing cells in the early embryo; asymmetric cell division; genes controlling the early polarization of the embryo; establishment of the three embryonic axes; implantation of the embryo; epigenetic inactivation of chromosome X in women; gastrulation and organogenesis; specification of cells, induction and patterning of organs; growth; basic morphogen families – “the great five”; the significance of morphogen gradients for embryonic development; the role of Wnt/ $\beta$ -catenin pathway in development and anterior-posterior polarization of embryos, developmental abnormalities caused by defects of Wnt/ $\beta$ -catenin pathway; the role of Shh (Sonic Hedgehog) morphogen in development of the limb bones and formation of digits; the role of FGF (fibroblast growth factor) in skeletal development; skeletal dysplasias; basic transcription factors regulating the embryonic development.

*Recommended reading:*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 20: The Genetic Control of Animal Development (p. 558–575)*

## **26. Evolutionary Biology (O. Slabý)**

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*.

*Recommended reading:*

*Snustad P., Principles of Genetics (6<sup>th</sup> edition, 2011)*

*Chapter 23: Population Genetics (p. 641–651)*

*Chapter 24: Evolutionary Genetics (p. 672–679)*

### **COMPULSORY LITERATURE:**

- SLABÝ, Ondřej (Editor). **Medical Biology I. Cell and Molecular Biology**. 1st edition. Masaryk University Press, 2023. ISBN 978-80-280-0158-2

### **OPTIONAL 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, 5th edition, 2019.
- SNUSTAD, D. Peter a Michael J. SIMMONS. **Principles of genetics**. Sixth edition. Wiley, 2011.