UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

SYLLABUS DEL CORSO

Pathology and Medicine

2627-2-H4104D011-H4104D01104

Aims

The Pathology and Medicine course aims to provide 2nd-year students of the Medicine and Surgery degree programme with a solid understanding, at the biochemical, molecular and cellular level, of the etiopathogenetic mechanisms common to most human diseases, integrating general cell pathology, inflammation, clinical immunopathology and the biological basis of neoplastic transformation. Consistent with the scientific-biological profile of the course, the treatment of general oncology (epidemiology, environmental and chemical carcinogenesis) is limited to the essential conceptual core that is preparatory to understanding tumor immunoediting and immunotherapy. The learning objectives are organized according to the five Dublin Descriptors.

Knowledge and Understanding
Students will be expected to know the molecular and biochemical mechanisms of cellular adaptation and injury, the pathways of cell death (necrosis, apoptosis and alternative forms), the cellular and molecular mechanisms of acute and chronic inflammation, general hemodynamic pathophysiology, the molecular mechanisms of immunopathology (hypersensitivity, autoimmunity, immunodeficiencies, transplant rejection), and the biological-molecular basis of neoplastic transformation and tumor immunoediting.

Applying Knowledge and Understanding
Students will be expected to apply the molecular mechanisms studied to the pathogenetic interpretation of basic clinical-pathological pictures, to correlate biochemical and cellular findings (e.g. injury markers, inflammatory profiles, tumor biomarkers) with the underlying pathological process, and to recognize the biological rationale of the main modern diagnostic and immunotherapeutic strategies.

Making Judgements
Students will be expected to develop the ability to critically analyse the relationship between molecular mechanism and pathological manifestation, to distinguish between adaptive, reversible and irreversible cellular processes, and to formulate plausible pathogenetic hypotheses starting from complex clinical-molecular scenarios, including under conditions of diagnostic uncertainty.

Communication Skills

Students will be expected to present fundamental pathogenetic mechanisms using rigorous scientific terminology, to critically discuss translational medicine scientific papers, and to clearly and systematically communicate a complex pathogenetic pathway (from molecular mechanism to clinical manifestation) to a peer audience.

Learning Skills
Students will be expected to acquire a study method based on the integration of biochemistry, molecular biology and pathophysiology, developing the autonomy necessary for continuous updating on the molecular basis of human pathology and for the critical appraisal of the scientific literature during subsequent clinical studies.

Contents

The Pathology and Medicine course provides an integrated vision, with a rigorously biochemical, molecular and cellular approach, of the pathogenetic mechanisms common to most human diseases. The course opens with the general etiology and pathogenetic mechanisms of cell injury — oxidative stress, cellular adaptations and the various pathways of cell death (necrosis, apoptosis, autophagy, necroptosis, pyroptosis, ferroptosis) — before examining in depth the mechanisms of acute and chronic inflammation, tissue repair, and general hemodynamic pathophysiology (edema, thrombosis, embolism, shock). The central part of the course is devoted to clinical and molecular immunopathology, covering hypersensitivity reactions, mechanisms of immune tolerance and autoimmunity, primary and secondary immunodeficiencies, and transplant immunology. The course then addresses the biological-molecular basis of neoplastic transformation — limited to the essential preparatory core — in order to specifically examine tumor immunoediting and the biological principles of immunotherapy (checkpoint inhibitors, CAR-T). The course concludes with an overview of modern methods in contemporary pathology (quantitative immunohistochemistry, NGS, liquid biopsy, translational experimental models and CRISPR/Cas9), providing students with an integrated and up-to-date view of molecular pathology in the service of precision medicine.

Detailed program

The programme is organized into 30 lectures of 2 hours each (60 total contact hours), structured into five teaching macro-modules that follow a conceptual progression from general cell pathology to clinical immunopathology, culminating in the biological basis of tumors and modern diagnostic methods. Consistent with the degree programme's curricular constraint, the treatment of general oncology is limited to the essential biological-molecular core (Module 4, Lectures 24–27) that is preparatory to understanding immunoediting and immunotherapy. Both a concise macro-module overview and the detailed lecture-by-lecture calendar are provided below.

