UNIVERSITÀ DEGLI STUDI DI MILANO

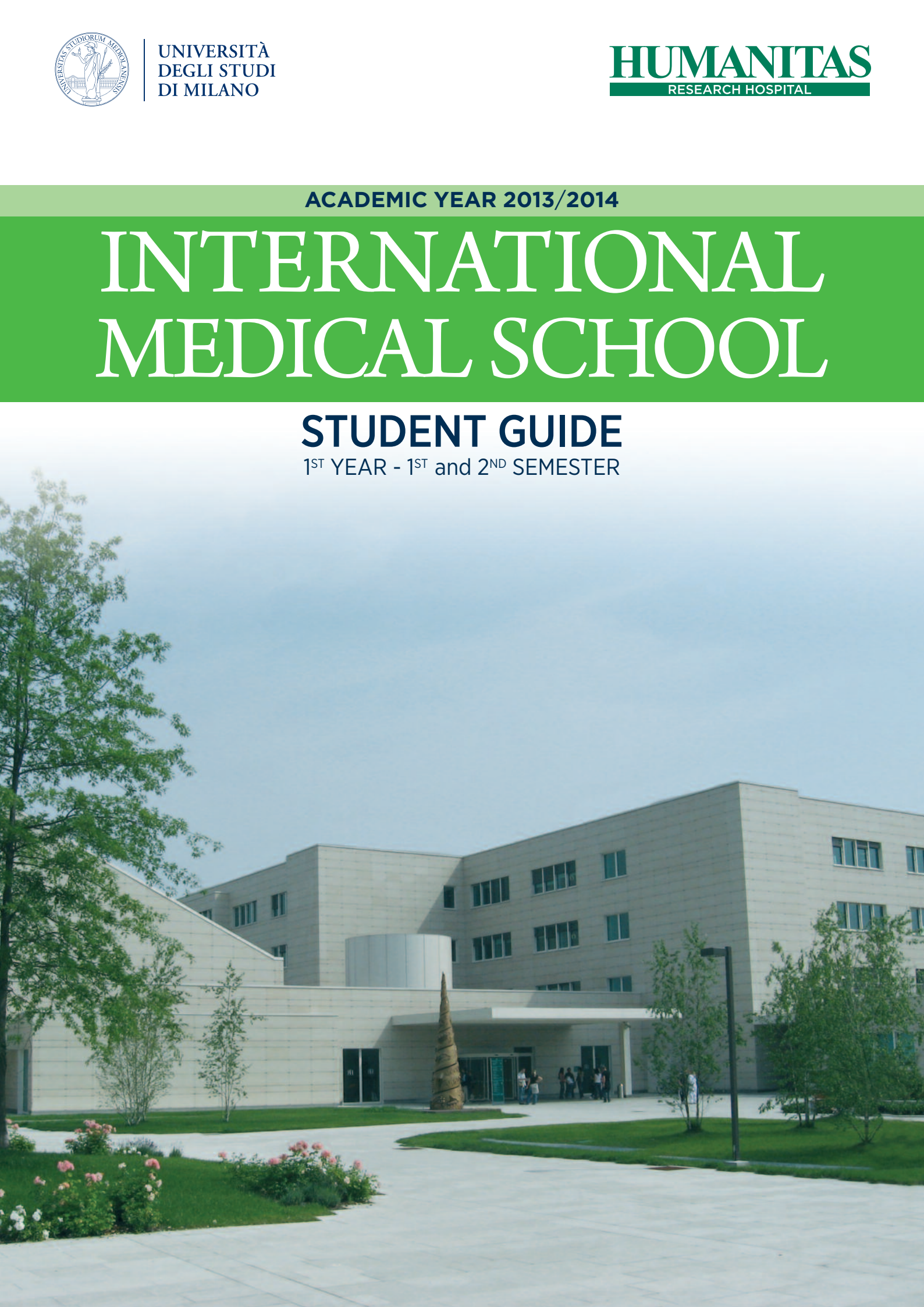
HUMANITAS RESEARCH HOSPITAL

ACADEMIC YEAR 2013/2014

INTERNATIONAL MEDICAL SCHOOL

STUDENT GUIDE

1ST YEAR - 1ST and 2ND SEMESTER



CONTENTS

1. INTRODUCTION TO MEDICAL PROFESSION

INTRODUCTION TO THE MEDICAL PROFESSION

Faculty: Bertazzi, Boniolo, Lippi, Selmi, Podda and Zannini.
Tutors: Montagna, Lleo, Oldani, Weber.

Year/Semester

1st year (1st semester)

Textbook

Magner L.N. *A History of Medicine* (second edition), Taylor & Francis Group, 2005, chapters: 1, 2 (Egypt only), 4-6, 9-14.
Furthermore, some journal articles will be provided during lessons and a pdf copy of them will be available on the course website: http://lzanniniIMP.ariel.ctu.unimi.it (please note that you can enter the course web site using your UNIMI e-mail address and your password).

Credits

4

Overview

This block is aimed at introducing medical students to doctoring and professionalism in medical practice. Since medical professionalism features not only knowledge and technical skills but also communication skills, responsiveness to patients and society, tolerance of ambiguity and anxiety, respect for patients and attentiveness, critical curiosity and reflection, students will also be trained in a narrative-based perspective. This means that role playing and film will be used in scheduled workshops as a fundamental tool for training students to 'read' the patient and his/her experience and to analyse their personal reactions to illness and suffering. Furthermore, students (mentored by doctors) will be given the opportunity to observe patients in the clinical context to deepen the illness experience. They will be asked to keep a journal of their short but significant clinical experience, since reflective writing has shown to be an essential tool in developing reflection in healthcare students/professionals and therefore professionalism.

Teaching methods

The block fosters active learning and places emphasis on a reflective approach. In addition to lectures, medical humanities workshops (based on discussion, film etc.) will be held to activate students' reflection on many topics related to the medical profession. Furthermore, students will be required to keep a journal of their brief observational experience in the clinical setting. Some extracts of these journals will be discussed in a small groups session, facilitated by the course tutors.

EXAMS

The exam consists of two steps:

1. a written short essay (minimum 500 words, maximum 1000) based on the ward experience that the student will write at home. This essay must be a reflective exercise on the early clinical experience of the student. Students will be trained on how to write the short essay during a workshop dedicated to this topic (see workshop C).
   The essay must delivered to the course coordinator (Prof. Lucia Zannini) during the last encounter, that will be held on December, the 17th. The student will deliver a printed copy of his/her essay, no electronic formats will be admitted. If the student will not be able to participate to the last encounter, he/she will have to deliver a printed copy of his/her essay to the Secretary (Micaela Filiberti), within the end of December 2013.
   The essay will receive a judgment by the teachers (insufficient, fair, good excellent) and not a mark. If the student will not deliver his/her essay within the end of December 2013, he/she will not be admitted to the exam.

2. *a written test* (about 60 multiple choice questions) that will be focused on the topics presented during the course's lessons (History of medicine, Internal medicine, Occupational/environmental medicine, Pedagogy, Philosophy of science,) and on the information contained in the textbook. The written test is aimed at verifying the achievement of some learning objectives by the students.

Timing and general organization of the exams

1st semester

In case students don't pass the summative exam in January they can take the exam in February.

Students who don't pass the exam in February can take the exam at the end of the II semester (June/July or September).

REGISTRATION TO WRITTEN EXAMS THROUGH THE SIFA SYSTEM IS MANDATORY.

Lectures & Workshops

The Block consists of 9 lectures, 3 mandatory workshops (A, B, C) and 1 small groups session. Learning objectives are listed for each lesson, representing the specific knowledge that the student will show to have acquired.

1. Introduction to the course.
   What are the origins of medicine? How do we study its evolution?
   Introducing History of Medicine. *Lippi & Zannini* (October, 9th 2013, 10:30-13:30)

Introduction to the course and review of the class syllabus.
Students will deal with the different sources (paleopathological, iconographical and literary sources) used to reconstruct the History of Medicine: they will acquire a basic knowledge of the different theories concerning Medicine in the West from classical antiquity to the twentieth century,learning to work with historical sources, and how to identify and read primary sources.
Learning objectives

- Define medical professionalism and describe its different components.
- Discuss history (and humanities as a whole) as a research discipline that enriches understanding of present-day medicine.
- Stimulate a sense of scepticism with regard to the "dogma" of the rest of the medical curriculum and against a concept of progress as a continuous self-overcome.
- Illustrate the different theories concerning medicine in the West from classical antiquity to the twentieth century.
- Describe how to work with historical sources, and how to identify and read primary sources.

2. Introduction to the doctor-patient relationship and medical professionalism.
   Podda, Lleo and Montagna (October, 11th 2013, 11:30-13:30).

Analysis of a simulated doctor-patient relationship and completion of an observation grid. Taking medical notes from the diagnosis of the disease and understanding the illness experience.
Learning objectives

- Describe the general features of the doctor-patient encounter;
- Discriminate questions when taking medical histories aimed at investigating biological, psychological and sociological aspects of illness;

A. WORKSHOP: Movie analysis and discussion (attendance required). *Podda, Selmi & Zannini* (October, 16th 2013, 11:30-13:30 14:30-16:30).
Medical Interviewing Skills. Giving bad news to patients. The psychosocial impact of terminal illness. Balancing work and personal life. Training medical students and residents.

B. Workshop: Ethical dilemmas and disagreements at the patient's bedside: how to cope with them (attendance required). *Boniolo* (October, 17th 2013, 14:30-16:30).
After discussing the difference between a moral position and a moral prejudice, the topic of the decisions in cases of ethical dilemmas and disagreements concerning diagnostic or therapeutic choices will be analyses.

3. Work, environment & health. *Bertazzi* (October, 21st 2013, 11:30-13:30).

The lecture will highlight the epidemiological evidence and the mechanistic models (physiological, biochemical and molecular) that describe the tight relation linking human environment and human health. This can be made by combining historical examples of disaster occurrence (Minamata, Seveso, Chernobyl, asbestos epidemics,) and advanced knowledge on the mechanistic pathways explaining the work-environment-health relation.

Learning objectives:

- Increase awareness of the relevance that the history, the culture, and the natural, built and social environments have in the process of disease causation and health promotion for individual people and the community as a whole.
- Document the many ways in which this awareness positively affects the medical practice, in both the approach to the patient and in the diagnostic and therapeutic processes.

4. When and where did medicine emerge as a profession? The Greek world. *Lippi* (October, 22nd 2013, 11:30-13:30).

Students will explore how different ideas about medicine contribute to different types of doctor/patient interactions,. They will learn about the emergence of western medicine as a profession, the history of medical education, the role of science in shaping and legitimizing medical practice. They will learn about the medical market place and how patients have navigated their way among a range of caregivers and health professionals from the past to the present, throwing light on the so named Hippocratic oath.

