

# **Human Anatomy & Histology**

General histology and histogenesis: stem cells, differentiation and tissue organization. Classification and general characteristics of the four fundamental tissue types.

General Aspects: Anatomical terminology. Plans and axes of the human body. Parenchymal and hollow organs.

Cardiovascular System: Heart and pericardium. Small and large circulation. Coronary arteries. Generalities on the course of the aorta artery and of the vena cava.

Lymphatic System: Organization. Microscopic anatomy of lymphnodes, tonsils, thymus and spleen. Respiratory System: Overview of nasal cavities and larynx. Microscopic and macroscopic anatomy of trachea, bronchi and lungs.

Digestive System: Overview of the oral cavity and salivary glands. Microscopic and macroscopic anatomy of stomach, small intestine, large intestine, peritoneum, liver and pancreas.

Urinary System: Microscopic and macroscopic anatomy of the kidney, ureters and urinary bladder. Female Genital System: Microscopic and macroscopic anatomy of the ovaries, uterine tubes and uterus.

Male Genital system: Microscopic and macroscopic anatomy of the testis, sperm tract and related glands.

# **Human Physiology**

Transcellular and paracellular exchange processes: Fluid compartments of the body. Ionic composition of the intracellular and extracellular fluids. Selective permeability of the cell membrane. Transport of water and solutes across the cell membrane. Passive transport: simple diffusion and Fick's law; osmosis, facilitated diffusion (uniporters). Primary active transport: ATP-driven pumps. Secondary active transport: symporters; antiporters. Transport of water and solutes across epithelia. Capillary filtration according to the Starling-Landis hypothesis.

Resting membrane potential and action potential: Electrochemical equilibrium and Nernst equation. Membrane potential and Goldman equation. Voltage-dependent channels and excitability in cells of the nervous system, skeletal muscle, smooth muscle and heart. Genesis of the action potential: threshold membrane potential and self-regenerating mechanisms. Ionic conductances in the various phases of the action potential. Cycle of membrane excitability: refractory periods. Propagation of the action potential.

Synaptic transmission: Electrical synapses. Chemical synapses: synthesis, release and inactivation of neurotransmitters. Classification of neurotransmitters. Membrane receptors. Effects of binding of neurotransmitters to ionotropic and metabotropic receptors: excitatory and inhibitory postsynaptic potentials, changes in cellular metabolism and gene expression. Spatial and temporal summation of postsynaptic potentials. Presynaptic inhibition and facilitation. Synaptic transmission at the neuromuscular junction.



Sensory receptors: Classification of sensory receptors. Adequate stimulus and stimulation threshold. Signal transduction: generator potential and action potential propagation in nerve fibers. Encoding the intensity of sensory stimulation. Adaptation in sensory receptors. Receptive field of sensory receptors.

General somatic and special senses receptors: Receptors and afferent fibers of the tactile, kinesthetic, thermal and pain sensibility. Cellular organization of the retina and mechanism of phototransduction. Photopic and scotopic vision. Functional anatomy of the cochlea and vestibular apparatus. Transduction of sound and cochlear tonotopy Auditory thresholds. Responses of vestibular receptors to linear and angular acceleration.

Skeletal, smooth and cardiac muscle: Skeletal muscle: activation of the contractile mechanism; excitation-contraction coupling; innervation of fibers; muscle twitch and tetanic contraction; gradation of contractile force; isometric and isotonic contraction; length-tension relationship. Cardiac muscle: activation of the contractile mechanism; excitation-contraction coupling; length-tension relationship. Smooth muscle: classification; activation of the contractile mechanism; nervous and humoral regulation of contraction.