Concise Macro-module Overview
Macro-module Lectures Hours Key contents
Module 1 – Cell pathology, injury and molecular death Lectures 1–7 14h Etiology of cell injury, oxidative stress, cellular adaptations, necrosis, apoptosis, alternative forms of cell death, senescence
Module 2 – Inflammation, repair and general pathophysiology Lectures 8–15 16h Acute and chronic inflammation, chemical and plasma mediators, fever, tissue repair, hemodynamic pathophysiology
Module 3 – Clinical and molecular immunopathology Lectures 16–23 16h Hypersensitivity I–IV, immune tolerance, autoimmunity, primary/secondary immunodeficiencies, transplant immunology
Module 4 – Biological basis of tumors, immuno-oncology and immunotherapy Lectures 24–27 8h Basic tumor biology, oncogenes/tumor suppressors, immunoediting, immunotherapy (checkpoint inhibitors, CAR-T)
Module 5 – Modern methods in contemporary pathology Lectures 28–30 6h Quantitative IHC, immunofluorescence, NGS, digital PCR, liquid biopsy, translational models and CRISPR/Cas9

Module 1 — Cell Pathology, Injury and Molecular Death (Lectures 1–7)
General Etiology of Cell Injury. Physical, chemical and biological causes of cell injury; molecular mechanisms of

hypoxic injury; collapse of ATP production and consequences for cellular ionic and energetic homeostasis.
Oxidative Stress. Biochemistry of reactive oxygen species (ROS); mechanisms of lipid peroxidation and DNA damage; enzymatic and non-enzymatic cellular antioxidant systems; molecular basis of reperfusion injury.
Cellular Homeostasis and Adaptations. Molecular mechanisms of hypertrophy, hyperplasia, atrophy and metaplasia as adaptive responses to cellular injury and stress; signaling pathways involved; biological significance and limits of adaptation.
Irreversible Cell Death: Necrosis. Biochemical mechanisms of necrosis; cellular and nuclear morphological alterations; main morphological types of necrosis (coagulative, liquefactive) and their etiopathogenetic correlation.
Programmed Cell Death: Apoptosis. Intrinsic (mitochondrial) and extrinsic (death receptor) pathways of apoptosis; caspase activation cascade; genetic regulation by the Bcl-2 family (pro- and anti-apoptotic proteins).
Alternative Forms of Cell Death and Homeostatic Responses. Autophagy: molecular mechanisms and homeostatic role; Necroptosis and the RIPK1/RIPK3/MLKL pathway; Pyroptosis and the inflammasome; Ferroptosis and iron- and lipid-peroxidation-dependent cell death.
Cellular Senescence and Aging. Molecular basis of replicative aging and the role of telomeres/telomerase; accumulation of genetic damage and stress-induced senescence; premature aging syndromes (Werner syndrome, Hutchinson-Gilford Progeria).

Module 2 — Inflammation, Repair and General Pathophysiology (Lectures 8–15)
Acute Inflammation (Angioflogosis). Vascular changes in acute inflammation; mechanisms of exudate formation; kinetics of leukocyte recruitment: rolling, adhesion, diapedesis and chemotaxis.
Phagocytosis and Cellular Chemical Mediators of Inflammation. Molecular mechanisms of phagocytosis and intracellular killing; cellular mediators of inflammation: histamine, serotonin; arachidonic acid metabolites (cyclooxygenase and lipoxygenase pathways: prostaglandins and leukotrienes).
Plasma Mediators of Inflammation. The complement system in inflammation; the kinin cascade (kallikrein-kinin system); interactions between the coagulation system and the inflammatory response.
Chronic Inflammation (Histoflogosis). Cellular features of chronic inflammation (macrophages, lymphocytes, plasma cells); causes and classification of immune-mediated and foreign-body granulomas; pathogenesis of abscesses and ulcers.
Systemic Response to Inflammation. Pathophysiology of fever: endogenous and exogenous pyrogens, the hypothalamic PGE2 signaling pathway; non-pyrogenic hyperthermia; synthesis and biological role of acute-phase proteins (CRP, fibrinogen).
Tissue Repair and Regeneration. Wound healing by primary and secondary intention; role of angiogenesis in repair; extracellular matrix (ECM) remodeling; molecular pathogenesis of fibrosis.
Hemodynamic Pathophysiology I. Alterations of fluid balance and blood flow; pathogenesis of edema and analysis of the Starling equation; mechanisms of active hyperemia and passive congestion.
Hemodynamic Pathophysiology II. Physiological hemostasis: the platelet phase and the enzymatic coagulation cascade; pathogenesis of thrombosis (Virchow's Triad); mechanisms of embolism, tissue infarction and systemic shock.