Learning objectives:

- Describe how medicine moved from the idea of “disease” to “diseases”
- Discuss the Hippocratic revolution and development of “scientific medicine”
- Describe the birth of Western medical ethics

5. From Broad Street Pump to epigenetics. *Bertazzi* (October, 23rd 2013, 11:30-13:30).

The lecture will give account of the research methods that made possible the discovery of the links between environmental factors and population health, from epidemiology to molecular biology. It will describe their developments over time, discuss how they can be useful even today, and give examples of how the different research methods can be combined to gain deeper insight into the risks posed by the environment to human health.

Learning objectives:

- Provide an overview of the interactions of environmental risk factors with the genome and the epigenome in the human body.
- Overview and make acquaintance of the main research methods available to explore and describe those interactions.

6. When and where hospitals were born? *Lippi* (October, 24th 2013, 11:30-13:30).

Students will appreciate the history and evolution of health care systems, focusing on how health care came into being, understanding the forces that have shaped the management of hospitals and health systems in the past, underlining the role of the pioneers of EBM.

They will discuss various approaches to the understanding of the history of disease, realizing how both the epidemiology of diseases and ideas about them are shaped by social, economic and cultural forces, as well as by changing understandings of medical science.

Learning objectives

- Discuss the history and evolution of health care systems, focusing on how health care came into being, understanding the forces that have shaped the management of hospitals and health systems in the past, underlining the role of the pioneers of EBM.
- Discuss various approaches to the understanding of the history of disease;
- Describe how both the epidemiology of diseases and ideas about them are shaped by social, economic and cultural forces, as well as by changing understandings of medical science.

7. When did Medicine discover the "human body"? Medicine in the Renaissance and the birth of Anatomy. *Lippi* (October, 28th 2013, 14:30-16:30).

Students will understand how works of art are influenced by social, political, economic and educational factors, discussing the use of images in a medical environment. They will be requested to comment on the associations between art, medicine and health, and on their past and present, reflecting on the role of Art in Hospital in healthcare. They will start from the basic history of the practice of anatomical dissection, learning how it has been integrated into medical education and recognizing the historical

evolution of anatomy as an important component of medicine, identifying the relationship between art and anatomy and considering the different approaches of medicine as art or as science.

Learning objectives:

- Highlight fundamental changes in the approach to the study of anatomy
- Understand the critical relationship between art and medicine
- Explain the secret message of the works of art, which reveal particular aspects of medicine and society

C. Workshop: Introduction to reflective writing to enhance early clinical experience (attendance required). *Podda, Selmi and Zannini, Oldani* (November, 4th 2013, 14:30-16:30).

The role of reflection in learning from clinical practice. Writing a journal as a core strategy for learning from experience. Features of a reflexive journal. Writing exercises.

At the end of the workshop, Dr. Oldani will explain to the students the organization of the early clinical experience.

8. How did scientific discoveries of the XX century affect the modern medicine? Lippi (November, 6th 2013, 11:30-13:30).

Student will face with the epistemological revolution of the XX.th century, focusing on the shaping of the biological pattern of medicine and the causes of its current crisis.

They will acquire the awareness of history (and humanities as a whole) as a research discipline that enriches understanding of present-day medicine, together with a sense of skepticism with regard to the "dogma" of the rest of the medical curriculum and against a concept of progress as a continuous self-overcome.

Learning objectives:

- Understand the reason of criticism towards contemporary medicine
- Realize why people always more often turn to complementary medicine
- Discern special pathways to let Medical Humanities affirm themselves

9. Environmental risks today: asbestos, air pollution, chemical carcinogens. *Bertazzi* (November, 7th 2013, 16:30-18:30).

The lecture will point out which are today the most relevant environmental risk factors, either because of the severity of the effects or because of the number of people exposed to them. It will also illustrate their occurrence in different settings and populations, and their impact on the burden of disease in different countries. Students will be provided with examples on how scientific research can support public health and policy decisions.

Learning objectives:

- Practically show how critical, valid and updated information on the most relevant exogenous risk factors can be acquired.

- Review the translational potential of environmental health findings for the health of individuals and for public health policies.

10. Small groups session: Tutorials on journal writing. Prof. Zannini & tutors from the Hospital's Units (December, 17th 2013, 14:30-16:30).

Tutorials will be held when all the students have completed the observational experience in the clinical context.

Early Clinical Experience

Students will have a brief observational experience in the clinical setting: they will be divided in small groups and mentored by tutors. They will be provided with an observational grid that will help them in organizing reflections on their early clinical experience . During the observational experience, students will also be required to keep a journal, that will be discussed in the last course lecture (small groups session), facilitated by the course's tutors.

2. HUMAN BODY 1st and 2nd Semesters

HUMAN BODY

Faculty: Barajon, Dellavia, Gagliano, Sforza

Year/Semester
1st year/1st and 2nd semester, 2nd year/1st semester, 4th year /2nd semester

Credits
20

Textbooks
Moore & Dalley
Clinically Oriented Anatomy
Lippincott Williams & Wilkins, 2009

Gray's Anatomy The Anatomical Basis Of Clinical Practice
Churchill Livingstone, 2008

Gray's Anatomy for Students
Churchill Livingstone; 2 edition (February 25, 2009)

Ross and Pawlina
Histology A Text And Atlas - With Correlated Cell And Molecular Biology
Lippincott Williams & Wilkins, 2006

Wheater's Functional Histology: A Text And Colour Atlas .Barbara
Churchill Livingstone, 2006

Langman's Medical Embriology
Lippincott Williams & Wilkins; 12th Edition, 2011

Larsen's Human Embryology
Churchill Livingstone, 2008

Overview
The block addresses the organization of the human body from the cellular and tissue level (cytology and histology) to the organ/system level (anatomy), including how this organization comes into being during development (embryology).
The course integrates the systematic and topographic approach in relation to the clinical practice. The core of knowledge acquired during this block is fundamental to understand the functions and pathologies of the different organs and systems.

Part of Neuroanatomy and of Anatomy of the Head and Neck regions will be integrated in blocks of the second year (Functions) and fourth year (Neurosciences, Head and Neck).
"Clinical drops" will be introduced in the lectures to exemplify how disruption of normal development and structure leads to pathology, so underline the relevance of anatomy in clinical practice.

General learning goals

- Describe cells, cell ultrastructure, and tissues and the functional aspects in relation to the morphological organization.
- Describe gametogenesis, fertilization, the early stages of embryonic development, and the key mechanisms leading to organogenesis.
- Illustrate the main morphological events and the relevant related molecular aspects characterizing the development of the body and its various organ systems in order to acquire the vision of the adult anatomy through a dynamic developmental view and understand the basis of congenital defects
- Illustrate the structural principles underlying the functions of organs and systems
- Illustrate the general principles of the body plan at both the systematic (organs and systems) and the topographic level (regions of the body and corresponding deep spaces)

Learning/teaching methods

- Lectures
- Tutorial activities at the light microscope

EXAMS

Multiple choice tests and oral assessment, slide diagnosis at the light microscope. At the end of the first semester students will be evaluated through a multiple choice test for their ability to describe and recognize histological preparations at the light microscope. In case of failure, it will be possible to retake the test before the beginning of the second semester. A second multiple choice test will be performed at the end of the second semester. Students that will have successfully passed both tests will be admitted to the oral exam. Before each oral exam session it will be possible to retake both tests. In case of failure of the oral exam, the tests will be kept valid.

Registration to final exams is mandatory through SIFA.
Registration through SIFA is not required for intermediate tests.

Modules 1st semester

Cells and Tissues

Overview

During the module cell morphology and tissue organization of human cells and tissues will be discussed, as well as the main methods and the instruments for the morphological analysis. On this basis the morphological and structural aspects of cell and tissues will be described in relation to their functional role.

Lesson 1: Presentation of the course. Introduction to histology. From tissue sample collection to the observation at the microscope.

Learning goals:

- Describe the main techniques used in histology.
- Describe the general aspects of histological specimen processing, such as inclusion, fixation and sectioning.
- Describe the main commonly used histological and histochemical stainings.

Lesson 2: A journey through the cell: from outside to cell compartments.

Learning goals:

- Describe the structure of cell membrane and the mechanisms of transport across the cell membrane.
- Describe the specialized functions of cell membrane.
- Describe the structure of both rough and smooth endoplasmic reticulum, and know their specific functions.
- Describe the structure of the Golgi apparatus and know its functions.
- Describe the structure of ribosomes and their specific functions.
- Recognize cell membrane, endoplasmic reticulum, Golgi apparatus and ribosomes at the electron microscope level.

Lesson 3: Special topic: Instruments for morphological analysis and biomedical applications: not “simple” microscopes.

Learning goals:

- Describe the main instruments for the morphological analysis and their application in the different fields of medicine for both research and diagnostic purposes.

Lesson 4: Vesicle trafficking. Exocytosis and endocytosis. Lysosomes. Peroxisomes. Mitochondria.

Learning goals:

- Describe vesicle trafficking and the mechanisms involved in directing vesicles to the different cell compartments.
- Describe the mechanisms of endocytosis.
- Describe the mechanisms of exocytosis.
- Describe the structure of lysosomes and peroxisomes, and their specific functions.
- Recognize lysosomes and peroxisomes at the electron microscope level.
- Describe the structure of mitochondria and their functions.

- Describe mitochondria morphology and localization in relation to cell type and cell function.
- Recognize mitochondria at the electron microscope level.

Lesson 5: The cytoskeleton.
Learning goals:

- Describe microfilaments with particular attention to their arrangement in apical specializations of epithelial cells, to cell motility and to their role in cell junctions supporting.
- Describe intermediate filaments, with particular attention to their role of stabilizing structures of cell junctions.
- Describe microtubules at the morphological and functional level, with particular attention to their arrangement in apical specializations of epithelial cells.

Clinical drop: epidermolysis bullosa simplex
Clinical drop: primary ciliary dyskinesia

Lesson 6: A journey through the cell: from the nucleus to the cell cycle.
Introduction to tissues.
Learning goals:

- Describe the shape of the nucleus in relation to cell morphology.
- Describe the nucleus and chromatin arrangement.
- Describe the nuclear envelope and the structure of the nuclear pore.
- Describe the nucleolus and its functional role.
- Describe the morphological aspect of the nucleus during mitosis and apoptosis.
- Define the phases of cell cycle.
- Describe the different cell population according to their pattern of growth.
- Describe the general relationships between cells, tissue, organs and systems.
- Describe the morphological aspect of the nucleus during mitosis and apoptosis.
- Define the phases of cell cycle.
- Describe the different cell population according to their pattern of growth.
- Describe the general relationships between cells, tissue, organs and systems.

Lesson 7: Apical and basolateral specialization of epithelial cells. Cell junctions.
Learning goals:

- Describe the general aspect and function of epithelial cells.
- Describe and recognize intercellular junctions at light and electron microscope levels.
- Describe occluding, anchoring, and gap junctions in epithelial cells and in different cell types, and discuss their functions.

Clinical drop: pemphigus foliaceus
Clinical drop: epithelial-to-mesenchymal transition

Lesson 8: Lining epithelia: classification and localizations.
Learning goals:

- Describe general aspects and functions of epithelia tissue: lining and secretory epithelia.
- Describe the general aspects and function of lining epithelia.
- Describe the types and the functions of epithelial cells.
- Describe the relationship between morphology and function in epithelial cells.

