MATHEMATICS
Mathematical Logic Elements. Set Theory. Applications between sets: graph of an application; composite applications, injective applications, surjective applications, inverse of an application. Real functions of a real variable. Monotony and invertibility. Inverse of exponential functions, local inverses of trigonometric functions. Neighborhoods, accumulation points, limits for functions and their properties. Infinite and infinitesimal functions. Continuous functions and their properties.
Differential calculus for real functions of real variables. Integral calculus for real functions of real variable. Scalar differential equations with separable and linear variables.
Linear algebra (vector spaces, linear systems, and principal techniques for discussion and solution).
Real functions of several real variables.
Elementary geometry of space: planes and lines, their Cartesian and parametric equations, abscissa coordinate on a line; mutual positions between lines and planes, distances between points, lines, and planes; symmetries. Real functions in several real variables: limits, continuity; partial derivatives, differentiability, level curves, gradient and directional derivative.

STATISTICS
Descriptive and inferential statistics. Simple and double distributions. Conditional distributions. Indices of position and variability. Relationships between variables: distributional and mean dependence. Regression line. Elements of Probability Calculus. Some discrete and continuous random variables. Law of large numbers and central limit theorem. Estimators and their properties. Confidence intervals. Test theory: hypothesis system, test statistic, critical region, significance level, test power. Test on the mean. Test on the difference between means. Chi-square test of independence. Inference on proportions. Frequency distributions, graphical analyses, position and variability indices. Relationships between variables: dependence in distribution and on average. Linear regression model. Elements of Probability Calculation. Inferential statistics: estimators and properties, central limit theorem, confidence intervals, test theory (hypothesis system, statistical test, critical region, level of significance). The fundamentals of epidemiology: concepts, definitions. Occurrence measures: incidence rate and prevalence.

GENERAL CHEMISTRY: Atoms, isotopes, ions; atomic and mass numbers. Molecules, compounds. Atomic and molar mass, moles; nomenclature. Balancing chemical reactions. Stoichiometry of reactions: limiting reagent; theoretical and percentage yield. Solution concentrations; Quantum-mechanical model of the atom: quantum numbers, orbitals; electron configurations (exclusion principle and Hund's rule); periodic properties of elements. Chemical bonding: 1) Ionic bond. 2) Covalent bond: Lewis and resonance formulas; VSEPR theory; valence bond and molecular orbital theory. 3) Hydrogen bond. Chemical equilibrium in homogeneous and heterogeneous reactions; equilibrium constant; gas-phase equilibria; solution equilibria; Le Chatelier's principle. Acid-base equilibria: Definitions and types of acids and bases; pH. Hydrolysis reactions; buffer solution; acid-base titrations. Slightly soluble compounds: Solubility product and molar solubility. Effect of common ion, pH, and complex ion formation on solubility.

ORGANIC CHEMISTRY: Functional groups and classes of organic compounds. Reactions in organic chemistry. Electrophiles, nucleophiles, and radicals. Saturated hydrocarbons: alkanes, alkyl groups, structural isomerism, cycloalkanes, cyclohexane, conformational isomerism, geometric cis/trans and E/Z isomerism, oxidation, halogenation. Stereochemistry: isomers, stereoisomers, enantiomers, chiral carbon atoms, polarized light and polarimeter, convention (+)/(-), perspective formulas, Fisher projections, R/S convention, racemic mixtures, diastereoisomers, meso compounds. Unsaturated hydrocarbons: alkenes, reactivity towards electrophiles, geometric cis/trans and E/Z isomerism, carbocations, electrophilic addition, hydrogenation, oxidation; alkynes. Aromatic hydrocarbons: benzene, resonance, aromaticity, reactivity towards electrophiles, aromatic electrophilic substitution, substituent effects. Alkyl halides: reactivity towards nucleophiles, alkyl nucleophilic substitution, ionic elimination. Alcohols: acidity and basicity, reactivity towards nucleophiles, nucleophilic substitutions, dehydration. Phenols: acidity and basicity, antioxidant activity, oxidation. Thiols: acidity, oxidation. Ethers: cleavage. Sulfides: oxidation. Amines: basicity, reactions. Aldehydes and ketones: carbonyl group, reactivity towards nucleophiles, nucleophilic addition, oxidation, reduction, keto-enol tautomerism, aldol condensation. Carboxylic acids and derivatives: acids, esters, amides, acyl halides, anhydrides, nitriles, acyl nucleophilic substitution, reactivity order of derivatives, Claisen condensation. Introduction to heterocycles.
Structure, nomenclature, and properties of the main classes of biomolecules. Classification of carbohydrates and stereochemistry series in monosaccharides. Mutarotation, formation and hydrolysis of glycosides, reduction and oxidation of monosaccharides. Epimerization reaction and aldose/ketose conversion. Vitamin C and natural glycosides. Examples of natural disaccharides (maltose, lactose, sucrose) and polysaccharides (starch, cellulose, chitin, and acidic polysaccharides). Primary structure of proteins. Amino acids: stereochemistry, acid-base equilibria, and formation of the peptide bond. Cleavage of disulfide bonds and peptide bond with chemical and enzymatic methods. Saponifiable lipids (waxes, triglycerides, phospholipids, sphingolipids), structural characteristics, and supramolecular aspects. Hydrolysis reaction and rancidity of oils. Structure and properties of non-saponifiable lipids: cholesterol and steroid compounds, vitamins, and introduction to terpenes and eicosanoids. Structure of nitrogenous bases and sugars in nucleic acids. Nomenclature of nucleosides and nucleotides and