Module 3 — Clinical and Molecular Immunopathology (Lectures 16–23)
Type I and Type II Hypersensitivity. Type I: IgE-mediated anaphylactic reactions, mast cell activation and degranulation; Type II: antibody-mediated cytotoxic hypersensitivity, effector mechanisms and pathological correlates.
Type III and Type IV Hypersensitivity. Type III: hypersensitivity mediated by circulating immune complexes, pathogenesis of the Arthus reaction; Type IV: delayed-type cell-mediated hypersensitivity, role of T lymphocytes and macrophages in tissue damage.
Molecular Mechanisms of Immune Tolerance. Central tolerance: thymic and bone-marrow selection; peripheral tolerance: clonal anergy, regulatory T-cell (Treg)-mediated suppression, peripheral clonal deletion.
Molecular Pathogenesis of Autoimmune Diseases. Mechanisms of immune tolerance breakdown; molecular mimicry; genetic susceptibility and the role of HLA haplotypes; environmental triggering and modulating factors.
Models of Systemic and Organ-Specific Autoimmunity. Molecular analysis and pathogenesis of Systemic Lupus Erythematosus (SLE): autoantibodies and immune complexes; molecular analysis and pathogenesis of Multiple Sclerosis: immune-mediated demyelination.
Primary or Congenital Immunodeficiencies. Molecular classification of antibody deficiencies; severe combined immunodeficiencies (combined B/T-cell defects); molecular defects of phagocytosis; genotype-phenotype

correlations in the main syndromes.
Secondary or Acquired Immunodeficiencies. Molecular pathogenesis of HIV infection; viral replication cycle within CD4+ T lymphocytes; mechanisms of immune exhaustion and clinical-molecular progression toward AIDS.
Transplant Immunology. Biological basis of non-self recognition: direct and indirect allorecognition; molecular mechanisms of hyperacute, acute and chronic rejection; pathogenesis of Graft-versus-Host Disease (GVHD).

Module 4 — Biological Basis of Tumors, Immuno-Oncology and Immunotherapy (Lectures 24–27)
Introduction to Tumor Biology. Neoplasm nomenclature; biological and structural characteristics of benign and malignant neoplastic cells; the essential hallmarks of cancer; tumor-specific antigens (TSAs) and tumor-associated antigens (TAAs).
Genetic and Molecular Basis of Neoplastic Transformation. Alterations in cell-cycle control; activation of proto-oncogenes into oncogenes; inactivation of key tumor suppressors (p53 and Rb); molecular mechanisms of apoptosis evasion.
Immuno-Oncology: Tumor Immunoediting. The concept of tumor immunoediting and its three phases (Elimination, Equilibrium, Escape); molecular mechanisms of tumor immune evasion: MHC down-regulation, expression of inhibitory checkpoints (PD-L1, CTLA-4).
Biological Principles of Cancer Immunotherapy. Therapeutic monoclonal antibodies; immune checkpoint inhibitors (anti-PD-1/PD-L1, anti-CTLA-4) and their molecular rationale; biological overview of CAR-T cell technology.

Module 5 — Modern Methods in Contemporary Pathology (Lectures 28–30)
Advanced Histopathological Techniques. Principles and applications of quantitative immunohistochemistry (IHC); principles of immunofluorescence; identification of tissue biomarkers and therapeutic targets (e.g. HER2, PD-L1).
Predictive and Diagnostic Molecular Pathology. The use of Digital PCR; Next Generation Sequencing (NGS) for the identification of mutational profiles; biological principles of liquid biopsy and circulating tumor DNA (ctDNA).
Translational Experimental Models. Use of in vitro cellular models; in vivo animal models for the study of human disease; CRISPR/Cas9 genome editing in the dissection of pathogenetic pathways; methodological and concluding summary of the course.

Prerequisites

A correct understanding of the course contents requires that students possess solid preparatory knowledge in the following basic disciplines, normally acquired during the 1st year of the degree programme:
• Biochemistry: structure and function of biological macromolecules, enzymology, cellular bioenergetics (ATP metabolism), principles of membrane biochemistry and signal transduction.
• Cell biology: structural and functional organization of the eukaryotic cell, the cell cycle, intercellular communication, molecular basis of transcription and translation.
• Histology: microscopic organization of epithelial, connective, muscle and nervous tissues; structure of primary and secondary lymphoid organs.
• Human genetics: principles of Mendelian and molecular genetics, organization of the human genome, basis of genetic mutations and their transmission.
• Knowledge of the basic contents of Immunology (immune system organization, antibodies, MHC, lymphocyte development) is also recommended, as it is preparatory to fully understanding the immunopathology and immuno-oncology modules of this course.

