Degree in Medicine and Surgery

Course: General Pathology
Disciplinary scientific sector: MED/04 (6CFU) e MED/46 (2CFU)
CFU : 8
Coordinator Prof. Roberto Bei

General Pathology (MED/04)
Prof. Roberto Bei (3CFU) roberto.bei@unicamillus.org
Prof. Monica Benvenuto (1CFU) gabriella.dorazi@unicamillus.org
Prof. Delia Goletti (2CFU) delia.goletti@unicamillus.org

Laboratory Medicine Technical Sciences (MED/46)
Prof. Emiliano Fabiani (2CFU) emiliano.fabiani@unicamillus.org

PREREQUISITES
Previous knowledge and competence in the following subjects: Human Anatomy, Histology and Embryology, Physiology, Biology and Genetics, Biochemistry and Molecular Biology. Basic concepts concerning the structure and functions of nucleic acids (DNA and RNA) and proteins are also needed.

LEARNING OBJECTIVES
The learning objectives of the Course in GENERAL PATHOLOGY are to enable the student to understand the molecular mechanisms of cell damage, the response of the cell and the organism to damage, the molecular basis of the neoplastic transformation, and the causes of human diseases, interpreting the fundamental pathogenetic mechanisms. In addition, the objectives of the course are the understanding of basic laboratory techniques; cellular isolation methods; standard molecular biology techniques; correct and efficient storage of biological samples; how to apply diagnostic technologies needed to help the assessment of the diagnosis and prognosis of patient.

LEARNING OUTCOMES
Knowledge and understanding
At the end of the course, the student must know and understand autonomously the molecular mechanisms of cellular damage, cell (cellular stress, necrosis, apoptosis) and organism response to damage, the molecular basis of the neoplastic transformation, the activation of the immune response and the pathogenetic mechanisms of the most important human diseases.
In addition, the student has to know:
• to manipulate, amplify and store bacterial cells
• to manipulate, amplify and store eukaryotic cells
• to evaluate the human karyotype using conventional and molecular cytogenetic methods
• to understand the flow cytometry data in the haematology field
• to isolate nucleic acids (DNA and RNA) and proteins
• to qualitatively and quantitatively amplify nucleic acids
• to evaluate the diagnostic and prognostic role of gene mutations in oncology
• to understand the data achieved from the use of both old and new generation sequencing

Applying knowledge and understanding

The student must be able to apply his/her knowledge to analyze and understand the alterations of the cellular, immunological and genetic mechanisms underlying the human pathologies. In addition, the student will be able to use the knowledge acquired for the in-depth study of aspects relating to the specific field to which the student will dedicate himself in the professional activity.

Communication skills
The student must be able to communicate information, ideas, problems and solutions to interlocutors, both specialists and non-specialists, in relation to the molecular mechanisms of cellular damage, neoplastic transformation, and to the pathophysiological mechanisms of diseases. In addition, the student will be able to use the specific scientific terminology.

Making judgements
The student must be able to use the acquired knowledge to identify and explain the molecular, immunological and pathophysiological mechanisms that lead to a disease. The acquisition of autonomy of judgment will be acquired through the analysis of examples of damage and human pathologies.

Learning skills
The student will have to understand the mechanisms and effects of cellular damage, the mechanisms underlying the process of carcinogenesis and have memorized the knowledge that will allow understanding of the pathophysiology of diseases. These skills will be developed favoring a critical discussion of the topics.

COURSE SYLLABUS
General Pathology (MED/04)
Etiology:

- Concept of disease: state of health and causes of disease.Concept of etiology and pathogenesis.
- Genetic disorders: mutations, mendelian disorders, disorders with multifactorial inheritance, normal karyotype, cytogenetic disorders, single-gene disorders with non classic inheritance. Diagnosis of genetic diseases.
- Infectious diseases: general principles of pathogenesis. Viral infections. Bacterial infections. Fungal infections. Parasitic infections.
- Environmental pathology: recognition of occupational and environmental diseases. Mechanisms of toxicity. Phase I reactions. Common environmental and occupational exposures. Personal exposures: tobacco use, alcohol abuse, therapeutic drugs, outdoor air pollution, industrial exposures, agricultural hazards, natural toxins. Radiation injury: ionizing radiation, ultraviolet radiation. Physical environment: mechanical force, thermal injuries (hyperthermia. Hypothermia). Electrical injuries. Decompression (caisson) disease.

Cellular Pathology:

- Cellular adaptations, cell injury, and cell death. Cellular responses to stress and noxious stimuli. Cellular adaptations of growth and differentiation: hyperplasia, hypertrophy, atrophy, metaplasia. Overview of cell injury and cell death: causes of cell injury. Mechanisms of cell injury. Reversible and irreversible cell injury. Morphology of cell injury and necrosis. Examples of cell injury and necrosis: ischemic and hypoxic injury, ischemia-reperfusion injury, chemical injury. Apoptosis: causes of apoptosis, morphology, biochemical features of apoptosis, mechanisms of apoptosis, examples of apoptosis.