examples of important biochemical intermediates. Representation of oligonucleotides and stability of oligoribonucleotides. Structure of nucleic acids.

BIOCHEMISTRY

Proteins. Structure and general properties of amino acids. Classification of amino acids. Modified amino acids. Peptide bond and polypeptides. Structural hierarchy of proteins. Primary, secondary, tertiary, and quaternary structure of proteins; protein motifs and domains, post-translational modifications; prosthetic groups. Structural domains and structure-function relationship. Denaturation. Protein folding.

Proteins involved in the transport of oxygen and other biologically relevant ligands. Allosterism and mechanisms of cooperative binding. Allosteric effectors.

Enzymatic proteins. Catalysis and enzyme kinetics. Michaelis-Menten model. Meaning and determination of vmax, Km, and kcat. Energetic profile of an enzymatic reaction. Catalytic mechanisms. Regulation of enzyme activity and inhibition mechanisms.

Carbohydrates. (Monosaccharides, disaccharides, and polysaccharides; Glycosidic bond: overview). Glycoproteins, glycolipids, proteoglycans.

Lipids and membranes. Structure and properties of lipids (fatty acids, triacylglycerols, waxes). Membrane lipids (glycerophospholipids, sphingolipids, glycosphingolipids, cholesterol). Fat-soluble vitamins. Membrane structure and properties. Fluidity and asymmetry of membranes. Membrane proteins and their structure. Overview of transport mechanisms.

Cell signaling. Examples of molecular mechanisms of enzymatic catalysis and signal transduction.

Purification of recombinant proteins: overview of principles and basic techniques for the isolation of macromolecules.

Concepts of metabolism: chemical kinetics, enzymes, biological oxidations. Glycolysis; Krebs cycle (Citric acid cycle); Gluconeogenesis and Glycogenolysis; Oxidative Phosphorylation; Lipid Absorption and Catabolism; Lipogenesis and Biosynthesis of Sterols; Amino Acid Metabolism; Nucleic Acid Metabolism; Integration of metabolism in diet and fasting.

