

Degree course in Medicine and Surgery

Integrated Course: **General Pathology**

Scientific Disciplinary Sector (SDS): **MED/04 e MED/46**

ECTS: **8**

Coordinator: **Professor Federica Wolf**

Patologia Generale

SDS: MED/04

Professor **Federica Wolf** (4 CFU)

federica.wolf@unicamillus.org

Professor **Gabriella D'Orazi** (1 CFU)

gabriella.dorazi@unicamillus.org

Professor **Cristina Capuano** (1 CFU)

cristinacapuano9@gmail.com

Laboratory Medicine Technical Sciences

SDS: MED/46

Professor **Emiliano Fabiani** (2 CFU)

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 biology and molecular basis of the neoplastic transformation, and the causes of human diseases, interpreting the fundamental pathogenetic mechanisms. In addition, we will also introduce basic principles of pathophysiology of the major systems as circulation, hepatobiliary and metabolism. Objectives of the course are also 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 biological and molecular basis of the neoplastic transformation, the pathogenetic mechanisms of the most important human diseases. The student must also know the basic mechanisms of pathophysiological events of the major systems such as circulatory, hepatobiliary and metabolic. In addition, the student has to know the principle and use of:

- manipulation, amplification and store of bacterial and eukaryotic cells
- the use of conventional and molecular cytogenetic methods to evaluate the human karyotype
- the use of flow cytometry data in the haematology field
- the isolation of nucleic acids (DNA and RNA) and proteins
- the use of qualitatively and quantitatively amplification of nucleic acids
- to evaluate the diagnostic and prognostic role of gene mutations in oncology

- to understand the data 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 on specific setting.

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. Classification and 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.
- Pathophysiology of major systems. Circulation: edema, hemostasis, thrombosis, hemorrhagia, atherosclerosis, emboli, infarct, shock. Hepato-biliary: liver functions and related diseases, jaundice, cholestasis, hepatitis, cirrhosis, hepatic failure. Metabolism: diabetes.

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 additional support by the teacher through e-mail or explanations during office hours. During the lessons will be shown slides containing topics of the program that will guide students to achieve the objectives. A part of the lesson will be dedicated to explaining the topic, when possible practical examples in the form of simple clinical cases, while another will be devoted to questions from students active participation will be encouraged to implement active learning. At the beginning of the lesson the teacher will clarify the objectives and the learning outcomes, 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 (single best answer) followed by oral test. The questions test will award points for each correct answer. Eighteen points will be required to be admitted to the oral exam.

There will be 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. Specifically : it will 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

External activities are not provided, but teachers can suggest website for learning or exercising.

Scientific seminars will be organize to introduce and train the students to scientific methodology.

Optional credits will be awarded to participants.

READING MATERIALS

The teachers will provide handouts. Students will study the topics of the course, using the following suggested textbook:



UNICAMILLUS

-Robbins & Cotran, Pathologic Basis of Disease, X edition, Elsevier 2017

-Rubin's Pathology: Clinicopathologic Foundations of Medicine, VII edition, Woulter's