Inflammation:

- Acute inflammation: historical highlights, stimuli for acute inflammation; vascular changes (changes in vascular flow and caliber, vascular leakage); cellular events: leukocyte extravasation (leukocyte adhesion and transmigration) and phagocytosis. Adhesion molecules involved in the inflammatory response. Chemotaxis. Defects in leukocyte functions.
- Chemical mediators of inflammation: vasoactive amines, plasma proteins, arachidonic acid metabolites: prostaglandins, leukotrienes, and lipoxins, platelet-activating factor (PAF), cytokines and chemokines, nitric oxide (NO), lysosomal constituents of leukocytes, oxygen-derived free radicals, neuropeptides. Disorders of the complement system.
- Outcomes of acute inflammation. Morphologic patterns of acute inflammation.
- Chronic inflammation: causes of chronic inflammation, morphologic features, mononuclear cell infiltration, cells involved in chronic inflammation. Granulomatous inflammation, lymphatics in inflammation.
- Systemic effects of inflammation, consequences of defective or excessive inflammation.

Tissue renewal and repair. Regeneration, healing, and fibrosis: Definitions. Control of normal cell proliferation and tissue growth. Mechanisms of tissue regeneration. Extracellular matrix and cell-matrix interactions. Repair by healing. Scar formation and fibrosis. Cutaneous wound healing. Overview of repair responses after injury and inflammation

Thermoregulation: Neurophysiology of thermoregulation. Body's thermoregulatory set-point. Pyrogens. Fever. Types of fevers.

Neoplasia:

- Definitions. Nomenclature of tumors. Biology of tumor growth: benign and malignant neoplasms. Differentiation and anaplasia, rates of growth.
- Epidemiology: cancer incidence, geographic and environmental factors, genetic predisposition to cancer, chronic inflammation and cancer, precancerous conditions.
- Molecular basis of cancer: essential alterations for malignant transformation, the normal cell cycle, self-sufficiency in growth signals: oncogenes. Insensitivity to growth inhibitory signals. Tumor suppressor genes. Retinoblastoma as a paradigm for the two-hit hypothesis of oncogenesis. Selected tumor suppressor genes involved in human neoplasms. p53: guardian of the genome. Evasion of apoptosis. DNA repair defects and genomic instability in cancer cells. Limitless replicative potential: telomerase. Development of sustained angiogenesis. Invasion and metastasis. Stromal microenvironment and carcinogenesis. Dysregulation of cancer-associated genes.
- Molecular basis of multistep carcinogenesis: gatekeeper and caretaker genes. Tumor progression and heterogeneity. Carcinogenic agents and their cellular interactions: chemical carcinogenesis, metabolic activation of carcinogens. Molecular targets of chemical carcinogens. Major chemical carcinogens. Radiation carcinogenesis: ultraviolet rays, ionizing radiation. Microbial carcinogenesis: oncogenic DNA viruses, oncogenic RNA viruses. Host defense against tumors: tumor immunity, tumor antigens, antitumor effector mechanisms. Immune surveillance. Effects of tumors on the host local and hormonal effects. Grading and staging of tumors.

Laboratory Medicine Technical Sciences (MED/46)

- Bacterial cell culture techniques
- Eukaryotic cell culture techniques
- Preparation of slides for light microscopy: tissues inclusion, microtome cutting

- Immunohistochemistry techniques
- Primary and secondary antibodies
- Peripheral blood sampling and bone marrow aspirate
- Isolation of mononuclear and polymorphonuclear cells
- Stem cells isolation: culture, amplification and cryopreservation
- Cytofluorimetry
- Karyotype aberrations: conventional and molecular cytogenetics (FISH)
- Diagnostic and prognostic role of molecular biology in oncology
- Extraction and storage of nucleic acids (DNA and RNA)
- Basic techniques in molecular biology: nucleic acids amplification
- Qualitative analysis (PCR and RT-PCR)
- Quantitative analysis (Q-PCR and Q-RT-PCR)
- Minimal Residual Disease (MRD)
- Gene mutations
- Sanger sequencing
- New generation sequencing and personalized medicine: applications, progress, costs and benefits

COURSE STRUCTURE

The teacher will conduct lectures for a maximum of two hours for a total of 80 hours. The course includes lectures and continuous support by the teacher in the classroom and through e-mail or explanations during office hours. During the lessons will be shown slides containing topics of the program that will allow students to achieve the Educational Goals. The teacher will illustrate the slides providing the tools to achieve the Educational Goals. A part of the lesson will be dedicated to explaining the topic, while another will be devoted to questions from students and to the discussion of the topic. At the end of the lesson the teacher will summarize the essential elements of each topic necessary to meet the learning outcomes.

COURSE GRADE DETERMINATION

The knowledge acquired by the student will be evaluated through multiple choice test followed by oral test for the module Laboratory Medicine Technical Sciences. The 30 questions test will award 1 point for each correct answer. Eighteen points will be required to be admitted to the oral exam.
There is only an oral exam for the General Pathology module.
In the oral session, the student has to answer to several questions in such a way as to demonstrate the acquisition of the knowledge and skills described in the learning outcomes. It will also be evaluated: autonomy of judgment, communication skills and learning ability as indicated in the Dublin descriptors.
The judgment will be expressed in a mark out of thirty, obtained from the weighted average according to the CFU between the marks of the individual modules.

OPTIONAL ACTIVITIES

Optional or external activities are not provided.

READING MATERIALS

The teachers will provide handouts. Students also will be able to study the topics of the course, using a text of General Pathology:

-Robbins & Cotran, Pathologic Basis of Disease.

-Rubin's Pathology: Clinicopathologic Foundations of Medicine