PHYSICS

Quantities and physical quantities measures, units of measurement systems, dimensional analysis. Kinematics. Reference systems. Motion of a material point. Vector calculus review. Vector equation of motion, equation of trajectory, and time law. The velocity vector. Velocity representation. The acceleration vector. Acceleration representation. Uniform motion and motion with constant scalar acceleration. Rectilinear and circular motions. Simple harmonic motion. Motion with constant acceleration: free fall. The principles of Dynamics. Forces. Constraint reactions. Static and dynamic friction, elastic forces. Inertial reference systems. Circular motion and centripetal forces. The simple pendulum. Energy and Work of a force. Power. Work of the resultant of a set of forces. Kinetic energy. Kinetic energy theorem. Conservative forces. Potential energy. Calculation of the work of a conservative force. Mechanical energy and its conservation. Non-conservative forces. Statics of a material point. Fluids. Scalar and vector fields. Pascal's and Stevin's laws. Archimedes' principle. Fluids in motion. Bernoulli's theorem. Viscosity. Poiseuille's law and sedimentation. Surface tension. Laplace's law and capillarity. Electrostatics. Electric charge. Coulomb's law. Electric fields. Electric potential. Gauss's theorem. Motion of charges in an electric field. Equipotential surfaces. Conductors and insulators. Conductors in electrostatic equilibrium. Dielectric polarization. Electric capacity. Capacity of an isolated conductor. Capacitors. Capacity of a flat capacitor. Capacitors in series and parallel. Energy density of an electric field. Electric currents and circuits Current intensity. Resistance. Conductors and Ohm's law. Direct voltage generators. Electromotive force and internal resistance. Energy dissipated in a resistor, Joule effect. Resistors in series and parallel. Kirchhoff's rules. RC circuit. Magnetostatics The magnetic field. Gauss's theorem for the magnetic field. Lorentz force. Motion of a charge in a magnetic field. First and second Laplace laws. Mechanical moments of coils in a magnetic field. Sources of the magnetic field. Forces between circuits. Ampère's law. Magnetic fields produced by wires and solenoids. Faraday's law of electromagnetic induction. RL circuits. Energy density of a magnetic field. Maxwell's equations in integral form. Overview of electromagnetic waves. Optics Huygens-Fresnel principle. Interference of waves emitted by 2 sources and by N sources. Diffraction from a slit. Diffraction grating. Polarization. Reflection. Refraction. Dispersion.

CELL BIOLOGY

Main characteristics of Prokaryotes and Eukaryotes. Cell dimensions and observation methods; separation of cells, organelles, and macromolecules. Main characteristics of biological macromolecules useful for understanding cellular organization and functioning.

Biological membranes: chemical composition, ultrastructure, molecular organization. Permeability and membrane transport.

Cell integration in tissues through cell-cell and cell-matrix adhesions (junctions and adhesion molecules, extracellular matrix). Specializations of the cell surface: microvilli, cilia, and flagella.

Cytoskeletal systems (microtubules, microfilaments, and intermediate filaments, motor proteins); interaction between actin and myosin in skeletal muscle cells and non-muscle cells.

The system of internal cellular membranes: structure and functions of the endoplasmic reticulum, Golgi apparatus, and lysosomes. Signal sequence and post-translational modifications of proteins; native conformation and chaperone proteins. Vesicular transport (mechanisms of vesicle formation: types of coating and targeting signals). Autophagy and turnover of cellular organelles. Exocytosis: constitutive and regulated secretion. Endocytosis and endosomal compartment.
Mitochondria and chloroplasts: origin, organization, and functions.
Nucleus: nuclear envelope, nuclear pore complex, chromatin organization, nucleo-cytoplasmic transport. Nucleolus: morphology and function.
The cell cycle: main activities of the cell in the various phases (G1-S-G2, M). Cell division: mitosis and cytokinesis; meiosis and gamete formation. Regulation of the cell cycle: the role of cyclins and activation of cyclin-dependent kinases; cell cycle checkpoints. Cell proliferation, internal and external signals. Stem cells.
Apoptosis: morphological and biochemical aspects; apoptosis control mechanisms; activation of initiator and effector caspases.
Cell-cell communication. Main signaling pathways and signal transduction mechanisms.

