UNICAMILLUS

Degree in Medicine and Surgery

Course: **BIOCHEMISTRY**
Code: **BIOS-07/A, BIOS-08/A**
Number of CFU: **12**

Reference Professor: **Prof.** Giacomo Lazzarino e-mail: giacomo.lazzarino@unicamillus.org

Module: **Biochemistry**
SSD course: **BIOS-07/A**

Prof. Giacomo Lazzarino **(3 CFU)** e-mail: giacomo.lazzarino@unicamillus.org
Prof. Barbara Tavazzi **(3 CFU)** e-mail:barbara.tavazzi@unicamillus.org
Prof. Maria Patrizia Stoppelli **(2 CFU)** e-mail: mariapatrizia.stoppelli@unicamillus.org

Credits: **8**

Module: **Molecular Biology**
SSD course: **BIOS-08/A**

Prof. Emiliano Maiani **(2 CFU)** e-mail: emiliano.maiani@unicamillus.org
Prof. Maria Rosaria Capobianchi **(1CFU)** e-mail: maria.capobianchi@unicamillus.org
Prof. Lucia Buccarello **(1 CFU)** e-mail: lucia.buccarello@unicamillus.org

Credits: **4**

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, oxidation-reduction reactions and electrochemical potentials, hybridization of the carbon atom, aromatic compounds, properties of the main functional groups (-OH, -SH, -COH, -C=O, -COOH, -CH3, -NH2), 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 procaryotic and eucaryotic 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 both non-physiological conditions (prolonged fasting, physical effort) and pathological conditions.

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.

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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 occurring in eukaryotic cells;
- Knowledge of the role of different "fuels" for the 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 eucaryotic cells and microorganisms;
- Knowledge of the molecular regulation mechanisms of genome replication and expression;
- Knowledge of the DNA repair mechanisms
- 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:

- Properly 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 purposes.

Communication skills

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

- Communicate scientific contents in a clear and unambiguous way, using an 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 to the topics covered by the course.

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 the primary structure of proteins and their 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 (O2, CO2). 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. Km, Vmax, turnover number, Kcat/Km. Reversible and irreversible inhibition. Multimeric enzymes and allosteric regulation. Multi-enzymatic complexes. Regulation of enzymatic activity. Isoenzymes. Active and passive transport mechanisms: transport of substances across biological membranes. 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 biochemical reactions of glycolysis – Regulation of glycolysis. The glucose transporter family – GLUT. Hormonal control of glucose metabolism. Glycolysis and cancer – Warburg effect. Reactions of the pentose phosphate shunt and its biochemical importance. Glycogen metabolism: biosynthesis and degradation – glycogen phosphorylase and its hormonal control. Gluconeogenesis and other carbohydrate biosynthetic pathways. Homolactic 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 iron-sulphur 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. Mitochondria as generator of reactive oxygen species (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 and regulation. Protein degradation: the role of pH and digestive enzymes. Protein turnover and degradation in lysosomes and proteasome. 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. Metabolism of purines and pyrimidines. Heme metabolism: biosynthesis and degradation and related pathologies. Structure and function of biliary salts. Bioenergetics and regulation of fuel metabolism – energy metabolism disorders.

Molecular Biology

Structure of DNA and RNA. Chemical and physical properties of nucleic acids and nucleotides. Topological properties of DNA. DNA supercoiling, linking number, euchromatin and heterochromatin, chromatin structure, Histones, nucleosomes. Epigenetic modifications of histones, histone acetyltransferases and deacetylases. Methylation of DNA and histones.
Genomic structure in eukaryotes. Genome and exome. DNA replication. Semi-conservative and bidirectional synthesis of DNA. Mechanism of action of DNA polymerases. Proof reading mechanisms. Duplication of the leading and lagging strand, Okazaki fragments.

