Degree in Medicine and Surgery
Course: **BIOCHEMISTRY**
Credits: **12**

Module: **Biochemistry**
SSD course: **BIO/10**
Credits: **8**
Professor's name: **Prof. Giacomo Lazzarino** e-mail: **giacomo.lazzarino@unicamillus.org**
Prof. Barbara Tavazzi e-mail: **barbara.tavazzi@unicamillus.org**

Module: **Molecular Biology**
SSD course: **BIO/11**
Credits: **4**
Professor's name: **Prof. Maria Rosaria Capobianchi** e-mail: **maria.capobianchi@unicamillus.org**
Prof. Costanza Montagna e-mail: **costanza.montagna@unicamillus.org**

PREREQUISITES

In order to learn contents of this course, it is necessary to have an appropriate knowledge of the fundamental concepts acquired in the course of Chemistry and Introduction to Biochemistry, including: chemical bonds, chemical kinetics, acid-base equilibrium in solution, pH, oxide-reduction reactions and electrochemical potentials, hybridization of the carbon atom, aromatic compounds, properties of the main functional groups (-OH, -SH, -COH, -C=O, -COOH, $-CH_3$, $-NH_2$), isomerism (conformational, geometric, position, functional group, stereoisomerism).
Furthermore, the student must be aware of fundamental concepts of the Biology and Genetics course. Specifically: organization of procariotic and eucariotic cells; structure and functions of DNA and RNA; genetic code and relevant properties; cell cycle and its regulation; genetic mutations (substitutions, insertion, deletion of nucleotides).

LEARNING OBJECTIVES

To acquire knowledge on the structure, function and regulation of biological macromolecules. To acquire knowledge of the general mechanisms of regulation of metabolism. To acquire knowledge of the main metabolic pathways and cycles with particular regard to carbohydrate, lipid and amino acid metabolism. Understanding the significance of metabolic alterations in non-physiological conditions (prolonged fasting, physical effort).
To acquire learn basic knowledge on fundamental processes of molecular biology and their regulation, necessary to understand:

- The pathogenic mechanisms of diseases
- Molecular mechanisms involved in the therapeutic intervention
- Biotechnology applications of medical relevance, including the principal methods for the study of nucleic acids and of their application for diagnostic and research purpose.

LEARNING OUTCOMES

Knowledge and understanding

At the end of this teaching, the student will acquire:

- Knowledge of the structure and function of the main biological macromolecules

- Knowledge of the principles of enzymatic catalysis
- Knowledge of the different metabolic cycles that occur in eukaryotic cells
- Knowledge of the role of different "fuels" in energy production
- Knowledge of the role of the mitochondrion as the power plant of the cell and the basis of mitochondrial dysfunction
- Knowledge of the biosynthetic pathways of the main molecules of biochemical interest
- Knowledge of the molecular basis of biological processes of eucariotic cells and microorganisms.
- Knowledge of the molecular regulation mechanisms of genome replication and expression
- Knowledge of the structure and function of nucleic acids and proteins
- Knowledge of the fundamental molecular techniques and applications for diagnostic and study purpose

Applying knowledge and understanding
At the end of this teaching, the student will be able to:

- Adequately interpret the importance of biochemical processes alterations, as a cause of various pathological conditions.
- Use the acquired knowledge for an in-depth study of aspects related to his future professional activity
- Understand the molecular basis of human diseases
- Understand medical approaches to molecular medicine and translational research.
- Understand application of molecular techniques for diagnostic purpose

Communication skills
At the end of this teaching, the student will be expected to:

- Communicate scientific contents in a clear and unambiguous way, using appropriate technical language

Making judgments
At the end of this teaching, the student will be able to:

- Carry out assessments of the topics covered.
- Autonomously interpret the data pertaining the topics covered by the course

Learning skills
At the end of the course, the student will have:

- acquired skills and learning methods suitable for the deepening and improvement of their skills
- developed the ability to deepen the topics through the consultation of the scientific literature

COURSE SYLLABUS

Biochemistry
Recalls of inorganic and organic chemistry –Chemical bonds. Carbohydrates – structure and function. Lipids – structure and function. Nucleotides, Purines and pyrimidines – structure and function. Amino acids – structure and function. Peptide bond and its characteristics. Peptides of biological relevance. Proteins – structure and function. Classification. Primary structure. Secondary structures: alfa-helix, beta-strand, collagen helix. Tertiary structure. Quaternary structure. Relationship between primary structure and conformation. Denaturation and renaturation. Protein

