MEDICINE AND SURGERY

Course: Mechanisms of disease
Year (1st-2nd-3rd-4th-5th-6th): 2nd
Period (1st-2nd semester – annual): _annual
Credits: 22

Objectives

Knowledge and understanding:

The course will offer an integrated introduction to causes of cell, tissue and organ injury (cellular pathology) and the major genetic causes and microbial agents that cause human diseases (medical genetics and microbiology), the principal mechanisms of responses to injury and defense (inflammation and immunity), and the general processes of the most relevant causes of human diseases (immunopathology, vascular pathology and oncology).

Application of knowledge and understanding:

At the end of the course students will gain understanding of:

- how the body reacts to physical and biological agents to recover homeostasis
- general pathological mechanisms leading to cell injury and death
- molecular and cellular basis for inflammatory disease states
- normal and abnormal functions of the innate and adaptive immune system
- body's immune reactions to infections
- molecular basis for neoplastic disease
- pathological mechanisms leading to thrombosis, atherosclerosis, ischemia, infarction

Making judgements; Communication skills; Learning skills.

By the end of the course students will have

- developed some abilities to communicate and work in team
- acquired some learning skills such as study in a group, organize knowledge, revise and retain information, select information.

Prerequisites

Knowledge of cell biology, cell physiology, histology and anatomy

Contents

The course can be divided into 5 modules: general pathology (cellular pathology, innate immunity and inflammation, vascular pathology) microbiology (basic and clinical), immunology and immunopathology, tumor biology and medical genetics. The syllabus is organized by learning outcomes specific for each lecture or for a group of lectures

FIRST SEMESTER

CELLULAR PATHOLOGY (prof Raffaella Bonecchi)

Learning objectives

At the end of these lectures and activities, students should be able to

- Discuss the pathogenesis of hyperplasia, hypertrophy, atrophy, and metaplasia, and compare and contrast their possible physiologic and pathologic causes.
- Explain causes of cellular injury and describe cellular alterations during injury
- Demonstrate understanding of cellular changes during injury and cell death

Lessons

1. **Mechanisms of cellular adaptation**

- Adaptation of cellular growth and differentiation
- Hypertrophy, hyperplasia, atrophy, metaplasia

PPP portfolio: Chest pain (cardiac hypertrophy), Abnormal vaginal bleeding (Endometrial hyperplasia)

2. Cell injury and cell death

- Causes of cell injury
- Hypoxia exposure and ATP depletion
- Oxidative stress and damage from reactive oxygen species
- Nitrosative stress and damage from reactive nitrogen species
- Mitochondrial damage

3. Programmed cell death

- Apoptosis
- Necroptosis, pyroptosis and autophagy

4. Recap on cell pathology

INNATE IMMUNITY AND INFLAMMATION (prof Raffaella Bonecchi, prof Alberto Mantovani, prof Seppo Meri)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe and discuss each of the following cell type in terms of the associated type of inflammation and their role therein: mast cells/basophils neutrophils and eosinophils monocytes/macrophages, NK cells and dendritic cells
- Describe the classic vascular changes and cellular events of the acute inflammation and and discuss the receptors and ligands that are responsible for these events.
- Define and use in proper context: abscess, chemotaxis, cytokine, edema, exudate, granulation tissue, granuloma, inflammation, margination, phagocytosis, purulent, pus, pyogenic, resolution, transudate, ulcer.
- Discuss the following chemical mediators of inflammation, in terms of origin (cells vs. plasma) and chief in vivo functions: vasoactive amines, complement system, arachidonic acid metabolites, platelet activating factor, cytokines/chemokines nitric oxide, lysosomal granule contents oxygen-derived free radicals
- Describe the steps involved in the isolation and destruction of an infectious agent by cells of the innate immunity. Describe important molecules involved in the process (opsonins, phagocytic receptors)
- Compare and contrast acute, chronic, and granulomatous inflammation in terms of: etiology, pathogenesis, histologic appearance, laboratory findings, characteristic cells involved, outcome, systemic effects.
- Describe the phases of tissue repair and cutaneous wound healing, the mechanisms of healing by first intention (primary union) and second intention (secondary union) and possible clinical consequences of abnormal wound healing.