- Classify the different epithelia that cover or line an organ, and describe their localization.
- Describe the structure of epidermis and the cell types that are contained.
- Describe the structure and function of the basement membrane.
- Describe stem cells in the epithelia tissue: localization recognition and function.

Lesson 9: Exocrine glands.
Learning goals:

- Describe the general aspect and function of exocrine glands.
- Distinguish unicellular from multicellular exocrine glands.
- Compare the histological aspect and microscopic structure of the major multicellular exocrine glands.
- Describe the interrelationship and functions of the intercalated duct, striated duct, and interlobular duct.

Lesson 10: Endocrine glands.
Learning goals:

- Describe the general aspect and function of endocrine glands.
- Describe the cytological and histological characteristics of the endocrine glands, and recognize their structure.
- Describe the functional role of the hypophyseal portal circulation in the regulation of pituitary secretions.
- Describe the functional role of the nervous system in coordinating the actions of the endocrine glands.

Lesson 11: Connective tissue: cellular components and extracellular matrix.
Learning goals:

- Describe the general organization of the connective tissue.
- Describe the key morphological and functional differences between epithelia and connective tissue.
- Identify the cellular components of connective tissue and describe their functional role.
- Describe the components of the extracellular matrix, and their interrelationship.

Clinical drop: extracellular matrix remodeling in tumor invasion and fibrosis

Lesson 12: Connective tissu: proper connective tissue
Learning goals:

- Illustrate the classification, the properties and typical locations of the various types of connective tissues: loose, dense regular, dense irregular, adipose, elastic, and reticular.
- Describe the localization and understand the functional roles of the different connective tissues.

Lesson 13: Specialized connective tissue: cartilage.
Learning goals:

- Describe how the cellular and extracellular components of cartilage contribute to its structure and function.
- Describe the mechanisms of cartilage growth.
- Recognize the three classifications of cartilage tissue.
- Describe the main localizations of cartilage in the human body.

Lesson 14: Specialized connective tissue: bone and osteogenesis.
Learning goals:

- Describe the cellular and extracellular components of bone, and discuss how they contribute to the structure and function of this tissue.
- Recognize the differences between compact and spongy bone, and compare their functions.
- Describe the periosteum and its functional role.
- Describe the mechanisms of bone growth.
- Describe the mechanisms of bone remodeling and repair.

Lesson 15: Specialized connective tissue: blood and hemopoiesis.
Learning goals:

- Describe the components and the general functions of blood.
- Distinguish red blood cells, white blood cells and platelets, and describe their functional role.
- Describe the cytological and histological aspect of red blood cells, white blood cells and platelets
- Describe the main steps of hemostasis.
- Describe the developmental precursors of erythrocytes, leukocytes and platelets.
- Distinguish the morphological changes that occur during differentiation into an erythrocyte and a granulocyte.

Lesson 16: Lymphoid organs (lymph nodes, spleen, thymus, tonsils).
Learning goals:

- Describe the structure of the lymph node and how it accommodates its function.
- Recognize how the structure of the spleen accommodates its function.
- Recognize how the structure of the thymus accommodates its function.
- Distinguish the structural and functional organization of the MALT.

Lesson 17: Muscle: skeletal and cardiac muscle tissues.
Learning goals:

- Describe the components of skeletal muscle, and understand their functions.
- Describe the structure of myofibrils.
- Describe the sarcomere structure and the principles of striated muscle contraction.
- Describe the arrangement of the sarcoplasmic reticulum and its function during muscle contraction.
- Recognize skeletal muscle in histological preparations.
- Distinguish the endomysium, perimysium and epimysium structure and function in a skeletal muscle.
- Distinguish the morphological criteria to recognize skeletal and cardiac muscle in histological preparations.
- Describe the functional differences between skeletal and cardiac muscle.

Lesson 18: Muscle: smooth muscle tissue. Nervous tissue (Neurons. Nerve fibers)
Learning goals:

- Illustrate the morphological criteria to recognize cardiac and smooth muscle in histological preparations.
- Discuss the functional differences between skeletal, smooth and cardiac muscle.
- Describe the main localizations of smooth muscle tissue.
- Illustrate the general principles of smooth muscle contraction.
- Describe the structure and the general function of neurons.
- Describe the structural relationships between the axon, myelin sheath, node of Ranvier, Schmidt-Lantermann clefts, and the Schwann cell.
- Describe the process of myelination and myeline function.
- Recognize nervous tissue in histological sections.
- Illustrate the general structure of a peripheral nerve.
- Distinguish the endoneurium, perineurium and epineurium of a peripheral nerve.

Lesson 19: Nervous tissue (Synapses. Neuroglia. Peripheral nerve terminals).
Learning goals:

- Describe the structure of synapses and their role in the transmission of nerve impulse
- Describe the morphology and the general function of glial cells, and their relationship with neurons.
- Describe the blood-brain barrier and its role.
- Recognize specialized sensory neuronal endings and their main localization.

Lesson 20: Principles of organ architecture.
Learning goals:

- Describe the general architecture of organs.

General Embryology

Overview

During the module the key mechanisms leading to both male and female gametogenesis, and to fertilization will be discussed, as well as the early stages of the human embryonic development.

Lesson 1: Introduction. Male gametogenesis. Testes and cycle of the seminiferous epithelium. Introduction to genital ducts.
Learning goals:

- Describe the general histological organization of the testis and epididymis.
- Describe the process of spermatogenesis.
- Distinguish the structural changes that occur in the spermatids during spermiogenesis.
- Describe the various cell types of the seminiferous tubule and of the interstitium of the testis.
- Describe the relationship between the Sertoli cells and developing sperm cells.
- Compare the structure and function of the epididymis and genital ducts.
- Describe the "blood-testis" barrier and explain why it is important.

Lesson 2: Female gametogenesis. Ovary and uterus. Maturation of follicles and menstrual cycle

Learning goals:

- Describe the histological organization of the ovaries.
- Describe the process of oogenesis, folliculogenesis, and ovulation.
- Discuss the relationship of the ovarian follicle, corpus luteum and corpus albicans.
- Illustrate the changes in the ovaries during ageing process.
- Describe those cells involved in steroid production within the ovary.
- Describe the hypothalamus-pituitary-ovarian axis and how this relates to monthly changes in the ovaries.
- Describe the general structure of the uterus and uterine tubes.
- Describe the cyclic changes of the endometrium.
- Describe the hypothalamus-pituitary-ovarian axis and how this relates to monthly changes in the uterus.

Lesson 3: Fertilization. Early stages of the embryo development. Segmentation. Morula. Blastocyst implantation

Learning goals:

- Describe the process of fertilization and the phases of zygote cleavage.
- Describe the implantation and continuation of embryonic development.
- Describe the formation of the amniotic cavity and of the embryonic disc.

Lesson 4: Embryo annexes

Learning goals:

- Describe the amniotic cavity.
- Describe the allantois.
- Describe the chorionic villi and their functional role.
- Describe the placenta and the fetal placental circulation.

Lesson 5: Gastrulation. Becoming trilaminar

Learning goals:

- Describe the role of primitive streak and primitive node and the formation of the body axes
- Developmental defects: situs inversus and Kartagener syndrome
- Describe the formation of the three primitive layers
- Describe the notochord and its role.
- Describe the formation of the neural plate and neural tube.
- Developmental defects: sirenomielia
- Describe the destiny of the neural crest
- Clinical drops: epithelio-mesenchymal transition

System Development And Organ Structure

Overview

During the module some major topics in organogenesis will be discussed as to understand the main morphological events and the related molecular aspects characterizing the development of the body and its various organ systems. On this

basis, the morphological and structural features of mature organs will be described stressing functional aspects.

Lesson 1. The 4th week: establishing the body plan. Planning is everything
Learning goals:

- Illustrate the concept of organogenesis
- Describe the destiny of the three embryonic layers
- Illustrate the concept of segmentation
- Describe the outcome of the folding of the embryo: formation of the intestinal tube, formation of the body cavities, formation of the body wall
- *Developmental defects: gastroschisis and omphalocele*
- Describe the formation and general organization of the embryonic circulation
- *Clinical drops: vasculogenesis and angiogenesis*
  Explain some basic molecular aspects characterizing the establishment of the body plan

Lesson 2. Development of the digestive system. *A place for everything and everything in its right place*
Learning goals:

- Illustrate how the different portion of the digestive system develop from the primitive gut
- Describe the positioning of the different organs in the body cavities
- *Developmental defects: congenital diaphragmatic hernia*
- Describe the formation of the peritoneum
- Explain some basics molecular aspects characterizing the histogenesis of the organs
- Illustrate the basis of the most common malformations of the digestive system
- *Developmental defects: stenosis, atresia, abnormal rotations, fistulae, diverticuli, familial adenomatous polyposis and colon cancer*

Lesson 3. Macroscopic aspects, functional architecture and structure of the esophagus, gastrointestinal tract, pancreas and liver (Part I). Through stormy seas and acid rains.
Learning goals:

- Illustrate the pharynx
- Illustrate the general structural organization of the digestive system in relation to the functions of digestion and absorption
- Illustrate the morphology of the pharynx in relation to its dual function (respiratory and digestive tracts)
- Describe the external and internal morphology of the esophagus and stomach and to know their histological structure
- Describe the cell types of the stomach glands and their function
- *Clinical drops: reflux esophagitis, pernicious anemia and peptic ulcer disease*
- Describe the distribution of gastroenteroendocrine cells and their role
- *Clinical drops: Zollinger-Ellison syndrome*

Lesson 4. Overview of the pharynx, macroscopic aspects, functional architecture and structure of the esophagus, gastrointestinal tract, pancreas and liver (Part I) : strange landscapes and narrow passageways…

Learning goals:

- Describe the external and internal morphology of the small and large intestine and to know their histological structure
- Describe the structure of the intestinal villi and crypts and the major cell types of their epithelial lining
- *Clinical drops: inflammatory bowel diseases*
- Describe the organization of the lymphoid tissue in the intestinal wall: the GALT (gut-associated lymphoid tissue
- *Clinical drops: the microbial self and the others*
- Describe the basic organization of the enteric nervous system
- *Clinical drops: Hirschsrpung's disease*
- Describe the internal morphology of the rectum and anal canal
- *Clinical drops: the epithelial transformation zone*

Lesson 5. Topic: Overview of the pharynx, Macroscopic aspects, functional architecture and structure of the esophagus, gastrointestinal tract , pancreas and liver (Part II): strange landscapes and narrow passageways...
Learning goals:

- Describe the macroscopic aspect of the liver and to discuss the organization of its parenchyma in relation to the different types of hepatic lobules
- Describe the gallbladder and the intraepatic and extrapatic billiary tracts
- *Clinical drops: the liver acinus*
- Describe the macroscopic aspect of the pancreas and discuss the organization of its parenchyma in relation to its endocrine and exocrine function
- *Clinical drops: acute pancreatitis and cystic fibrosis*