folding. Protein misfolding and related pathologies – β-amyloid, Alzheimer's disease. Fibrous proteins. Globular proteins. Hemoproteins involved in the transport of gases (O_2, CO_2). The heme group. Tridimensional structures of myoglobin and hemoglobin. Mechanism of oxygen binding to myoglobin and hemoglobin. Oxygen affinity. Saturation curves, Bohr effect, cooperativity, Hill plot, homotropic and heterotropic interactions. The effect of 2,3-DPG. The Monod-Wyman and Changeux (MWC) model and the sequential model. T and R states. Heterogeneity of circulating hemoglobin. Methemoglobin reductase, reduced glutathione (GSH) and NADPH for the maintenance of hemoglobin functions. Deficit of G-6-PDH, oxidation of hemoglobin, malaria. Hemoglobinopathies. Enzymes – Classification. Coenzymes and vitamins. Avitaminosis and related pathologies. Enzymatic catalysis and regulation. The Michaelis-Menten equation. K_m, V_{max}, turnover number, K_{cat}/K_m. Reversible and irreversible inhibition. Multimeric enzymes and allosteric regulation. Multi-enzymatic complexes. Regulation of enzymatic activity. Isoenzymes. Introduction to metabolism – general organization. Understanding pathways and metabolic maps. Catabolism and anabolism. Bioenergetics. Energetically relevant molecules. Use of biochemical energy within the cell. Examples of regulation of metabolic sequences. Glucose as the fuel for energy production. The glucose transporter family – GLUT. Hormonal control of glucose metabolism. The biochemical reactions of glycolysis – Regulation of glycolysis. Glycolysis and cancer – Warburg effect. Reactions of the pentose phosphate shunt and its biochemical importance. Degradation of glycogen – glycogen phosphorylase and its hormonal control. Gluconeogenesis and other carbohydrate biosynthetic pathways. Lactic fermentation and alcoholic fermentation. Anaerobic metabolism. Mechanism of pyruvate oxidation – the pyruvate dehydrogenase complex. Reactions of the citric acid cycle – Regulation of the cycle. Oxidative phosphorylation – The mitochondrion as the energetic plant of the cell. The scale of redox potential of biologically relevant molecules. The machinery for the electron transport: structure and function of the complexes I, II, III and IV. The sulphur-iron centers. The Q-cycle in the complex III. The electrochemical potential in electron transport. Oxygen utilization. The ATP synthase: structure and mechanism of action. The stoichiometry of electron transport, proton transport, oxygen consumption and ATP production. Brief introduction to mitochondrial dysfunction – the Mitochondrial Quality Control network in the control of mitochondrial dynamics (fusion, fission and mitophagy); mitochondria as generator of reactive oxygen species (ROS). The intrinsic pathway of apoptosis. ROS, oxidative stress, antioxidants and nutrition. Absorption and transport of dietary lipids. Activation of lipolysis and transport of free fatty acids. Activation and transport of free fatty acids in mitochondria. The role of carnitine. The beta-oxidation reactions. Ketogenesis. Synthesis of fatty acids – Regulation of fatty acids metabolism. The biosynthesis of phospholipids. Cholesterol metabolism Transamination and trans-deamination of amino acids. Selected examples of amino acid bio-transformations: production of dopamine, adrenaline and noradrenaline from tyrosine; arginine as the source of nitric oxide. The urea cycle. Degradation of nucleotides. Catabolism of purines and pyrimidines and related pathologies –Lesch-Nyhan syndrome, Adenosine deaminase deficiency. Degradation of heme: structure and function of biliary salts. Bioenergetics and regulation of fuel metabolism – energy metabolism disorders.

Molecular Biology

Structure and replication of DNA; genome and exome; genome organization: viruses, bacteria, eucariotic cells; genome alteration and mechanisms of evolution; mechanisms of DNA repair; control of gene expression: promoters and enhancers.
Structure and function of various RNA species; mRNA processing.
Genome editing and gene therapy concepts, development and application of CRISPR/Cas9 technique. Fundamentals of protein synthesis: translation initiation, elongation and termination; post-translational modifications.

DNA and RNA study methods: targeted enzymatic amplification and detection of nucleic acids; DNA sequencing, classical and high throughput next generation methods (NGS); use of sequencing for diagnostic, epidemiologic and forensic applications.

COURSE STRUCTURE

The course is structured in 120 hours (80 hours of biochemistry and 40 hours of molecular biology) of frontal teaching, divided into 2-hour lessons basing on the academic calendar. Lectures will include theoretical lessons on the topics of the program.

COURSE GRADE DETERMINATION

The final exam will consist of a written test followed by an oral exam. The written test will consist of 30 questions with multiple-choice and open-ended answers (20 biochemistry questions and 10 molecular biology questions); for each correct answer, 1 point will be assigned. For every wrong or missing answer, 0 points will be assigned. The final score of the written test will be given by the sum of the scores of each correct answer. To access the oral exam the student must score at least 18 points. During the oral exam, the examining commission will assess the student's ability to correctly present knowledge acquired during the integrated course of biochemistry and molecular biology, and the ability to apply knowledge in the medical field.
Ability to making judgments, communication skills and learning skills will be also evaluated, as indicated in the Dublin descriptors.

OPTIONAL ACTIVITIES

In addition to the frontal teaching activity, students will be able to take advantage of 2 hours of reception with the professor of biochemistry (Prof. Lazzarino and Prof. Tavazzi from 10:00 AM to 11:30 AM every Tuesday), and with the professors of molecular biology (Prof. Capobianchi and Prof. Montagna, students are received by appointment by writing via email).

READING MATERIALS

Biochemistry

- David L. Nelson; Michael M. Cox. "Lehninger Principles of Biochemistry" Seventh Edition – 2017. W. H. Freeman
- Voet D, Voet JG, Pratt CW. "Principles of Biochemistry (international student version)" IV edition – John Wiley and Sons Inc.
- Christopher K. Mathews , Van Holde, K. E. "Biochemistry" IV edition –2012. Pearson.

Molecular Biology

- WATSON James D , BAKER Tania A , BELL Stephen P , GANN Alexander , LEVINE Michael , LOSICK Richard Molecular Biology of the Gene (7th ed) COLD SPRING HARBOR LABORATORY PRESS
- Michael M. Cox, Jennifer Doudna, Michael O'Donnell. Molecular Biology: Principles and Practice; W H Freeman & Co; 2 edition (16 March 2015)