Teaching form

• Interactive lectures (30 lectures × 2 hours, for a total of 60 hours), supported by structured multimedia

presentations and summary diagrams of the biochemical, molecular and cellular mechanisms covered.
• Critical analysis and discussion of international translational medicine scientific papers, selected to illustrate the clinical application of the molecular mechanisms studied and to encourage critical reading of the primary biomedical literature.
• Use of an institutional e-learning platform for sharing teaching materials (lecture slides, in-depth scientific articles, summary diagrams) and for formative self-assessment quizzes.
• Interactive teaching moments (guided questions, quick-response questions during lectures) to promote active participation and ongoing monitoring of learning.
• Possible seminar-style deep dives into frontier topics in molecular pathology (e.g. precision medicine, liquid biopsy), depending on schedule availability.

Textbook and teaching resource

Recommended Textbooks
• Kumar V., Abbas A.K., Aster J.C. — Robbins and Cotran Pathologic Basis of Disease, 10th Edition, Elsevier (main reference textbook).
• Pontieri G.M. — Patologia Generale, Piccin (supplementary text for general pathophysiology topics).
• Abbas A.K., Lichtman A.H., Pillai S. — Cellular and Molecular Immunology (latest edition), Elsevier (for the immunological foundations applied to immunopathology).

Supplementary Materials
• Lecture slides made available on the institutional e-learning platform after each lecture.
• A selection of translational medicine scientific articles (up-to-date reviews from indexed journals, e.g. Nature Reviews Disease Primers, New England Journal of Medicine) on specific topics of the programme, progressively distributed throughout the course.
• Summary diagrams and concept maps prepared by the instructor for the most complex molecular mechanisms (e.g. the caspase cascade, tumor immunoediting, immune checkpoint pathways).
• Self-assessment materials (sample multiple-choice and open-ended questions).

Semester

The Pathology and Medicine course is delivered during the **Second Semester** of the 2nd year of the Single Cycle Master's Degree Programme in Medicine and Surgery, according to the academic calendar approved annually by the Degree Programme Council. The distribution of the 30 lectures throughout the semester is planned to ensure an adequate progression of content across the five macro-modules and a suitable study interval before the examination session.

Assessment method

Examination Structure
• Written examination, consisting of a multiple-choice section (aimed at verifying the acquisition of basic knowledge across all programme topics) integrated with an open-ended question, specifically designed to assess the student's ability to establish well-reasoned connections between molecular mechanism and pathological manifestation (molecule-to-pathology connection). The minimum passing threshold for the written examination is set at 60% of the overall score.
• Oral examination, to be taken after passing the written examination, aimed at verifying the student's ability to

present pathogenetic mechanisms coherently, to integrate knowledge from different modules of the programme (e.g. cell injury, inflammation, immunopathology, molecular oncology), and to critically discuss the clinical-diagnostic implications of the mechanisms studied.

Grading Criteria
The final grade is expressed on a 30-point scale (trentesimi), with the possible award of honours (lode) for outstanding performance. The final grade takes into account the following criteria:
• Correctness and completeness of the knowledge demonstrated in the written test and oral examination.
• Ability to establish well-reasoned connections between molecular/biochemical mechanism and pathological manifestation (a criterion specifically assessed in the open-ended question).
• Ability to integrate reasoning across the different modules of the programme (cell pathology, inflammation, immunopathology, molecular oncology, diagnostic methods).
• Appropriate scientific language and clarity of presentation during the oral examination.
• Honours (lode) are awarded when, in addition to fully meeting the above criteria, the student demonstrates particular critical judgement and the ability to make interdisciplinary connections, including with reference to the scientific papers discussed during the course.

Office hours

The instructor is available to meet students according to the following modalities:
• Weekly in-person office hours, by appointment arranged via institutional e-mail, at the instructor's office.
• Availability for remote consultations (videoconference via the institutional platform), upon reasoned request arranged in advance.
• Asynchronous communication via institutional e-mail and via the messaging tools of the course's e-learning platform, with a response guaranteed within ordinary technical timeframes.
• The weekly in-person office hours schedule is communicated at the beginning of each semester via the Department website and the course's e-learning platform, and is subject to updates in case of overlap with other institutional commitments.

Sustainable Development Goals

GOOD HEALTH AND WELL-BEING | QUALITY EDUCATION | INDUSTRY, INNOVATION AND INFRASTRUCTURE | REDUCED INEQUALITIES | PARTNERSHIPS FOR THE GOALS