Lessons

1. Origin of innate immune cells: hematopoiesis (Bonecchi)

- The hematopoietic niche
- The hematopoietic stem cell
- Hematopoietic lineages
- Cytokines and growth factors
- The normal blood counts
- Leukocytosis and leukopenia

2. The acute inflammatory response (Mantovani)

- Cardinal signs of acute inflammation
- Blood flow alterations and vascular permeability
- The endothelium as a reactive biological structure

3. Collaborative lesson on cells mediators of inflammation (Bonecchi-Jaillon)

- Mast cells
- Neutrophils
- Macrophages
- NK cells

4. Soluble mediators of inflammation (Bonecchi)

- Molecular mediators active on vessels
- Molecular mediators active on leukocytes
- Primary inflammatory cytokines
- Eicosanoids

PPP portfolio: fever

5. Chemokines and leukocyte recruitment (Bonecchi)

- Adhesion molecules and cell adhesion
- Migration and chemoattractants

6. Pathogen recognition in innate immunity (Mantovani)

- Pathogen-Associated Molecular Patterns
- Structure and signalling properties of Pattern Recognition Receptors
- Structure and signalling properties of opsonic receptors
- Pentraxins
- Genetic defects in pathogen recognition
- Danger-Associated Molecular Patterns and their receptors

7. The complement system (Seppo Meri)

- Activation pathways
- Functions
- Regulatory mechanisms
- Genetic defects in the complement system

8. Pathogen killing (Bonecchi)

- Mechanisms of cell-mediated cytotoxicity
- Phagocytosis and degranulation
- Oxygen-dependent mechanisms
- Oxygen-independent mechanisms
- Opsonic agents
- Genetic defects in pathogen killing

9. Resolution of the inflammatory response (Bonecchi)

- Anti-inflammatory cytokines
- Tissue repair and fibrosis

10. Chronic inflammation, fibrosis and tissue renewal (Bonecchi)

- Cellular and molecular effectors of chronic inflammation
- The chronic inflammatory response and immune polarization
- Fibrosis
- Stem cells and tissue renewal
- Growth factors and tissue regeneration

11. Acute phase reaction and systemic inflammation (Mantovani)

a. Fever
b. Leukocytosis
c. Acute phase proteins

PPP portfolio: Fever; shock, rush

12. **Collaborative lesson on sepsis (**Bonecchi, Mantovani and Garlanda**)**

13. **Recap lesson on inflammation (**Bonecchi**)**

14. **Small groups activity on WHIM syndrome** (Bonecchi, Kallikourdis)

BASIC CONCEPTS OF MICROBIOLOGY (Prof Cecilia Garlanda)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe the general categories of infective agents including bacteria, viruses, fungi, and parasites.
- Discuss the pathogenesis of infectious diseases by different types of microorganisms and compare and contrast their pathologic causes.

Lessons:

1 - Brief history of microbiology: from the early years of Microbiology, to the Golden and Modern ages of Microbiology. To describe how the discovery of the existence of microbes impacted on human life and survival.

2 - To describe cell structure and function in prokaryotic and eukaryotic cells: external structures, cell wall and Cytoplasm of bacterial and eukaryotic cells. To describe the relevance in the pathogenesis of infections.
PPP: fever, shock

3 - To describe major techniques to perform Microscopy and microbial staining

4 - To describe Microbe classification, Microbial nutrition and growth, metabolism, Growth requirements. To describe how Culturing microorganisms.

5 - To describe how we can Control microbial growth in the environment through physical and chemical methods, and in the body through antimicrobial drugs. To describe the mechanisms of action of principal classes of antimicrobial drugs and the resistance to antimicrobial drugs.

6 - To characterize and classify prokaryotes: To describe General characteristics and Modern classification of bacteria relevant in medical microbiology.