Lesson 6. Development of the lower respiratory tract. Shall we breath?
Learning goals:

- Illustrate the formation of the tracheobronchial tree and its segmental pattern
- *Developmental defects: tracheo-esophageal fistulas*
- Explain some basic molecular aspects characterizing the branching mechanism
- Describe the stages of lung maturation and their relation to breathing capacities
- Illustrate the mechanisms contributing to lung maturation
- Illustrate the basis of the most common malformations of the respiratory system
- *Clinical drops: premature birth and respiratory distress syndrome*

Lesson 7. Macroscopic aspects, functional architecture and structure of the lower respiratory tract. Every breath you take
Learning goals:

- Illustrate the outline of the respiratory pathways
- Describe the macroscopic aspects of the lungs and their lobes
- Describe the organization of the tracheo-bronchial tree
- Illustrate the histological features of the conductive portion and of the respiratory portions of the tracheobronchial tree
- *Clinical drops: asthma*
- Describe the morphofunctional aspects of the pulmonary lobule and acinus
- *Clinical drops: emphysema*
- Describe the microcirculation of the lungs

- Describe the structure of the alveoli and the structure of the gas-exchange barrier
- *Clinical drops: Acute Respiratory Distress Syndrome (ARDS)*

Lesson 8. Development of the urogenital system. Questions of water
Learning goals:

- Illustrate the formation of the three successive forms of the embryonic kidney and their destiny
- Describe the formation of the uriniferous tubule
- *Developmental defects: renal agenesia*
- Describe the positional changes of the kidney and related structures
- *Developmental defects: defects in migration and rotation of the kidneys*
- Describe the formation of the bladder and urethra
- *Developmental defects: exstrophy of the bladder, epispadia and ipospadia*
- Illustrate the development of the gonads and the establishment of their gender
- *Developmental defects: abnormalities of sexual differentiation*
- Describe the formation of the sexual duct system
- *Developmental defects: Malformations of the uterus*
- Describe the positional changes of the gonads
- *Developmental defects: cryptorchidism, congenital inguinal hernia*
- Describe the formation of the external genitalia

Lesson 9. Macroscopic aspects, functional architecture and structure of the kidney, ureters and lower urinary tract. The cathedral of water
Learning goals:

- Describe the macroscopic aspect of the kidney
- Describe the structural organization of the kidney parenchyma and its vascular supply in relation to process of blood filtration and urine production
- Describe the macrosocopic aspect and the general structure of the excretory pathways: calyxes pelvis, ureters and bladder.
- Describe the male and female urethra
- *Clinical drops: urolithiasis*

The morpho-functional description of the different segments of the nephron and collecting ducts, of the structural aspects of the filtration barrier and of the iuxta-glomerular apparatus will be integrated during the second year in the course "Functions"

Lesson 10. Macroscopic aspects, functional architecture and structure of the male and female reproductive system. Procreation and recreation
Learning goals:

- Describe the different components of the female reproductive system
- Describe the morphology of the ovary, uterine tubes, uterus and vagina
- Describe the structure of these organs and their cyclic changes
- *Clinical drops: the transformation zone of the uterine cervix and cancer*
- Describe the different components of the male reproductive system
- Describe the morphology of the testicle, epididmus, spermatic pathways and accessory glands

- Describe the main structural aspects of the epididimus, spermatic pathways and accessory glands
- Describe the different portions of the male urethra and the penis
- *Clinical drops: Prostate hyperplasia and cancer*

Lesson 11. The primordial pharynx and the pharyngeal apparatus. Once there was a fish...
Learning goals:

- Describe the pharyngeal apparatus and its relation to the primordial pharynx
- Illustrate how the different components of the pharyngeal apparatus contribute to the formation of various structures of the head and neck
- *Developmental defects: Cleft palate*
- Describe the development of the thyroid gland
- Describe the development of the thymus
- *Developmental defects: DiGeorge syndrome*
- Describe the morphology and the main structural aspects of the larynx
- Describe the most common anomalies of the pharyngeal apparatus

Lesson 12. Structure of blood vessels and lymphatic vessels. Coming and going
Learning goals:

- Describe the structure of arteries and vein in relation to their function
- *Clinical drops: atherosclerosis*
- Describe the different types of capillaries in relation to their function
- Describe the structure of lymphatic vessels
- *Clinical drops: edema*

Lesson 13. Layout of the vascular system. Home-plumbing
Learning goals:

- Describe the general layout of the arterial, venous and lymphatic system

Lesson 14. Topic: Development of the cardiovascular system, fetal circulation, neonatal circulation. The declaration of independency.
Learning goals:

- Illustrate the contribution of the heart fields and other sources to the heart formation
- Describe the formation of the heart tube and its looping
- Describe the basic events leading to the formation of the heart chambers and outflow tract
- *Developmental defects: septal defects, tetralogy of Fallot*
- Illustrate the concepts of vasculogenesis and angiogenesis in the formation of embryonic blood vessels
- Describe the general organization of the embryonic circulation and how it evolves into the fetal circulation
- Describe how the fetal circulation changes at birth
- *Developmental defects: patent ductus arteriosus*
- Describe the main congenital malformation of the heart and outflow tract

Lesson 15. Topic: Heart and pericardium. At the heart of it all.
Learning goals:

- Describe the external morphology of the heart
- Describe the internal cavities of the heart
- Describe the organization of the heart skeleton
- Describe the structure of the heart wall and the organization of the myocardium
- Describe the morphology of cardiac valves
- *Clinical drops: Heart Valve diseases*
- Describe the organization of the conductive system
- Describe the vascularization of the heart
- *Clinical drops: ischemic Heart Disease*
- Describe the morphology and structure of the pericardium

Practical/Histology 1: lining epithelia.
Learning goals:

- Describe the different components of a standard light microscope and to be able to use it.
- Describe and recognize at the microscope different simple and stratified epithelia.

Practical/Histology 2: exocrine and exocrine glands
Learning goals:

- Describe and recognize at the microscope different exocrine and endocrine glands.

Practical/Histology 3: connective tissue
Learning goals:

- Describe and recognize at the microscope different connective tissues.

Practical/Histology 4: muscle and nervous tissue.
Learning goals:

- Observe, describe and recognize at the microscope different muscle tissues.
- Observe, describe and recognize at the microscope neurons and glial cells.

Practical/Histology 5: revision of all the tissues.

- Observe, recognize and compare the different tissues.

Practical/Histology 6: revision of all the tissues.

- Observe, recognize and compare the different tissues.

Practical/Histology 7: interactive revision of all the tissues.

- Observe, recognize and compare the different tissues.

Practical/Microscopic Anatomy 1

- Practical at the light microscope: Exocrine glands

Practical/Microscopic Anatomy 2

- Practical at the light microscope: Endocrine glands

Practical/Microscopic Anatomy 3

- Practical at the light microscope: Digestive system

Practical/Microscopic Anatomy 4

- Practical at the light microscope: Respiratory system

Practical/Microscopic Anatomy 5

- Practical at the light microscope: lymphoid organs

Practical/Microscopic Anatomy 6

- Practical at the light microscope: Urinary system

Practical/Microscopic Anatomy 7

- Reproductive system

General Anatomy

Lesson 1. From tissues to body: organs and systems. Anatomical nomenclature
Learning goals:

- Define and describe the terms relative to the anatomical position
- Describe the anatomical planes
- Define and describe the terms used to describe the movements of the limbs and vertebral column

Lesson 2. Intercommunication between the body and the environment (skin and its appendages). From outside to inside: topographical hint
Learning goals:

- Define and describe the skin and its appendages and their regional characteristics
- Illustrate how we can interact with the environment
- Illustrate how we can protect ourselves from the environment
- Define and describe the various parts of the human body and their general content and arrangement.

SEMINARS

Exploring the digestive system Nico Pagano

Staminal cells in the heart Luigi Anastasia

Modules 2nd Semester

General Anatomy (continues)

Lesson 3. Bones: support, movement and protection.
Learning goals:

- Illustrate how the various bones, their components, growth, remodeling and repair, contribute to the general framework of human body.
- Describe the morphofunctional bases of the support, movement and protection functions of the bones in the trunk and limbs

Lesson 4. Joints: support and movement
Learning goals:

- Illustrate how joints can link bones together permitting and/ or limiting their reciprocal movements
- Describe the morphofunctional bases of the movement and support functions of the various joints in the trunk and limbs

Lesson 5. Skeletal muscles: support, movement and protection
Learning goals:

- Illustrate how the various skeletal muscles and their components contribute to the general construction of human body.
- Illustrate the morphofunctional bases of the movement and support functions of the various muscles in the trunk and limbs

Lesson 6 and 7.The skull:bones, fossae and general architecture, part I and part II
Learning goals:

- Describe the position and main characteristics of the major bones of the skull, and their reciprocal joints.
- Describe the boundaries, walls and floors of the cranial fossae.
- Identify the external and internal features of the cranial foraminae and list the structures that each transmits.

Practical/General anatomy 1and 2: The skull, part I and II
Learning goals:

- Describe and recognize the position and main characteristics of the major bones of the skull, and their reciprocal joints.
- Describe and recognize the boundaries, walls and floors of the cranial fossae.
- Describe and recognize the external and internal features of the cranial foraminae and list the structures that each transmits.

Regional Anatomy

Overview
During the course a description of regional anatomy in relation to the clinical practice will be made. The anatomical structures of the back, thorax, abdomen and limbs will be analyzed in their relations and reciprocal interdependence together with the principles

methods for non destructive clinical image analysis. In the 4th year/second semester the same approach will be used for Had and Neck.

Lesson 1. Trunk: the back
Learning goals:

- Describe the anatomical relations between the vertebrae, the spinal cord, and the spinal nerves.
- Describe the cervical, brachial, lumbosacral, and pudendum plexa, their position, anatomical relations and significance

Lesson 2 and 3 Trunk: the thorax, part I and II
Learning goals:

- Describe the main anatomical characteristics of the thorax and its surface anatomy
- Describe the topographical and anatomical divisions of the thoracic cavity, the surface markings of the main thoracic organs, and their anatomical relations
- Illustrate the position of the heart, great vessels and oesophagus in the mediastinum
  Illustrate the position and relations of the pleura, lungs, trachea and bronchi
- Illustrate the position and relations of the diaphragm, and its role in respiratory movements

Lesson 4, 5 and 6 Trunk: the abdomen and pelvis, part I, II and III
Learning goals:

- Describe the main anatomical characteristics of the abdomen and pelvis, and their surface anatomy
- Describe the topographical and anatomical divisions of the abdominal cavity, the surface markings of the main abdominal organs, and their anatomical relations
- Illustrate the position of the gastrointestinal tract, abdominal viscera, and urogenital system in the abdomen
- Describe the peritoneum, its ligaments, and the peritoneal cavity
- Illustrate the position and relations of the various organs with the peritoneal cavity

Lesson 7,8, 9 and 10. Pectoral and pelvic girdles, upper and lower limb
Learning goals:

- Describe the main anatomical characteristics of the upper and lower limbs, thoracic and pelvic girdles, and their surface anatomy.
- Describe the fascial compartments delimiting the major muscle groups of the upper and lower limbs, and to explain the functional importance of those compartments and their contents.
- Describe the movements of the pectoral and pelvic girdles, and of upper and lower limbs; to identify and describe the muscles responsible for the movements and summarise their main attachments and somatic motor nerve supply.
- Describe the origin, course and distribution of the major arteries and veins of the upper and lower limbs and their branches; classify and contrast the functions of the deep and superficial veins.
- Describe the origin, course and function of the principal nerves of the upper and lower limbs.