PHYSIOLOGY AND ANATOMY
Histology. Epithelial Tissue: Morphological, structural, and ultrastructural description; classification; function; and location of epithelia a) lining, b) exocrine and endocrine glands, c) sensory, d) highly specialized epithelia.
Connective Tissue: a) Proper connective tissues: loose fibrillar, reticular, elastic, dense connective, unilocular and multilocular adipose; b) Cartilaginous tissue; c) Non-lamellar and lamellar bone tissue, compact and cancellous bone tissue. Direct and indirect ossification; d) Blood: plasma and formed elements.
Muscle Tissue: Morphological organization and classification (smooth muscle tissue, skeletal striated muscle tissue, and cardiac muscle tissue), structure of myofibrils.
Nervous Tissue: Morphology of neurons and their classification. Glial cells. Nerve structure. Synapses. Anatomical and functional organization of the CNS and PNS.
Human Anatomy. General principles of human body organization. Systems and organs. Subdivision of the human body; external examination and internal examination. Musculoskeletal system, circulatory and blood system, digestive system, respiratory system, urinary system, endocrine system (Pituitary gland, Thyroid gland, Parathyroid glands, Adrenal glands), reproductive system (male and female).
Anatomy of Laboratory Animals. Comparative aspects of the anatomical characteristics of the most commonly used species in biotechnological research, with particular attention to the digestive, respiratory, urinary, male and female reproductive, endocrine, and integumentary systems.
Physiology. Cell-Environment Interactions: General premises, transmembrane transports, chemical signal transduction. Excitability: Ionic flows and transmembrane potentials, action potential, ion channels.
Cell-to-Cell Communication: Action potential spikes in neurons and nerve fibers, conversion of environmental stimuli into electrical signals, synaptic transmission, chemical communication between cells.
Nervous System: Anatomical organization, motor system, sensory system, autonomic system, and higher nervous functions.
Endocrine System: Hormones and major glands, sex hormones.
Muscular System: Motor proteins, skeletal muscle, biomechanics of muscle fibers, smooth muscle, cardiac muscle.
Cardiovascular System: Cardiac electrophysiology, cardiac mechanics, heart regulation, circulation.
Respiratory System: Anatomical description, respiratory mechanics and ventilation, alveolar exchange, gas transport in blood, nervous and chemical control of respiratory activity, acid-base balance and respiratory function.
Urinary System: Water-electrolyte homeostasis, anatomical organization, renal physiology (filtration, reabsorption, secretion), acid-base balance, and renal function.

PATHOLOGY
Definition of etiology and pathogenesis. Types of damage. Cellular response to non-lethal damage.
Adaptive cellular responses: hypoxia, ischemia, preconditioning; hyperplasia, hypertrophy, atrophy, metaplasia. Main histopathological aspects.
Irreversible damage: necrosis, apoptosis or programmed cell death. Damage from ischemia and reperfusion.
Organism defenses against pathogens and non-pathogens. The inflammasome. Pyroptosis. Chemotaxis. Phagocytosis. Acute inflammation. Chemical mediators of inflammation. Chronic inflammation. Main histopathological aspects.
Regenerative and reparative processes. Scarring and fibrosis. Dysfunction of reparative processes: liver cirrhosis.
Neoplastic proliferation. General aspects of classification and epidemiology of neoplasms. Local and systemic effects of neoplasms. Molecular basis of tumors. Oncogenes and tumor suppressor genes. Physical, chemical, viral, and hormonal carcinogenesis.
Physiology and pathology of hemostasis. Endothelial dysfunction. Role of vascular endothelium, platelets, and coagulation factors in hemostasis. Bleeding disorders. Thrombosis and thrombophilic states. Atheroma. Risk factors for atherosclerosis.
Pathophysiology of the hematopoietic system (anemia, hemoglobinopathies, disorders of heme and hemoglobin synthesis)
General pathophysiology of the heart: heart failure
Pathophysiology of the endocrine system: hypo- and hypersecretion of hormones; hormonal resistance.

MICROBIOLOGY

Overview of bacteria, Archaea, viruses, and subviral agents. Structure and function of prokaryotic cell components. Growth, nutritional requirements, cultivation, isolation, identification/characterization of microorganisms. Bacterial metabolism. Cell division/differentiation in prokaryotes. Microbial genetics/plasticity of the bacterial genome. Antimicrobial agents: control of microbial growth using chemical and physical agents. Mechanisms of action of antibiotics and antimetabolites. Overview of resistance mechanisms. Interaction between microorganisms, microbe-host, and microbial ecology: quorum sensing, biofilm, elements of pathogenesis/virulence. General characteristics of Archaea and biotechnological applications. Overview of fungi with a focus on yeasts and molds and their applications in biotechnology. Introduction to parasitology. Overview of viruses that infect eukaryotic cells: classification, general characteristics, and replicative strategies. Interactions between virus and host cell. Isolation and cultivation of viruses. Antiviral drugs and mechanisms of resistance. Bacteriophages: general characteristics and mechanisms of bacterial resistance to infection (restriction enzymes, CRISPR-Cas9 mechanisms).