7 - To characterize and classify eukaryotes: To describe General characteristics of Protozoa and Fungi relevant in medical mycology, Parasitic helmints, and Insects
8 - To characterize and classify viruses, viroids and prions: To describe General characteristics, Classification, Replication and culture of viruses. To describe Viroids and Prions

9 - To describe mechanisms of Infection, characteristics of infectious diseases and the principles of epidemiology. To describe principles of Immunization and immune testing

MEDICAL MICROBIOLOGY (prof Cecilia Garlanda)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe Gram positive bacteria and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations
- Compare mechanisms characteristic of infection with particular categories of bacteria.
- Describe Gram negative bacteria and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations

Lessons

1 - Pathogenic Gram-positive bacteria

- Staphylococcus
- Streptococcus

PPP portfolio: cough, rash, fever, chest pain, shortness of breath, abdominal pain, loss of consciousness, shock, sore throat, diarrhea, headache.

2 - Pathogenic Gram-positive bacteria

- Enterococcus
- Bacillus
- Clostridium
- Listeria
- Micoplasma

PPP portfolio: cough, fever, chest pain, shortness of breath, abdominal pain, loss of consciousness, shock, diarrhea, dysuria.

3 - Pathogenic Gram-positive bacteria

- Corynebacterium
- Propionibacterium
- Mycobacterium
- Nocardia and Actinomyces

PPP portfolio: cough, rash, fever, chest pain, shortness of breath, sore throat, unexplained weight loss.

4 - Pathogenic Gram-negative cocci

- Neisseria

PPP portfolio: abnormal vaginal discharge, rash, fever, pelvic pain, loss of consciousness, shock, sore throat, headache, seizure.

5 - Pathogenic Gram-negative bacilli

- Anaerobic bacilli: Opportunistic Enterobacteriaceae

PPP portfolio: cough, rash, fever, chest pain, shortness of breath, abdominal pain, shock, diarrhea, dysuria.

6 - Pathogenic Gram-negative bacilli

- Anaerobic bacilli: Pathogenic Enterobacteriaceae, Pasteurellaceae

PPP portfolio: fever, abdominal pain, diarrhea, loss of consciousness, headache, seizure, cough, chest pain, shortness of breath.

7 - Pathogenic Gram-negative bacilli

- Aerobic bacilli: Bartonella, Brucella, Bordetella, Burkholderia, Pseudomonads
- Francisella, Legionella, Coxiella
- Anaerobic bacilli: Bacteroides, Prevotella

PPP portfolio: cough, fever, chest pain, shortness of breath, dysuria, abdominal pain, diarrhea.

MEDICAL GENETICS (prof. Rosanna Asselta)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe apparently unexplained phenomena now enclosed in the term Epigenetics
- Describe the Waddington epigenetic landscape
- Learn the difference between epigenetic and genetic modification
- Describe the enzymatic pathways responsible for DNA methylation
- Describe different functions of DNA methylation
- Describe the developmental process from the DNA methylation point of view
- Describe how genomic imprinting works
- Learn the most common genetic diseases associated with genomic imprinting problems
- Understand the different mechanisms leading to UPD
- Describe the enzymatic pathways responsible for histone modifications
- Understand the concept of "Histone code"
- Learn the most common genetic diseases associated with aberrant pattern of histone modifications
- Describe the organization of the nucleus, in terms of pores, lamina, and internal structures/granules
- Describe chromosome territories and TADs
- Learn the most common genetic diseases associated with a disorganization of the nucleus structure
- Describe the most common classes of Regulatory RNAs
- Learn the basic modes of sex determination
- Describe the molecular mechanisms leading to X inactivation
- Describe how environmental factors can influence the epigenome
- Describe the basic molecular mechanism leading to cancer
- Describe the genetic landscape of cancers
- Describe the most common inherited cancer syndromes and their molecular mechanisms
- Learn the basic steps that are taken during a genetic counselling for cancer predisposition
- Being able to distinguish differences between FISH, NGS, dPCR (etc)
- Learn the concept of liquid biopsy
- Describe the biogenesis of microRNA
- Describe the 4 main mechanisms leading to miRNA-based genetic disorders
- Being able to explain the CeRNA hypothesis
- Acquire confidence with online tools for medical doctor and researchers in the field of molecular genetics

Lessons

1. Epigenetics: principal mechanisms and factors

- DNA methylation and hydroxymethylation
- Histone and chromatin modifications
- Non-coding RNA
- RNA editing