Practical/Regional anatomy 1 and 2: Trunk & the back, part I and II
Learning goals:

- Describe and recognize the main anatomical features of vertebrae and their joints
- Describe and recognize the structures, regions, functions and movements of the vertebral column.
- Describe and recognize the principal muscle groups and ligaments of the vertebral column
- Describe and recognize the anatomical relations between the vertebrae, the spinal cord, and the spinal nerves.
- Describe and recognize the cervical, brachial, lumbosacral, and pudendum plexa, their position, anatomical relations and significance

Practical/Regional anatomy 3 and 4: Trunk: the thorax I and II
Learning goals:

- Describe and recognize the main anatomical characteristics of the thorax and its surface anatomy
- To observe, describe and recognize the main anatomical skeletal, cartilaginous and ligamentous features of thorax
- Describe and recognize the joint and movements of the thorax
- Describe and recognize the principal muscle groups of the thorax
- Describe and recognize the position and relations of the diaphragm
- Describe and recognize the position of the heart, great vessels and oesophagus in the mediastinum
- Describe and recognize the position and relations of the pleura, lungs, trachea and bronchi

Practical/Regional anatomy 5 and 6: Trunk: the abdomen and pelvis I and II
Learning goals:

- Describe and recognize the anatomical characteristics of the abdomen and pelvis, and their surface anatomy
- Describe and recognize the main anatomical skeletal, cartilaginous and ligamentous features of abdomen and pelvis
- Describe and recognize the joint and movements of the abdomen and pelvis
- Describe and recognize the principal muscle groups of the abdomen and pelvis
- Describe and recognize the position and anatomical relations of the gastrointestinal tract, abdominal viscera, and urogenital system in the abdomen

Practical/Regional anatomy 7,8 and 9: Upper and lower limb I, II and III
Learning goals:

- Describe and recognize the main anatomical characteristics of the upper and lower limbs, thoracic and pelvic girdles, and their surface anatomy
- Describe and recognize the main anatomical skeletal, cartilaginous and ligamentous features of the upper and lower limbs
- Describe and recognize the joints and movements of the upper and lower limbs
- Describe and recognize the major muscle groups of the upper and lower limbs, and their relations with the vessels and nerves
- Describe and recognize the major arteries and veins of the upper and lower limbs and their branches
- Describe and recognize the principal nerves of the upper and lower limbs

NEUROANATOMY

Overview

The neuroanatomy course is divided into three modules. The first module takes place during the second semester of the first year. Its general learning goal is to understand, starting from a developmental perspective, the macroscopic anatomy and internal architecture of the central nervous system and to know the organization of the peripheral nervous system

Lesson 1. Phylogenesis and general organization

Learning goals:

- Describe the phylogenesis of nerve cells and primitive neural circuits
- Describe the process of centralization and cephalization of nerve cells
- Describe the formation of the tubular nervous system and brain vesicles
- To illustrate the general morpho/functional organization of the nervous system in relation to its phylogenesis
- Describe the general organization of the gray and white matter
- List most common neurotransmitters/neuromodulators

Lesson 2 and 3. Development of the nervous system I and II

Learning goals

- Describe the different phases of neurulation
- *Developmental defects: defects of closure of the neural tube, cyclopia*
- Describe the process of histogenesis in the neural tube
- Describe the fundamental cross sectional organization of the developing neural tube
- Describe the process of myelination
- Describe the development of the spinal nerve and of the peripheral nervous system
- Describe the basic macroscopic events through which the neural tube undergoes to form the different portions of the central nervous system and the ventricular system
- Illustrate the events that lead to the organization of the gray and white matter in the different portions of the central nervous system: spinal cord, brainstem and brain
- Describe the basic prenatal and postnatal steps characterizing the morpho-functional maturation of the nervous system
- *Developmental defects: lissencephaly*

Lesson 4: Spinal cord, spinal nerves

Learning goals:

- Describe the relation of the spinal cord with the vertebral canal
- Describe the spinal segment, the ventral and dorsal roots and their level of exit
- Describe the meninges, the meningeal spaces and their content
- *Clinical drops: vertebral metastases*
- Describe the lumbar cistern and the composition of the cerebrospinal fluid
- *Clinical drops: tapping the cerebrospinal fluid*
- Describe the macroscopic aspect of the spinal cord

- Describe the laminar and columnar organization of the gray matter
- Describe the main cell types of the gray matter
- *Functional drops: spinal reflexes*
- Describe the organization of the white matter and the position of the most important ascending and descending pathways

Lesson 5. Peripheral nervous system: spinal plexuses
Learning goals

- Describe the formation of the spinal nerve and the destiny of its terminal and collateral branches
- Illustrate the formation of spinal plexuses
- Describe the position and composition of the spinal plexuses and their territory of innervation
- Highlight the main aspects of the course and territory of innervations of the most important peripheral nerves
- *Clinical drops: injuries of the brachial and lumbosacral plexuses*

Lesson 6. Peripheral nervous system: Autonomic nervous system
Learning goals

- Describe the general organization of the autonomic nervous system
- Describe the neurochemical organization of the autonomic nervous system
- *Functional drops: fight and flight vs rest and digest*
- Describe the specific organization of the sympathetic and parasympathetic outflow pathways
- Describe the position of viscerosensory neurons and the destiny of viscerosensory fibers
- Describe the organization of the enteric nervous system
- *Clinical drops: referred pain*

Lesson 7 and 8. Brainstem and cerebellum part I and II
Learning goals:

- Illustrate the content and organization of the posterior cranial fossa
- Describe the organization of the meninges in relation to the suvratentorial and infratentorial compartments of the neurocranium and to the formation of the venous sinuses
- *Clinical drops: herniations*
- Describe the internal organization of the brainstem with respect to cranial nerve nuclei, specific nuclei, and ascending and descending pathways
- Describe the surface anatomy of the brainstem, the origin of the cranial nerves and their exit points with respect to the skull foramina
- Illustrate the sensory and motor organization of the cranial nerves and their territory of innervations
- Describe the surface anatomy of the cerebellum and its division in lobes
- Describe the relation of the cerebellum to the brainstem and 4th ventricle
- Describe the morphology of the 4th ventricle and its communications
- Describe the structure of a choroid plexus and the formation and circulation of the cerebrospinal fluid
- *Clinical drops: hydrocephalus*

- Illustrate the organization of the cerebellar gray and white matter and introduce the organization of the cerebellar cortex

Lesson 9 and 10.Telencephalon and diencephalon part I and II
Learning goals:

- Discuss the developmental aspect of the prosencephalic vesicle most relevant to understand the organization and reciprocal relationship of the telencephalic emispheres and diencephalon
- Describe the surface anatomy of the telencephalon and its subdivision in lobes and gyri
- Describe the position of the primary and secondary motor and sensory areas in the lobes
- Describe the organization of the white matter of the cerebral emispheres into projecting, association and commissural fibers
- Describe the organization and relationships of the basal ganglia location and relations of the basal ganglia
- Describe the organization of the cerebral cortex with special reference to the neocortex and its layers and cell types
- *Clinical drops: disruption of inhibitory circuits in the brain and disease*
- Describe the morphology of the lateral ventricles
- To describe the diencephalon and the third ventricle
- Discuss the subdivisions of the diencephalon and the relevant aspects of their structural organization in relation to their function
- Describe the position and function of circumventricular organs
- *Clinical drops: vomiting*

SEMINARS

Cell to cell communication in brain development	Michela Matteoli
Functional neuroanatomy	Lorenzo Bello
Clinical aspects of pelvic girdles pathology	Nicola Portinaro
People from Bones	Cristina Cattaneo

3. FROM ATOMS TO CELLS 1st and 2nd Seemsters

FROM ATOMS TO CELLS

Year/Semester

1stYear/1st and 2nd semester

Credits: 25

Faculty

Laura Riboni	("Biochemistry") (Coordinator)
Roberto Cerbino	("Physics")
Federica Compostella	("Chemistry")
Stefano Duga	("Molecular Biology")
Palma Finelli	("Medical Genetics")
Paola Giussani	("Biochemistry")
Fabio Grassi	("Cell Biology")
Anna Marozzi	("Human Genetics")

Overview

A&C is an integrated course that covers the biological processes and inheritance mechanisms supporting life. The block starts with the modules of "Physics" and "Chemistry", the main goal being to provide basic principles underling the life and the features of the living matter. The course goes on by addressing the multiple levels of organisation, from macromolecules, supra-molecular assemblies and cell compartments, to cells and organisms. Specific topics include bio-molecular diversity, function and turnover, structure and regulation of genes, chromosomes and genomes, cellular compartmentalisation, dynamics and communication, cellular metabolism and energy relationships, regulation and interconnections of metabolic pathways, biological variation, mutation, selection and evolution, and the genetic basis of inherited diseases. The topics of the course will be presented in a conceptual and methodological framework largely shared by modern Physics, Chemistry, Biochemistry, Molecular and Cellular Biology, and Human Genetics to promote interdisciplinary thinking across fields.

If you have specific questions related to lecture material you are encouraged to direct them to the instructor who is the content expert. Talk with us early and often; we will listen and make changes where appropriate. The coordinator is responsible for all difficulties concerning the course. Please feel free to contact Prof. Riboni (laura.riboni@unimi.it) with questions or concerns.

Teaching methods

- Lectures

- Small Group Activities
- Labs
- PBL
- Seminars

Textbooks

Physics

- M. Zinke-Allmang, K. Sills, R. Nejat, E. Galiano-Riveros, Physics for the life sciences (2nd edn.), Nelson (2012) ISBN: 978-0-17-650268-3
- Paul Davidovits, Physics in Biology and Medicine (4th edn.), Academic Press (2013) ISBN: 978-0-12-386513-7

Chemistry

- Atkins P., Jones L. "Chemical Principles: The Quest for Insight" (3rd edn.), Freeman & Co: New York and Basingstoke, 2004; a Handout of Chemistry will be available.

Molecular and Cellular Biology

- Alberts B, et al. "Essential Cell Biology" (3rd edn.), Garland Science, 2009

Biochemistry

- Lieberman M. and Marks A. "Marks' basic medical biochemistry: a clinical approach" (2009) Lippincott Williams & Wilkins
- Devlin TM "Textbook of Biochemistry with Clinical Correlations" (7th edn.), Wiley, 2010

Human and Medical Genetics

- Thompson & Thompson - Genetics in Medicine. 7thedn., Saunders, 2008

Exams

Students' evaluation will be assessed through a multiple choice examinations in two parts, including:

1) 1st semester exam (modules of Physics, Chemistry, Molecular Biology)
2) 2nd semester exam (modules of Cell Biology, Biochemistry, Human and Medical Genetics).