GENETICS

Different branches of genetics: formal, molecular, genomic, population genetics. Basic and applied genetic research.

Structure and function of genetic material: Identification of DNA as genetic material. Basic components of nucleic acids, comparison between DNA and RNA. DNA structure: the Watson-Crick model. RNA genomes. Genome organization in phages, Prokaryotes, and Eukaryotes.

DNA replication: replication models; enzymology of replication in E. coli; replication in E. coli and Eukaryotes.

Gene structure variations; gene mutations; adaptation versus selection. Definition of mutation; spontaneous and induced mutations; types of spontaneous mutations and consequences: tautomerism, base loss, in/del; consequences of different mutation types in a protein-coding sequence; mutagenic agents (radiation; direct and indirect chemical agents). Mutants in genetic studies: visible mutants; conditional mutants; nutritional mutants; resistance mutants. Chromosomal alterations: types and consequences.

Formal genetics: Mendelian inheritance: genotype-environment relationship in phenotype determination. Transmission of autosomal and sex-linked traits. Mendelian inheritance in humans: pedigree analysis. Extension of Mendelian genetic analysis: multiple alleles, lethal alleles, gene interactions. Molecular basis of dominance and recessiveness. Penetrance and expressivity. Semidominant diseases and digenic inheritance.Complementation and allelism test for new mutations; examples of complementation tests.

Genetic recombination: gene linkage and crossing-over. Genetic mapping in Eukaryotes: two and three-marker crosses. Coefficients of coincidence and interference. Map function. Advanced genetic mapping in Eukaryotes: yeast and human analysis. Mutation research techniques. Study of small mutations: Sanger and Next Generation Sequencing techniques Study of deletions/duplications. Non-Mendelian Diseases:

Mitochondrial genetics: Maternal inheritance, heteroplasmy, threshold effect, random drift. Nuclear genes controlling the biogenesis of the respiratory chain. Triplet expansion diseases: anticipation phenomenon, molecular basis of main forms (Fragile X, Huntington's disease, Myotonic Dystrophy).

Genomic imprinting diseases. Uniparental disomy and its implications. Molecular basis of Prader-Willi Syndrome and Angelman Syndrome.

Chromosomal Abnormalities: Classification of chromosomal abnormalities. Chromosomal examination, FISH, Array-CGH. Molecular basis of chromosomal rearrangements.

Functional genomics. Model organisms in biomedicine. Mouse as a model organism.

Functional genomics through transgenesis in mice: principles and applications

Mouse characteristics (genome, life cycle, embryonic development, strains). Mouse transgenesis: use and applications of DNA microinjection into oocytes. Mouse mutagenesis: targeted or random mutagenesis.

ES cells

Early embryonic development of mice. Characteristics of the blastocyst. Cell lineages and derivation of ES cells: programmed differentiation of ES cells in vitro; embryoid bodies. Applications.

Gene targeting

Applications of gene targeting. Targeted mutagenesis through homologous recombination in ES cells. Types of constructs. Production of knockout mice from ES cells. Preparation of constructs, selectable markers, positive-negative selection. Phenotype interpretation: dependence on genetic background; "absence of phenotype," genetic redundancy, and compensatory mechanisms; lethal phenotypes. Site-specific recombination: the Cre/lox system. Conditional gene targeting: tissue-specific and inducible knockout. Knock-in and introduction of fine mutations. Chromosomal engineering.

MOLECULAR BIOLOGY

Biological Macromolecules: Chemical bonds and properties of macromolecules, Interactions between macromolecules. Basic principles for the isolation and characterization of biological macromolecules. DNA structure: DNA structures; alternative local conformations, unpaired structures, curvature; DNA topology and DNA topoisomerase. RNA structure: tRNA, ribosomal RNA, molecular mimicry. DNA repair: Types of lesions; repair pathways and mechanisms. DNA Recombination: Homologous recombination in prokaryotes; non-homologous recombination; site-specific recombination (lambda phage). Transcription In Prokaryotes: RNA polymerase;