2. Epigenetic regulation during development

- Genomic imprinting
- Uniparental disomy; mechanisms and examples

3. **X-inactivation and sex determination**

4. **Genetics of cancer – basic principles**

5. **RNA-based disease**

PPP portfolio: Abnormalities of Mood (How the environment and the epigenome can influence mood), Obesity (Prader-Willi Syndrome)

ADAPTIVE IMMUNITY (KALLIKOURDIS)

Learning Objectives

At the end of the lecture course, students should be able to:

- Understand and explain to others the function of adaptive immunity, *with all its associated features and physiopathological facets* (see below).
- Understand the key biological problems that drove the evolutionary selection of adaptive immunity as an answer to these problems.
- Be able to identify mechanisms driven by adaptive immunity when faced with a complex clinical problem.

LECTURES:

1. Introduction to adaptive immunity:
- key concepts

2. MHC, antigen processing and presentation:
- Intro and link to other lectures
- Initiation of adaptive responses
- Antigen presentation; lymph nodes
- Nomenclature and historic overview of MHC studies
- Haplotypes
- Dominant epitopes; superantigens
- Topology issues
- MHC processing for Class I and Class II
- Cross-presentation.

3. Dendritic cells/antigen presenting cells (delivered by Prof Bonecchi)
- Origin and heterogeneity of dendritic cells
- Maturation and function
- Clinical use.

4. T cell development and functions - Lecture 1
- T cell development
- Generation of T cell receptor diversity
- Assembly of the mature TCR
- Thymic selection (an introduction)
- T cell signalling (T cell activation).

5. T cell development and functions - Lecture 2
- T cell functions
- Immune synapses
- Costimulation - checkpoint blockade
- Cytotoxic function.

6. B cell development and functions - Lecture 1

- BCR diversification
- B cell development

7. B cell development and functions - Lecture 2

- Th-B cell interactions; germinal centers
- affinity maturation/somatic hypermutation, class-switch recombination, AID and Neuberger.
- class switching and polarization of responses
- Memory B cells
- Antibody structure and function; integration with innate immunity
- Monoclonal antibodies and Cesar Milstein; uses in diagnostics and therapy; patent of the technology
- Humanized monoclonal antibodies; Neuberger and Winter
- Future directions of monoclonal antibody technologies, bispecific antibodies, fully humanized antibodies.

8. Polarization and memory:

- Th1 Th2 Th17, innate/adaptive immunity coordination
- Nomenclature issues on M2-like vs Th2 and Treg
- Development and function of polarized responses
- Clinical examples
- Autoimmunity
- Allergy (Atopy)
- Memory responses
- Vaccines

PPP portfolio: obesity, rash, shock

9. Tolerance and negative regulation of immune responses:

- Central tolerance; Peripheral tolerance
- Intracellular mechanisms of immunoregulation: via signaling; via degradation; via inhibition of costimulation
- Mechanisms of peripheral tolerance at the level of cell-cell interactions
- Treg cells
- Other suppressive populations

PPP portfolio: Rash, Chest Pain, Shock, Cough, Shortness of Breath or Dyspnea, Sore Throat

10A. Small Team Work – Flipped Classroom: Immunological issues in reproduction

10B. Immunology of pregnancy:

- Immune evasion mechanisms
- Medawar
- Treg
- Consequences of maternal-fetal tolerance for the evolution of immune system control

MUCOSAL IMMUNE SYSTEM AND MICROBIOTA (Rescigno)

At the end of the lecture course, students should be able to:

- Understand the structure of the mucosal immune system (the sites where the response is initiated)
- Understand how immune responses are initiated or repressed at mucosal sites
- Understand how immune homeostasis is carried out at mucosal sites.
- Understand the bases of several disorders initiated at mucosal surfaces (allergies, asthma, metabolic disorder, etc.)
- Understand what is the microbiota, its activities on our well-being and how we tolerate