# **Cellular and Molecular Biology**

The Eukaryotic Cell: Structure and functions of cellular organelles and differences with prokaryotic cells. The Cytoskeleton and Cellular Movement. The Cell Surface and Cell-Cell Interactions. The Nucleus, DNA Replication, and Mitosis. The Cell Cycle and Its Regulation. Apoptosis. The Flow of Genetic Information and the Central Dogma of Biology. Transmembrane Transport Mechanisms. The Endoplasmic Reticulum, the Golgi Apparatus, and Lysosomes. Cell Regulation and Communication. Signals and Their Transduction. Differentiation and Stemness. Reproduction and Meiosis.

Structure, components and properties of nucleic acids. Gene structures. Central dogma. Genetic code. tRNA structure and synthetases. Ribosome. Protein synthesis: stages of translation initiation factors in prokaryotes and eukaryotes, elongation, translocation, termination. Codon-anticodon interactions. Transcription in prokaryotes: The RNA polymerase and transcription. Structure and function of sigma factors. Structure of the promoter. Termination. Antitermination. Bacterial operons and coordinated regulation: lac, trp. Structure and function of the Lac repressor. Operators. Catabolite repression. Antisense RNA. Phage strategies. Phage lambda. Structure of the CI repressor and lysogeny. Comparison of lytic and lysogenic cycles. Transcription in eukaryotes: RNA polymerase, transcription factors and regulatory elements. Replication. DNA polymerase I and III of E. coli. Other DNA polymerases. Repair systems. Recombination. Rec and Ruv systems. DNA topology.

Gene organization. Introns and exons, pseudogenes, gene clusters (globin genes and ribosomal genes). Structure and function of repeated DNA sequences. Transcription. Classes of RNA polymerases. Structure of RNA polymerase II. Promoter organization of class I, II and III. General



transcription factors and their function. TBP structure in the DNA complex. Transcription regulation. Inducible transcription factors. Enhancers. Protein interaction domains with DNA: structure and function. Chromatin. Chromatin structure. Nucleosome: X-ray structure and molecular components. Post-translational modification of histones. Translational and rotational nucleosomal positioning. Chromatin's role in transcription regulation. Transcript maturation. Intron classes. Splicing mechanism. Autosplicing mechanism of group I and II introns. Molecular mechanism of tRNA splicing.

### Biochemistry

The structure, properties, and functional role of the four main classes of biological macromolecules (carbohydrates, lipids, proteins and nucleic acids). Define mechanism, kinetics and regulation of enzyme reactions, and their role in biochemical processes. Describe the thermodynamic basis and mechanisms of cellular bioenergetics.

In brief the main topics are:

- Carbohydrates: Monosaccharides. Cyclic structures. Constitutional, configurational and conformational isomers. The glycosidic bond. Disaccharides and polysaccharides. Glycosaminoglycans.
- Lipids: Saturated, unsaturated and essential fatty acids. Triglycerides. Glycerophospholipids, sphingolipids, glycolipids. Cholesterol. Waxes.
- Aminoacids and proteins: classification, chemical structure and acid-base properties. Peptides and proteins: Structure, classification and properties of protein amino acids. Essential amino acids. The peptide bond. Primary, secondary, tertiary and quaternary structure of proteins. Denaturation and folding. Globular and fibrous proteins. Glycoproteins. Proteoglycans.
- Oxygen binding proteins: myoglobin and hemoglobin
- Enzymes and enzymology: Classification. Effects on reaction rate and thermodinamics. Enzyme kinetics and inhibition. Allosterism.
- Nucleotides and Nucleic Acids: Structure and nomenclature of nucleotides. Phosphodiester Bonds. Three-dimensional structure of DNA (A, B, and Z forms of DNA). RNA structures.
   Denaturation of nucleic acids. Nucleases: types and mechanisms of action. Mutations.
- Genes and Chromosomes: Genes and genome. Introns and Exons. DNA organization, supercoiling and topoisomerases, nucleosomes and histones. Mitochondrial DNA.
- DNA metabolism: DNA replication: rules and their meanings, mechanism of reaction.
  Functional characteristics of DNA polymerases and other enzymes and proteins involved in DNA replication (helicases, ligases); catalytic mechanism of ligases and phases of the replicative process. DNA repair. DNA recombination. Telomeres and telomerases. DNA genetic engineering with CRISPR/Cas9 technology.
- RNA metabolism: RNA polymerases. DNA-dependent synthesis of RNA (transcription). Transcription in prokaryotes and in eukaryotes. Promoters and transcription regulators.