subunits; inhibitors, mutants; closed and open complex; the promoter, conserved sequences; sigma factors. Operons, paradigmatic examples; lac, tryptophan, arabinose. Genetic regulation of lambda phage. Transcription in Eukaryotes: RNA polymerase I, II, and III. Common and distinctive features, activities, inhibitors; promoters, consensus sequences; enhancers, UAS sequences. Basic transcription factors, general and specific; main structural motifs for DNA binding, activation, multimerization. RNA maturation in Eukaryotes: Introns; splicing mechanisms; autosplicing; catalytic RNA, evolutionary implications; RNA-protein enzymes; small nuclear RNAs. Translation: Ribosomes: rRNA and tRNA; ribosomal proteins. Protein synthesis; initiation and elongation factors. Rho-dependent and independent termination; antitermination; PolyA and termination in eukaryotes. Chromatin Structure and Function, Epigenetics: Histones; nucleosomes, structural properties; topology; active chromatin, DNase hypersensitive sites; chromatin organization and gene expression; regulatory nucleosomes. Higher-order structures, nuclear matrix. Transcriptional and Post-Transcriptional Regulation: mRNA modifications: polyadenylation and CAP. Regulation in eukaryotes as a combinatorial system. Examples of regulation at the level of chromatin modifiers; RNA as a regulator, siRNA, miRNA, ceRNA.
Preparation of DNA fragments for cloning: isolation and purification of genomic DNA. Isolation and purification of total RNA and messenger RNA cDNA synthesis. Restriction endonucleases. Modification enzymes and PCR (Polymerase Chain Reaction). Electrophoretic separation for DNA visualization. Generation of Recombinant DNA: Natural plasmids and horizontal gene transfer. Vectors for cloning (plasmid vectors, transcription vectors, positive selection vectors, expression vectors, and phage vectors). DNA ligation. Strategies for DNA cloning: directed and non-directed cloning; DNA topoisomerase and cloning by recombination. Overview of genomic DNA and cDNA library creation. Introduction of recombinant dna into host cells: Bacterial transformation: natural and artificial competence. Isolation and purification of plasmid DNA. CRISPR Technology: Discovery of the CRISPR/Cas9 system and its mode of action. Genomic editing. Biotechnological and clinical-therapeutic applications of CRISPR/Cas9.

IMMUNOLOGY

Concept of disease and causative agent. Cellular pathology: the cell as the elementary patient. Alterations in size and number of cells, intracellular accumulation disorders (water, lipid, glycogenosis). Alterations of intracellular organelles. Programmed cell death, morphological aspects. Necrosis: molecular and morphological aspects. Pathological alterations of apoptotic mechanisms. Pyroptosis, NETosis, mitotic catastrophe. NLR and Inflammasome. Tissue and interstitial alterations: tissue necrosis, alterations of collagen, elastin, and proteoglycans, amyloidosis. Innate immunity. Surface, internal, humoral, and cellular. Tissue reactions to damage: Inflammation. Vascular and cellular phase. Acute and chronic inflammation. Tissue regeneration. Mucosal immunity and its alterations (IBD) - relationships between the IS and the intestinal microbiome - relationship between inflammation and neoplasia and between inflammation and obesity. Adaptive immunity: introduction to the innate and adaptive immune system. Cells of the immune system and the lymphatic system. Antigens and epitopes: chemical nature and classification. Molecules of the immune system that bind antigens: i) Antibodies. General structure. Classes, subclasses, and their function. Polymorphism. B Cell receptor (BCR). Interactions with the innate immune system. ii) T Cell Receptor (TCR). Structure and distribution. iii) Major Histocompatibility Complex (MHC) antigens. Class I and class II MHC. Genetic organization and polymorphism of MHC. Generation of immunoglobulin and TCR diversity: molecular mechanisms. Antigen recognition. Antigen-antibody interaction: molecular interactions, affinity, avidity, kinetics. Antigen presentation. Antigen Presenting Cells (APCs): nature and localization. Interaction between APCs and T lymphocytes. Role of cytokines in the T cell-APC interaction. T-dependent and T-independent antigens. Role of microbial signals (PAMPs) and danger signals (DAMPs) in innate and adaptive responses. Cell-mediated immune response. Regulation of the immune response: antigenic, antibody, immune complex, lymphocyte. Idiotypic, neuroendocrine, and genetic regulation of the immune response. Immune tolerance. Positive and negative thymic selection.