1. **Development and structure of Mucosal tissue**
   - Description of the mucosal associated lymphoid tissues
   - Nasal associated lymphoid tissue (NALT), Waldeyer's ring
   - Broncho-alveolar associated lymphoid tissue (BALT),
   - Gut associated lymphoid tissue (GALT), Peyer's Patches, Isolated lymphoid follicles
2. **Cellular constituents of the mucosal immune system I: Epithelial cells and antigen uptake**
   - Epithelial cells,
   - Bile acids and enterohepatic circulation,
   - Antigen uptake
   - Initiation of oral tolerance to food
3. **Cellular constituents of the mucosal immune system II**
   - Intraepithelial lymphocytes, dendritic cells, macrophages, Mast cells and neutrophils
   - Atypical CD8 T cells
   - gd T cells
   - iNK T cells
   - Innate lymphoid cells
   - ILC and chronic disorders
4. **Lymphocyte trafficking and oral tolerance**
   - Lamina propria lymphocytes
   - T regulatory cells (thymus derived and peripherally derived)
   - T regulatory cells and IBD
5. **ASTHMA**
   - Pathogenesis
   - Allergic and non-allergic airway inflammation
   - Atopic dermatitis and atopic rash
6. **The Microbiota and its impact on immune responses**
   - What it is
   - How to analyse the microbiota
   - Microbiota and Th17 and Tregs
   - Th17 and brain disorders
7. **The Microbiota and cancer**
   - How the microbiota impact on cancer
   - Protumorigenic and anti-tumorigenic bacteria
   - Microbiota and cancer treatment

PPP portfolio: food intolerance, celiac disease, inflammatory bowel disease, NAFLD/NASH, colorectal cancer, hepatocellular carcinoma, neurodegenerative disorders

MODULE OF IMMUNOPATHOLOGY (MANTOVANI e JAILLON)

Learning Objectives

At the end of the lecture course, students should:

- be able to understand and explain the general mechanisms and effector functions of the immune system.
- be able to understand and explain the causes and the pathogenesis of the main alterations of the immune response.
- be able to understand and explain the mechanisms involved in the rejection of tissue transplants.
- be able to understand and explain the mechanisms involved in the alterations of the immune system in tumors and the principles of immunotherapy.

- be able to understand and explain the importance of biomedical research in immunopathology and cancer.

1. Hypersensitivity reactions (1) (Jaillon)
- Overview of the normal immune response
- Classification of hypersensitivity diseases
- Immediate (type I) hypersensitivity

PPP portfolio: Rash, Chest Pain, Shock, Cough, Shortness of Breath or Dyspnea, Sore Throat

2. Hypersensitivity reactions (2) and autoimmune diseases (Jaillon)
- Antibody-mediated (type II) hypersensitivity
- Immune complex-mediated (type III) hypersensitivity
- T cell-mediated (type IV) hypersensitivity
- Autoimmune diseases: The central and peripheral tolerance
- Mechanisms of autoimmunity
- General features of the most common autoimmune diseases (Systemic Lupus Erythematosus)

PPP portfolio: Rash, Jaundice, Chest Pain, Fever, Shortness of Breath or Dyspnea

3. Rejection of tissue transplants and immunodeficiency syndromes (Jaillon)
- Rejection of tissue transplants: Generalities and definition, Type of rejection reactions
- Graft-versus-host disease
- Immunodeficiency syndromes: Primary immunodeficiencies
- Primary immunodeficiencies: Defect in innate immunity
- Primary immunodeficiencies: Defect in adaptive immunity
- Secondary immunodeficencies: Acquired immune deficiency syndrome (AIDS)

PPP portfolio: Rash, Chest Pain, Fever, Cough

4 Vaccines (Mantovani)

5. Immune responses to tumors and principles of cancer immunotherapy (Jaillon)
- Introduction
- The immunosurveillance hypothesis
- Defensive mechanisms against tumors
- Mechanisms of cancer immune evasion
- Cancer immunoediting
- Principles of cancer immunotherapy (antibodies, inhibitors of immune checkpoints, CAR-T cells)

6.Inflammation and cancer (Mantovani)
- Epidemiologic evidence
- Myeloid-derived suppressor cells
- Tumor-associated macrophages: origin and function
- Tumor-associated neutrophils

7. Innate immunity in translational medicine (Jaillon)
- Recognition and elimination of pathogens
- Role of neutrophils in tumors and response to therapy

MEDICAL MICROBIOLOGY (GARLANDA)

Microorganisms involved in human diseases: description of the microorganisms (bacteria, fungi, viruses, parasites), mechanisms of disease, major clinical consequences, epidemiology.