Each of the two written examinations will deal with all the topics and activities developed during the corresponding semester (lectures, labs, PBL and assigned readings).
Exam questions will be multiple choice. In general, there will be 5-6 questions/credit, and a total of 66 questions/exam.

The threshold scores for passing each of the two multiple choice tests is:
a) 40% of each of the corresponding modules (Physics, Chemistry, Molecular Biology for the 1st, and Cell Biology, Biochemistry, Human and Medical Genetics)
b) 36/66 on the whole.
Only students who pass the 1st semester exam are eligible for the second one.

Final mark

The final mark will be assigned as the average of the marks gained at the two written examinations.

Examination calendar

- The exam (1st + 2nd semester blocks in the same day) will be scheduled starting from June 2014.
- It will be possible to take only the 1st semester exam in a in separate session at the end of the first semester; in the period January-February 2014 (2 examinations).

Registration to exams

- through SIFA (mandatory) from June 2014
- only for the 1st semester exam (at the end of the 1st semester) at the student office.

Modules 1st semester

Physics

Overview

This course offers an introduction to Physics with an accent on medical applications. The course builds on prior knowledge of some important basic mathematics and physics concepts (see Prerequisites for a detailed list) that will be given for granted at the course start. The focus will be mostly on mechanics and thermodynamics, with a brief introduction to the importance of modeling and quantitative thinking in medicine and a conclusive part on feedback and control theory. Whenever possible, we will prefer scaling laws, order of magnitude estimates, back-of-the-envelope calculations to long and tedious calculations. The proposed approach is meant to privilege general concepts and ideas with strong applications toward understanding and explaining the working principles of the Human Body.

Prerequisites (mostly found in Chapter 1 and Appendix of Textbook 1)

- Mathematics: Powers and roots. Scientific notation. Decimal and significant figures. Solution of Algebraic Equations. Graphs. Plane Geometry and Trigonometric Functions. Series Expansions. Derivatives. Areas and volumes. The exponential function. Logarithms. Trigonometric identities. Integrals.
- Physics: Physical quantities and their measurement. Standards. Units and errors. Systems of units. The International system (SI). Vectors and operations with vectors (sum, difference and the three products)

Lectures

1) Introduction: quantitative thinking in medicine

Learning goals:

- Illustrate the link between physics and medicine
- Understand the importance of quantitative thinking in medicine
- Define the order of magnitude of a measurable quantity
- Define the properties of a standard man
- Become familiar with dimensional analysis, scaling laws and allometric rules
- Describe the laws of perception: Weber-Fechner law and Steven's law
- Introduce the decibel and its use in medical physics.

2) Forces and translational equilibrium

Learning goals:

- Discuss the concept of force and its properties
- Introduce typical forces such as the muscular force, gravity force, normal force, static friction, spring force
- Explain the role of tension forces and tendons
- Introduce translational equilibrium

3) Torques and rotational equilibrium

Learning goals:

- Define the center of mass of an extended body
- Describe forces and introduce torques
- Define rotational equilibrium
- Explain the levers of the human body

4) Moving bodies
Learning goals:

- Describe kinetic friction
- Introduce position, displacement, velocity and acceleration of moving bodies
- Introduce the three Newton laws and inertia

5) Momentum and energy
Learning goals:

- Define the momentum of a moving body
- Describe the motion of the center of mass of an extended body
- Introduce the concept of kinetic energy
- Introduce the concept of potential energy
- Define mechanical energy

6) Work and power
Learning goals:

- Define work and its relationship with the kinetic energy
- Understand the relationship between work and potential energy
- Realize the conditions for the conservation of mechanical energy
- Introduce dissipative forces
- Define the concept of power

7) Oscillations and Brownian motion
Learning goals:

- Introduce the uniform circular motion
- Define the simple harmonic motion as projection of a uniform circular motion
- Explain damping, forcing and resonance in oscillating systems
- Describe Brownian motion

8) Gases, air and breathing
Learning goals:

- Define gases and their properties: volume, pressure, temperature and thermal equilibrium
- Discuss the basic parameters of the human respiratory system
- Introduce the empirical gas laws
- Discuss the mechanical model of the ideal gas
- Introduce the internal energy of the ideal gas

9) Heat
Learning goals:

- Define the work made on and by a gas especially in connection with the respiration cycle
- Explain the 1st law of thermodynamics
- Discuss the thermal properties of matter
- Discuss the main heat transfer mechanisms

10) Entropy and free energy
Learning goals:

- Discuss thermodynamic processes
- Discuss the meaning of enthalpy and its connection with chemical reactions
- Discuss the concept of reversibility
- Explain the 2nd law of thermodynamics
- Discuss entropy as a measure of the “quality” of energy
- Introduce free energy

11) The body as a thermal machine
Learning goals:

- Discuss the conservation of energy in the human body
- Discuss the energy content of food and compare it with fuel and other sources of energy
- Define the basal metabolic rate
- Explain the main mechanisms of body heat loss

12) Basics of feed-back and control
Learning goals:

- Define open loop, feed-forward, feed-back (closed loop)
- Discuss the fundamentals of control theory
- Explain the PID algorithm
- Describe an application of control theory: controlling the temperature of the human body difference and the three products)

Chemistry

Overview

The chemistry module is intended to provide a rigorous introduction to the fundamentals of general and bio-organic chemistry. The structure of this module meets the requirements of the area of life sciences and aims to offer a foundation for further study in chemistry-related disciplines such as biology, biochemistry,…
In the first part of the course the special electronic characteristics of carbon atom and the nature of its bonds will be illustrated through structures and chemico-physical properties of the principal classes of organic compounds. The exam of a few inorganic and organic reactions will allow to understand the principles of chemical kinetics and chemical equilibrium. The role of catalysts will be illustrated with a few examples of reactions of organic compounds. The nature and properties of aqueous solutions will be evaluated and the most significant colligative property, i.e. the osmotic pressure, will be examined. Water self-ionization and the properties of acid/base and buffer solutions will be illustrated. Redox reactions in inorganic and organic chemistry and related energy will be discussed within the general frame of thermodynamics and electrochemistry. The second part of the course will describe the reactivity of the main classes of organic compounds, including isomerism and the stereochemical concepts related to organic molecules containing asymmetric carbon atoms. The content of this part will form the basis for understanding the structure and functions of the most relevant biomolecules, i.e. organic compounds found in living organisms.

Prerequisites:

Students are presumed to have a good background in high school chemistry and are expected to have previous knowledge on the following subjects:

- structure and periodic properties of the atoms
- relative atomic and molecular mass (atomic and molecular weight)
- covalent bond
- moles
- balance of reactions
- basic stoichiometric calculations
- solutions and molar concentration
- strong acids/bases
- pH

Lectures:

1) Discussion about Chemistry prerequisites

Learning goals:

- Discuss the structure of atoms
- Describe the electronic configuration of atoms
- Correlate the electronic configuration of atoms to their position in the periodic table
- Discuss the chemical properties of atoms and predict the formation of covalent/ionic bonds

2) Chemical bonds. Molecular and hybrid orbitals.

Learning goals:

- Describe how molecular and hybrid orbitals are derived from atomic orbitals
- Discuss the electronic properties of carbon atom to understand chemical bonding in organic chemistry (covalent bond)
- Describe the different types of hybrid orbitals and the shape of molecules.
- Discuss the structural features of complex molecules (haemoglobin). The coordinative bond.

3) Structures, nomenclatures and chemico-physical properties of organic compounds.

Learning goals:

- Discuss the meaning of "functional group" in organic chemistry
- Be able to recognize, name and write the structure of alkanes, alkenes, benzene, alcohols, thioalcohols, carbonyl compounds, carboxylic acids and amines.
- Describe the chemico-physical properties of alkanes and alcohols

4) Chemical reactions. Kinetics and equilibrium.

The concept of chemical equilibrium of a reversible reaction. Equilibrium constants.

Learning goals:

- Describe the chemical equation of a reaction
- Describe the speed of a reaction
- Distinguish between reversible and irreversible reactions
- Discuss the meaning of chemical equilibrium of a reversible reaction
- Be able to understand the meaning of the equilibrium constant value
- Discuss which are the parameters that can affect the equilibrium or the kinetics of a reaction

5) Activation energy and catalysis. The state quantities H and G.

Learning goals:

- Define the activation energy
- Describe a reaction diagram: exothermic and endothermic reactions
- Describe the general phenomenon of catalysis.
- Reactivity of alkenes: describe the mechanism of addition of water to a double bond to form an alcohol
- Describe the role of the catalysis of H^+ in the addition of water to a double bond
- Describe the meaning of endoergonic and exoergonic reaction

6) Water as a solvent. Properties of solutions: osmotic pressure. Water self-dissociation. Concept of pH. Strong acids and bases.

Learning goals:

- Describe the properties of aqueous solutions
- Discuss the meaning of isotonic and hypotonic (hypertonic) solutions
- Discuss the meaning and the value of the dissociation constant (Kw) of water
- Discuss the value of $[H^+]$ in pure water as a reference value for acid/base or neutral solution

- Define pH
- Describe the behaviour in water of strong acids and bases

7) Weak acids. The Brønsted-Lowry theory. Dissociation constants.
The Brønsted-Lowry theory: acids and conjugated bases. Solutions of weak acids and bases and related equilibrium constants (Ka and Kb).
Learning goals:

- Discuss the Brønsted-Lowry theory
- Recognize acids and their conjugated bases and viceversa
- Discuss weak acids/bases equilibrium in aqueous solutions (Ka and Kb)
- pH of strong and weak acid/base solutions

8) Polyprotic acids. Organic acids and bases.
Learning goals:

- Discuss that carbonic and phosphoric acids are polyprotic acids
- Recognize the meaning of the different dissociation constants of a polyprotic acid
- Discuss the importance of acid and basic functional group in organic chemistry and biochemistry (carboxylic acids, phosphoric acid and amines)

9) Buffer solutions: properties and pH.
Learning goals:

- Discuss the characteristics of the composition of a buffer solution and related properties
- Calculate the pH of a buffer solution
- Discuss the meaning of biological buffers, including those related to carbonic and phosphoric acids

10) Redox reactions
Learning goals:

- Discuss the meaning of oxidation and reduction
- Discuss the properties of oxidants/reductants
- Discuss that a redox reaction is the result of an exchange of electrons
- Discuss redox reactions in organic chemistry
- Calculate the oxidation number of a few oxidants/reductants
- Balance simple redox reactions

11) Redox reactions and related energy: principles of electrochemistry.
Energy related to redox reactions. Galvanic cells: the Daniell's cell. Standard reduction potentials. The Nernst equation as a mean to calculate biochemical redox potentials.
Learning goals:

- Discuss redox processes in terms of electrochemical processes
- Discuss how a simple galvanic cell works
- Discuss the meaning of standard reduction potential
- Discuss the meaning of Nernst equation
- Relate Nernst equation to biochemical redox potentials