Post-transcriptional modifications: significance and molecular mechanisms of splicing and of 5'-cap and polyA insertion; ribozymes. mRNA degradation. Reverse transcriptase. microRNAs and other non-coding RNAs: biogenesis, function, mechanisms of action and involvement in cancer.

 Protein Synthesis: The genetic code and its natural variations (mtDNA). Structure of ribosomes and peculiarity of tRNA. Protein synthesis: aminoacyl-tRNA synthase reaction; initiation, elongation, termination, folding and post-translational processing. Protein targeting and degradation (ubiquitin, proteases and proteasome). Protein synthesis through DNA recombinant technology.

# **Immunology**

Cell injury; cellular senescence; free radicals; autophagy; programmed and accidental cell death (apoptosis, necrosis, necroptosis, anoikis, pyroptosis, NETosis, entosis, ferroptosis); acute inflammation; systemic inflammation; resolution of inflammation; chronic inflammation; wound healing: regeneration, repair and granulation tissue; radiation; smoking.

# **General Pathology**

Lymphatic organs and immune system cells; innate and specific immunity; antigens; major histocompatibility complex; antigen processing and presentation; humoral and cell-mediated responses; antibodies; complement system; cytokines; immune tolerance.

#### **Human Genetics**

Mendelian inheritance

Mendel: Fundamental Principles of Heredity; experimental and analytical approach to Mendel's experiments.

Transmission of hereditary traits in humans: pedigree analysis; Mendelian segregation patterns (autosomal dominant, autosomal recessive, X-linked inheritance).

Concepts of somatic and germline lineage.

Inheritance linked to the X chromosome, X chromosome inactivation, gene dosage compensation, sex determination.

Extensions of Mendelian genetics

Modifications in dominance relationships (incomplete dominance, codominance); multiple alleles; the ABO blood group system; lethal genes; interaction between genes and environment; penetrance and expressivity, sex-influenced traits; imprinting.



Multiple genes affecting phenotype: gene interaction; epistasis and modified Mendelian ratios; complementation analysis; genetic heterogeneity. Continuous variation and multifactorial inheritance. Explanation of how Mendelian principles can account for continuous variation. Polygenic theory. Multifactorial traits.

Mitochondrial genome

Maternal inheritance; mitochondrial DNA

Recombination, Linkage, and Genetic Mapping

Independent assortment and linked genes; recombination as a result of crossing-over; genetic maps based on recombination frequency; relationship between crossing over and map units; effect of multiple crossovers; mapping functions; difference between genetic maps and physical maps.

Mutations and genetic variability

The molecular nature of alleles. Functional consequences of mutations (loss of function, gain of function). Concepts of haploinsufficiency and dominant negative effect; spontaneous and induced mutations; examples of physical and chemical mutagens and their mechanisms of action. Overview of major DNA repair mechanisms.

Chromosomes and their variability

Variations in chromosome number and structure: overview. Aneuploidies and chromosomal disorders in humans; consequences of chromosome missegregation in meiosis. Genomic structural variants (deletions, duplications, translocations): mechanisms of occurrence and their consequences.

Molecular analysis of genes and genomes

Overview of main genomic analysis techniques; cloning and construction of genomic libraries; physical and genetic genome maps; DNA sequencing (Sanger method); genome sequencing, Human Genome Project. Analysis of genomic variability.

Population genetics

Genetic variability in populations; allele and genotype frequencies. Hardy-Weinberg equilibrium. Evolutionary mechanisms that alter allele and genotype frequencies in populations (mutation, selection, genetic drift, migration, non-random mating, and inbreeding); balance between evolutionary forces.