Learning goals:

1 - **To describe Pathogenic**

- Rickettsias
- Chlamydias
- Spirochetes (Treponema, Borrelia, Leptospira)
- Vibrios (Vibrio, Campylobacter, Helicobacter)

PPP portfolio: rash, fever, cough, chest pain, abdominal pain, dysuria, loss of consciousness, diarrhea, headache.

2- **To describe Pathogenic fungi**

- Systemic mycoses caused by pathogenic fungi (Histoplasmosis, Blastomycosis, Coccidioidomycosis, Paracoccidioidomycosis)
- Systemic mycoses caused by opportunistic fungi (Pneumocystis, Candidiasis, Aspergillosis, Cryptococcosis, Zygomycosis)
- Cutaneous and subcutaneous mycosis
- Fungal intoxications and allergies

PPP portfolio: cough, rash, fever, chest pain, shortness of breath, loss of consciousness.

3 - Revising mechanism of pathogenesis of viruses

4 - To describe Pathogenic DNA viruses

- Poxviridae (Smallpox, Molluscum contagiosum)
- Herpesviridae (Varicella-Zoster, Epstain-Barr, Cytomegalovirus)
- Papillomaviridae (Papillomavirus)
- Polyomaviridae (Polyomavirus)
- Adenoviridae
- Hepadnaviridae (Hepatitis B)
- Parvoviridae

PPP portfolio: cough, rash, fever, chest pain, shortness of breath, abdominal pain, loss of consciousness, sore throat, headache, jaundice.

5 - To describe Pathogenic RNA viruses

- Nacked, positive ssRNA viruses: Picornaviridae, Caliciviridae, Astroviridae, Hepeviridae (Rhinoviruses, Enteroviruses, Hepatitis A, Hepatitis E)
- Enveloped positive ssRNA viruses with reverse transcriptase: Retroviridae (Lentiviruses-HIV)
- Enveloped unsegmented negative ssRNA viruses: Paramixoviridae, Rhabdoviridae, Filoviridae (Measles, Parainfluenza, Mumps, Respiratory syncitial virus, Rabies, Hemorragic fevers)
- Enveloped positive ssRNA viruses: Togaviridae, Flaviviridae, Coronaviridae
- Enveloped segmented negative ssRNA viruses: Bunyaviridae, Arenaviridae.
- Enveloped segmented negative ssRNA viruses: Orthomyxoviridae (Influenza)
- Nacked segmented dsRNA viruses: Reoviridae (Rotavirus, Coltiviruses)

PPP portfolio: cough, rash, fever, chest pain, shortness of breath, abdominal pain, loss of consciousness, shock, sore throat, diarrhea, headache, unexplained weight loss, jaundice, seizure.

6 - To describe pathogenic parasites (Meri)

To describe the epidemiology of the more important protozoan and helminthic parasites, life cycles, mechanisms of disease.

- Parasites protozoa (Apicomplexans: malaria)
- Parasites protozoa (Ciliates, Amoebae, Flagellates)
- Parasites (Helminths and Arthropod vectors)

PPP portfolio: cough, rash, fever, abdominal pain, loss of consciousness, diarrhea, headache, unexplained weight loss, jaundice, seizure, vaginal discharge.