Enzymes and proteins involved in DNA replication. Telomeres and telomerase. DNA repair mechanisms and therapeutic approaches targeting DNA repair.
Transcription, promoter sequence of RNA pol I, II and III in eukaryotes. Basic and specific/regulatory transcription factors. Promoter, enhancer, silencer. Interaction between proteins and DNA. Assembly of transcription complexes and role of transcription factors. Transcription regulation in prokaryotes and eukaryotes. Epigenetic regulation of gene expression. Exons and introns. Maturation of eukaryotic mRNA: capping, polyadenylation, intron removal (splicing). The spliceosome complex. rRNA and tRNA maturation. RNA interference and MicroRNA. Long non-coding RNA.
The genetic code: codons, reading frame. Nonsense, missense, and synonymous mutations. INDELS and frame shift. Chromosomal mutations.
Protein synthesis (translation). Amino acid activation, aminoacyl-tRNA synthetases. Initiation, elongation, and termination of translation in prokaryotes and eukaryotes, with initiation, elongation, and termination factors. Primary, secondary, tertiary, and quaternary structure of proteins. Intrinsically disordered proteins.
Molecular biology techniques: methods of studying DNA and RNA; enzymatic amplification and nucleic acid detection, application of enzymatic nucleic acid amplification techniques to diagnostic contexts; DNA sequencing and next-generation sequencing (NGS) methods; applications of sequence analysis to diagnostic, epidemiological, and forensic contexts. Recombinant DNA technologies: plasmids, restriction enzymes, cloning, expression vectors. DNA editing and CRISPR Cas-9. Application of recombinant DNA technologies to the study and therapy of human diseases. Ethical aspects related to the application of recombinant DNA.

COURSE STRUCTURE
The course is structured in 120 hours (80 hours of biochemistry and 40 hours of molecular biology) of frontal teaching basing on the academic calendar. Lectures will include theoretical lessons on program topics.

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/or 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 written test will last 45 minutes. The final score of the written test will be given by the sum of the scores of each correct answer and will be calculated in thirtieths. To access the oral exam the student must answer at least half of the questions correctly, corresponding to a score of 15 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.

The final score will be expressed in thirtieths.

The exam will be considered passed if the student totals a final score of 18/30 or higher.

The evaluation criteria considered will be: knowledge acquired, autonomy of making judgment, communication skills and learning ability.

Overall, the examination will be evaluated according to the following criteria:

Not sufficient: Poor or deficient knowledge and understanding of topics; limited ability to analyze and synthesize; frequent generalization of required contents; inability to use technical language.

18-20: Barely sufficient knowledge and understanding of topics, with evident imperfections; barely sufficient ability to analyze, synthesize and making judgment; poor ability to use technical language.

21-23: Sufficient knowledge and understanding of topics; sufficient ability to analyze and synthesize with ability to argue the required contents, with logic and coherence; sufficient ability to use technical language.

24-26: Fair knowledge and understanding of topics; fair ability to analyze and synthesize with ability to rigorously argue the required contents; fair ability to use technical language.

27-29: Good knowledge and understanding of the required contents; good ability to analyze and synthesize with ability to rigorously argue the required contents; good ability to use technical language.

30-30L: Excellent level of knowledge and understanding of the required contents with excellent analytical and synthesis skills with the ability to rigorously, innovatively and originally argue the required content; excellent ability to use technical language.

OPTIONAL ACTIVITIES
In addition to the frontal teaching activity, students will be able to take advantage of reception hours with the biochemistry professors (Prof. Lazzarino, Prof. Tavazzi and Prof. Stoppelli), and with the molecular biology professors (Prof. Maiani, Prof. Capobianchi and Prof. Buccarello). Students are received by appointment by writing via email.

SUGGESTED TEXTBOOKS:

Biochemistry

- David L. Nelson; Michael M. Cox. "Lehninger Principles of Biochemistry" 8th Edition – 2021. W. H. Freeman
- Voet D, Voet JG, Pratt CW. "Voet's Principles of Biochemistry, 5th Edition, Global Edition" – 2018. 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)
- Bruce Alberts et al., "Molecular Biology of the Cell", VII ed., WW Norton & Co.