12) Alkanes, alkenes and isomers. Reactivity alcohols, aldehydes and ketones.
Learning goals:

- Write simple structures of alkanes and related isomers
- Write simple structure of alkenes and related isomers
- Distinguish the different forms of isomerism
- Describe the most significant reactions of an alcohol: dehydration and oxidation
- Describe the reason of the different reactivity of an alcohol when compared to a phenol
- Describe the most significant reactions of aldehydes and ketones

13) Reactivity of carboxylic acids and amines. Reactions among functional groups
Learning goals:

- Write the structure of carboxylic acids derivatives (esters, anhydrides and amides) and describe the mechanism of formation.
- Describe the mechanism of nucleophilic substitution

14) Polyfunctional compounds: structures, stereochemistry and reactivity
Learning goals:

- Describe the stereochemistry of organic compounds.
- Define a chiral molecule
- Describe an asymmetric carbon atom and define its configuration
- Describe glyceraldehyde as a model for D,L-configuration
- Describe some polyfunctional compounds in the Krebs cycle and their reactivity

15) Carbohydrates 1
Structure, stereochemistry and reactivity of monosaccharides
Learning goals:

- Describe the structure of non-cyclic carbohydrates
- Discuss the differences between stereoisomers: enantiomers and diasteroisomers (epimers)
- Discuss the mechanism of ring-closure of a non-cyclic carbohydrate
- Discuss the difference between anomer and epimer
- Describe the oxidation and reduction of carbohydrates

16) Carbohydrates 2
Glycosides, disaccharides and polysaccharides.
Learning goals

- Discuss the mechanism of formation of a glycosidic bond.
- Discuss the main structural features of glycosides
- Describe the structure of a disaccharide
- Describe the structural features of polysaccharides (starch, cellulose, glycogen)

17) Nucleosides, nucleotides and nucleic acids.
D-ribose and D-2-deoxyribose. Purine and pyrimidine bases. Nucleosides. Nucleotides. AMP, ADP and ATP. Formation of the 3',5'-phosphoric bond between two nucleotides. Hydrogen bonds of double strand in DNA.
Learning goals:

- Discuss the main structural features of D-ribose and D-2-deoxyribose
- Discuss the main structural features of purine and pyrimidine bases
- Describe the formation of the glycosidic bond of a nucleoside
- Describe the formation of a nucleotide from a nucleoside
- Discuss the structural features of AMP, ADP and ATP, and the reactivity of the triphosphate group in ATP.
- Discuss how the 3',5'-phosphoric bond is formed between two nucleotides.
- Describe the hydrogen bondings of double strand in DNA

18) Amino acids and proteins 1
Structure of essential amino acids. Amino acid equilibrium in aqueous solution. Isoionic and isoelectric points.
Learning goals:

- Discuss the stereochemical features of alfa-L-amino acids
- Discuss amino acid structures

- Discuss amino acids equilibrium in aqueous solution
- Describe the isoionic and isoelectric point of an amino acid

19) Amino acids and proteins 2

Formation of the amide bond between two aminoacids. Structure and properties of the amide bond. Biosynthesis of the amide bond. Peptide and proteins. Protein structures. Denaturation of a protein.

Learning goals:

- Discuss the formation of the amide bond as a direct dehydration between two aminoacids
- Discuss the structure of the amide bond and its chemical properties
- Discuss the chemical features of the formation of an amide bond at physiological pH, and describe the steps of the biological synthesis of an amide bond
- Describe the differences between peptides and proteins
- Discuss the meaning of primary structure of a protein
- Describe the chemical features of the secondary structure of a protein
- Describe the intramolecular forces that contribute to the tertiary structure of a protein
- Discuss the meaning of denaturation of a protein

20) Lipids

Structure and nomenclature of fatty acids. Lipids: triglycerides and glycerophospholipids. Other lipids.

Learning goals:

- Discuss the amphiphilic nature of the anions of fatty acids and glycerophospholipids
- Write the structure of a simple triglyceride and of phosphatidylcholine
- Discuss the formation, hydrolysis and assembly of lipids
- Glycolipids

21) Overview on solutions

22) Overview on acids and bases

23) Overview on buffers

24) Questions and answers in bioorganic chemistry

Molecular Biology

Overview

Molecular biology deals with nucleic acids and proteins and how these molecules interact within the cell to promote proper growth, division, and development. The goal of this course is to provide students with a basic understanding of modern molecular biology both from the perspective of known molecular mechanisms regulating fundamental cellular processes, and from the applied perspective of using molecular biology as a laboratory tool. Special emphasis will be placed on molecular mechanisms that relate to nucleic acid structure-function relationships, chromatin and histone modifications, DNA replication and repair, RNA metabolism, and gene expression regulation. In addition, we will take an in-depth look at some rapidly evolving fields, including regulation of gene expression by chromatin structure and by small RNAs. The application of molecular biology as a tool to perform molecular genetic testing will also be discussed.

1. The nature of the genetic material

Topics

DNA as the genetic material. Structure of the genetic material, physicochemical properties of DNA molecules..

Learning Objectives

- Describe how DNA was demonstrated to be the genetic material
- Discuss the structure-function relationships of DNA molecules
- Describe the processes of denaturation and renaturation of DNA and illustrate how these phenomena are at the basis of nucleic acid hybridization techniques

2. Chromatin and chromosomes

Topics

The organization of DNA in the cell nucleus, chromatin structure, histones and histone modifications.

Learning Objectives

- Illustrate how the genetic material is organized in the cell nucleus
- Describe the levels of chromatin compaction
- Discuss the main chromatin modifications involved in gene expression regulation

3. The structure of eukaryotic genes

Topics

What is a gene? Structure of prokaryotic and eukaryotic genes. Main features of eukaryotic genes.

Learning Objectives

- Define gene as a transcriptional unit
- Discuss the existence of gene families and the concept of orthologs and paralogs
- Describe the typical structure of an eukaryotic gene and its main functional elements

4. The mechanism of DNA replication. Main classes of enzymes working on DNA

Topics

DNA Replication:Basic mechanism & enzymology. Semi-discontinuous replication, replication strategies, prokaryotic and eukaryotic DNA polymerases, priming. Origins of replication.

Learning Objectives

- Discuss the main classes of enzymes acting on nucleic acids: endo- and exonucleases, polymerases, ligases, modifying enzymes, etc.
- Discuss the role of enzymes acting on nucleic acids and their possible in vitro applications
- Discuss molecular mechanism of DNA replication
- Discuss the problems raised by DNA replication and how the different proteins participating in the process are able to solve them
- Discuss the relationship between DNA replication and cell cycle regulation

5. The mutability of the genome (DNA damage & repair)

Topics

Causes of mutation: spontaneous and induced. Agents that induce mutation. Common mutations due to DNA replication. Main mechanisms of DNA repair.

Learning Objectives

- Describe examples of the main categories of DNA damaging agents
- Describe mechanisms by which DNA can be damaged
- Discuss the relationship between DNA damage and DNA mutation
- Discuss the balance between mutation-inducing mechanisms and DNA repair and its role in evolution
- Discuss the cell responses to DNA damage
- Describe the main mechanisms of DNA repair and the specific damages they are apt to

6. RNA transcription and metabolism: the transcriptome

Topics

How information flows through macromolecules in the cell. Eukaryotic transcription: RNA polymerases, promoters & enhancers. Eukaryotic transcription factors - general & specific. Complexity of the transcriptome.

Learning Objectives

- Discuss the flow of genetic information
- Discuss the original and the revised enunciation of the “central dogma”
- Discuss the mechanism of RNA synthesis (transcription)
- Describe the main classes of RNAs present within cells and their functions, including new classes of small RNAs and their regulatory functions.
- Discuss the importance of studying gene expression by whole-trascriptome analysis

7. Alternative splicing in physiology and pathology (Seminar)

What is RNA splicing and why it has evolved and spread in higher eukaryote genomes. How alternative splicinggeneratesproteindiversity. RNA splicingregulation.

8. The genetic code

Topics

How can 4 nucleotides specify for 20 amino acids. The main properties of the genetic code. How mutations can affect the protein product of a nucleotide sequence. How protein synthesis takes place in the cell?

Learning Objectives

- Describe the properties of the genetic code
- Dicuss the mechanism of protein synthesis and its regulation
- Describe how mutations in DNA can affect protein sequences

9. Protein folding and post-translational modifications: the proteome

Topics

How proteins acquire their final conformation and their functional properties after synthesis. The complexity of the proteome and its relation with the genome and the transcriptome.

Learning Objectives

- Describe the main post-translational modifications and their function
- Discuss the relationship between post-translational modification and protein sorting
- Describe examples of post-translational modifications modifying protein function

10. The regulation of gene expression (part 1 & part 2)

Topics

How cells modulate gene expression. Levels of gene expression regulation: from chemical modification of DNA to post-transcriptional and post-translational regulation.

Learning Objectives

- Dicuss the importance of gene expression modulation in driving the processes of cellular differentiation and morphogenesis
- Dicuss the principles of transcriptional regulation in prokaryotes and eukaryotes
- Describe examples of transcriptional regulation
- Describe examples of diseases associated with anomalous transcriptional regulation of gene expression
- Dicuss the principles of post-transcriptional regulation in prokaryotes and eukaryotes
- Describe examples of post-transcriptional regulation
- Describe examples of diseases associated with anomalous post-transcriptional regulation of gene expression

11. Recombinant DNA (rDNA)

Topics

What is rDNA? Tools of rDNA technology, making a recombinant DNA molecule, DNA probes and hybridization, main applications of rDNA.

Learning Objectives

- Discuss the principles of rDNA technology
- Illustrate the concept of genomic and cDNA libraries
- Describe a cloning experiment
- Discuss what is a molecular probe and what is an hybridization experiment

12. Polymerase Chain Reaction (PCR) & DNA sequencing

The discovery of PCR, the principles of a PCR reaction, what can you do with PCR?
Sanger sequencing, next-generation sequencing, the future of genome sequencing. Applications of high-throughput sequencing.

Learning Objectives

- Discuss why DNA is amplified during a PCR reaction
- Illustrate the main applications of PCR
- Describe the theory of Sanger sequencing
- Compare traditional sequencing with massive parallel sequencing
- Describe the main applications of next-generation sequencing

Modules 2nd Semester

Cell Biology

Overview

The programme should allow the student to appreciate and understand the dynamic nature of the cell, including how it receives and responds to information from its environment. We will explain and compare different mechanisms of receptor activation and regulation with the aim of understanding intracellular signaling cascades and their impact on cellular activities, including cytoskeleton rearrangements, motility and changes in gene expression. We will also address mechanisms responsible for cell cycle regulation. Finally, we will provide an overview on how alterations of the described mechanisms can impact on physiological cellular behavior.

The eukaryotic cell.

Topics

Structure and functions of eukaryotic cell. Conservation of developmental programs among different species. Proteins. Self organization of molecules into the cell. The cytoskeleton.