7 - Collaborative lessons

Small group - Infections and cancer: Helicobacter, HPV, HBV, HCV (Garlanda, Jaillon, Kallikourdis, Bonecchi)

Small group - COVID 19 (Garlanda, Jaillon, Bonecchi)

MODULE OF TUMOR CELL BIOLOGY (JAILLON)

Learning Objectives

At the end of the lecture course, students should:

- be able to understand and explain the differences between benign and malignant tumors and their relative characteristics.
- be able to understand and explain the hallmarks of cancer.
- be able to understand the molecular and cellular mechanisms that lead to cancer.
- be able to give an overview of the cancer problem, the modern view on what cancer is, from a basic to a clinical perspective (staging and grading systems, cachexia, praneoplastic syndromes)

1. Introduction to tumors

- Definition
- Nomenclature
- Benign and malignant neoplasms
- Epidemiology of cancer

PPP portfolio: Obesity

2. Characteristics of benign and malignant tumors

- Differentiation and anaplasia. Metaplasia and dysplasia.
- Local invasion
- Metastasis, pathways of spread

3. Molecular basis of cancer 1

- Cellular and molecular hallmarks of cancer
- Genetic and epigenetic alterations
- Oncogenes and proto-oncogenes

4. Molecular basis of cancer 2

- Tumor suppressor genes
- Evasion of apoptosis
- Evasion of immune destruction
- Genome instability
- Metabolic alterations

5. Clinical aspect of patients with tumors

- Characteristics of neoplastic cachexia
- Paraneoplastic syndromes
- Grading and staging of tumors

PPP portfolio: Abdominal Pain, Chest Pain, Jaundice, Unexplained weight loss, Obesity, Abnormalities of Mood

VASCULAR PATHOLOGY (Bonecchi)

1. Angiogenesis

- Multipotent endothelial cells
- Angiogenesis and vasculogenesis
- Angiogenetic cytokines and their receptors

2. Tumor angiogenesis

- Role of angiogenesis to tumor survival and growth
- Soluble angiogenic factors and chemokines
- Endothelial progenitor cells and other relevant bone marrow-derived cells
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3 Hemostasis and coagulation

- Platelets
- Primary and secondary emostasis
- Coagulation cascade
- Fibrinolitic system

4. Thrombotic diseases

- Thrombus formation and evolution
- Clinical manifestations

5. Atherosclerosis

- Mechanisms of plaque generation
- Risk factors
- Clinical manifestations and complications

Teaching Methods

Lectures: the main purpose of lectures is to transfer knowledge to students by guiding them through the most relevant subjects of the disciplines. Collaborative lessons with teachers of the course and recap lessons will be done in order to increase the integration of the different modules. All lectures will be held synchronously, either in presence or using Teams.

Group work activities/activation of knowledge: the purpose of these activities is to activate and solidify knowledge acquired during lectures and independent study, in a collaborative learning setting. For these activities, students will be divided in groups that will remain the same through the semester. Participation is mandatory. Student that cannot be on Campus for reasons related to the pandemics will participate in teams.

Problem based learning (PBL) during each semester a PBL will be presented and discussed with students.

Students are encouraged to actively participate to the lectures with questions and comments.

Verification of learning

Exam

Students' evaluation will be assessed through multiple choice examinations at the end of the year. The faculty reserves the possibility to have also a intermediate test (optional) at the end of the first semester and an oral exam.

Intermediate Tests content

Content of IT1: (31 q): general pathology: cellular pathology + innate immunity (15q), microbiology (10q), medical genetics (6q)

Content of IT2 (35q): General pathology: vascular pathology (3q), microbiology (8q), immunology and immunopathology (17q), tumor biology (7q).

The content of the module of mucosal immune system and microbiota will be assessed in the immunology and microbiology questions.

ITs evaluation: each correct answer 0.5 points.

To pass the test you need to answer to at least 18 questions correctly with a threshold of 60% for each module

End of Semester Full Exam content and evaluation

Content of Full Exam (66 questions): general pathology (18q), microbiology (18 q), medical genetics and tumor cell biology (13q) immunology and immunopathology (17q).

Questions will include the whole program of the course

Full exam evaluation: 66 questions, each question 0.5 points.

To pass the test you need to answer to at least 36 questions correctly.

66 correct answers = 30 lode

A minimum of 60% correct answers in general pathology (10q), microbiology (10 q), medical genetics and tumor cell biology (7q) immunology and immunopathology (9q).

Texts

- Robbins, Pathological Basis of disease, 10th edition, 2020; Elsevier
- Cellular and molecular immunology 9th edition, 2017; Elsevier
- Bauman RW, Microbiology with Diseases by Taxonomy, 6th edition, Pearson