Learning Objectives

- Discuss the eukaryotic cell organization and the function of distinct compartment
- Explain phylogenetic relationship between species
- Discuss conservation of biological processes
- Discuss principles for organizing whole cells
- Discuss the role of long protein polymers in integrating cell functions

Signal transduction

Topics

Cell membrane structure. The rafts hypothesis. Protein kinases and the human kinome. Nature of intercellular communication and receptors. Second messengers.

Learning Objectives

- Discuss the eukaryotic cell membrane structure
- Explain the function and role of protein kinases in regulating the life of a eukaryotic cell
- Define the nature of intercellular communication
- Define modalities of signal transduction by different types of receptors
- Discuss the nature and significance of second messengers

The cell cycle

Topics

Cell cycle phases. Regulation of cell cycle by extracellular stimuli. Cell cycle checkpoints. Role and regulation of cyclins.

Learning Objectives

- Discuss cell cycle phases
- Discuss how extracellular stimuli can regulate cell cycle
- Discuss the significance of cell cycle checkpoints
- Discuss the role of cyclins in regulating cell cycle

Cell motility

Topics

Conservation of behavior and molecular basis of eukaryotic cell movement. Actin-based cell motility. Establishment of polarity. Dynamics and force generation in the eukaryotic cytoskeleton. Hijacking actin-based motility by pathogenic bacteria.

Learning Objectives

Illustrate filaments as dynamic structures

- Discuss how motors and filament assembly/disassembly to generate force

- Describe protrusion of the leading hedge of crawling cells
- Discuss function of cytoskeleton in physiological processes

Apoptosis

Topics

Differences between necrosis and apoptosis. Milestones in apoptosis research. Roles of apoptosis. Molecular regulation of apoptosis. Caspases. The apoptosome. The Bcl-2 family. Apoptotic cell engulfment. Extrinsic death pathway.

Learning Objectives

- Describe developmental, physiological and pathological processes in which apoptosis plays a crucial role
- Define upstream and downstream caspases
- Describe the apoptosome
- Discuss regulator, adaptor and effector molecules in apoptosis
- Discuss signals for elimination of apoptotic cells
- Discuss apoptosis and neoplastic transformation of the cell

Oncogenes and cancer

Topics

Hallmarks of cancer. In vitro contact inhibition and in vivo tumor progression. Control of cell proliferation in cancer. Environmental factors and cancer. The Ames test. Isolation of the first human oncogene. Classes of oncogenes. Mechanisms of proto-oncogenes activation. Chromosomal alterations and cancer. Multiple mutations in cancer progression. Tumor suppressor genes. Viral oncology. Stem cells and cancer stem cells.

Learning Objectives

- Discuss molecular mechanisms responsible for altered cell cycle regulation in tumors
- Define classes of oncogenes
- Discuss mechanisms of oncogenesis
- Discuss tumor progression by multiple mutations
- Discuss evolutionary diversity of cancers
- Illustrate neoplastic transformation by viruses
- Discuss the concept of cancer stem cell

Biochemistry

Overview

This module is designed to provide the medical students with a fundamental understanding of current concepts of cellular biochemistry that relate to human health and disease, and to orient them towards the applications of the acquired knowledge in solving clinical problems. Subjects encompass different aspects of the field, focusing on the metabolic events that control the functioning and homeostasis of cells in physiological conditions, and integrating the various aspects and their regulatory pathways.

Compartmentalize to function

Topics

Mechanisms and properties of cell compartmentalization. Dynamic organization and functional properties of cellular membranes (see “Signal transduction”, in Cell Biology).

Learning Objectives

- Illustrate the structure and organization of cellular membranes, and discuss their role in cell properties
- Explain why asymmetry, fluidity, dynamics and specialization are key membrane properties

- Discuss the role of the specific lipid, protein and carbohydrate components in conferring peculiar functions to cellular membranes
- Describe lateral and trans-bilayer motions of membrane lipids and recognize the role of microdomains as functional membrane compartments

Speeding up and regulating reactions

Topics

Principles of metabolic control. Enzyme properties and control in cell homeostasis. Isoenzymes and coenzymes. Medical implications of enzymes.

Learning Objectives

- Describe the fundamental aspects of enzymology that are central to metabolic pathways
- Illustrate the criteria of the international enzyme classification
- Describe the factors affecting enzymatic activity
- Illustrate coenzymes properties and their role in enzyme catalysis
- Define isoenzymes and explain their properties
- Describe mechanisms of inhibition of enzyme action
- Illustrate the regulation of enzyme activity and describe the properties of allosteric enzymes
- Recognize the clinical significance of enzymes

The work of crossing membranes: players and control

Topics

Molecular mechanisms of passive and active transport across cellular membranes.

Learning Objectives

- Describe energy change factors that influence rate and entity of transport across a membrane
- Explain the role of solute transport in homeostasis
- Illustrate mechanisms and control of simple diffusion, passive and active transport
- Recognize the main features of protein-mediated transport and describe the mechanisms of passive and active transport
- Define pores, channels and ionophores
- Describe the passive transmembrane transporters of glucose and of ions
- Describe the molecular mechanisms of active transport and their control
- Overview vesicular transport and information transfer through cell membrane (see “Signal transduction”, in Cell Biology).

Cell nutrients and strategies for energy transfer and use

Topics

Fundamentals of nutritional biochemistry: nutrient functions and requirements. Overview of metabolism and energetic strategies in human cells.

Learning Objectives

- Define nutrients and know functional types and roles
- Define and list essential nutrients, and recognize their importance in human health
- Explain how nutrient energy content can be evaluated, and describe measure units of energy in foods
- Define basal metabolic rate, factors influencing it, and describe how it can be measured
- Describe total energetic requirement, its components and energetic needs for physical activity
- Explain how cells turn nutrients into usable energy
- Define metabolism and discuss its different aims, features, and energetic strategies
- Describe catabolic and anabolic pathways, their interconnections and control
- Define high-energy compounds, and explain the role of ATP as energy transporter inside cells

- Explain the role of biological oxidation in homeostasis and describe the enzymes and coenzymes involved in it.

A key cycle for multiple roles: the tricarboxylic acid cycle

Topics

Bioenergetic and mitochondrial functions: mechanisms and regulation.

Learning Objectives

- Describe energetic flux and transformation in cells
- Illustrate the energetic role of mitochondria metabolism and the mechanisms of its control
- Explain how the oxidation of energetic fuels produces metabolic energy, and illustrate the key role of the TCA cycle in the whole process
- Describe the TCA cycle: substrates, products, cofactors, sites of energy recovery, and regulation
- Discuss the amphibolic role of the TCA cycle, and the role of anaplerotic reactions.

The respiratory chain: a strategy to recover energy

Topics

The mitochondrial electron transport chain functioning and control.

Learning Objectives

- Illustrate the mitochondrial respiratory chain, their components, organization, and properties
- Describe mitochondrial trans-membrane transporters, and the shuttle mechanisms for transfer of reducing equivalents from cytosol to mitochondria
- Describe the process of mitochondrial electron transfer, its control, and differences between NADH and $FADH_2$ as electron donors
- Explain why the electron transport chain releases energy and illustrate the different fates of released energy
- Describe inhibitors of mitochondrial respiratory chain and give examples
- Recognize the role for altered mitochondrial respiratory chain in human diseases (see “Human genetic variation integration”, in Human and Medical Genetics)
- Define free radicals and ROS, explain their formation and toxicity, and describe cell defenses against them.

The rotating molecular motor: ATP synthase

Topics

Mechanisms and regulation of oxidative phosphorylation. Structure, mechanism, and properties of ATP synthase.

Learning Objectives

- Describe ATP synthase structure and functional components
- Explain how the respiratory chain is coupled to ATP formation
- Describe mechanism of oxidative phosphorylation and know factors requirement
- Explain the ATP/ADP cycle, and the concept of respiratory control
- Outline the key role of oxygen in cells, and describe its different uses as metabolic substrate
- Illustrate how inhibitors and uncouplers of oxidative phosphorylation work
- Describe proteins encoded by the mitochondrial genome in humans and recognize the role for their physiological and pathological mutations.

Reactive oxygen species in health and disease

Topics

Production and effects of reactive oxygen species (ROS)

Learning Objectives

- Define ROS and describe their production and clearance
- Describe ROS effects in physiological and physio-pathological conditions

- Discuss nitric oxide production, functions and toxicity
- Discuss antioxidant defenses and redox homeostasis

The sweet side of catabolism: carbohydrates as cellular fuels

Topics

Carbohydrate digestion. Glucose phosphorylation and metabolic fates. Anaerobic and aerobic glycolysis and their control.

Learning Objectives

- Describe digestion and absorption of carbohydrates
- Explain glucose phosphorylation, its importance in metabolism, and its medical application in PET
- Describe the glycolytic pathway, recognizing the relevance of oxidation steps and substrate-level phosphorylation
- Describe the regulation of key glycolytic enzymes by local and hormonal control
- Describe energy production from anaerobic and aerobic glycolysis, and Pasteur effect
- Explain how pyruvate produced by glycolysis can be converted to lactate, acetyl-CoA and oxalacetate, and the control of these reactions

The ins and outs of glucose metabolism

Topics

Overview of metabolic origin and fates of glucose. Metabolism and control of fructose and galactose metabolism. Mechanism and rational of the pentose phosphate pathway.

Learning Objectives

- Describe the origins of fructose and galactose in human cells and the molecular mechanisms of their normal and abnormal metabolism (see “Mechanisms of inheritance”, in Human and Medical Genetics)
- List the different fates of nucleotide-activated sugars
- Discuss why the polyol pathway is necessary but also dangerous
- Describe the pentose phosphate pathway, its regulation, and differences with glycolysis
- Explain the importance of NADPH generation and its functional roles in different cells
- Describe glutathione structure and role in cell structure and functions

Lipid digestion and inter-organ transport

Topics

Biochemistry of lipid digestion and absorption. Mechanisms of transport of simple and complex lipids in blood and lymph. Lipoprotein structure, dynamic and metabolism.

Learning Objectives

- Define essential dietary lipids and explain their roles
- Describe biochemical and nutritional differences between saturated and unsaturated fats
- Describe emulsification, digestion and absorption of dietary lipids
- Describe structural properties, origin, entero-hepatic circulation, and role of bile acids
- Compare differences between absorption and transport of medium- and long-chain fatty acids
- Illustrate mechanisms of inter-organ lipid transport in biological fluids
- Describe lipoproteins: classification, composition, types, and roles
- Describe metabolism of different lipoproteins and recognize the medical significance of lipoprotein metabolism disorders.

Lipids as fuel

Topics

Fatty acid oxidation and metabolism of ketone bodies.

Learning Objectives

- Illustrate the role of triglycerides as circulating and stored fuel
- Describe mechanism and regulation of lipoprotein lipase and hormone sensitive lipase

- Overview fatty acid catabolism and explain the role of carnitine in it
- Describe fatty acid β-oxidation, its requirements and energetic yield
- Explain how β-oxidation is connected to the mitochondrial electron transport chain
- Discuss differences in oxidation of saturated, unsaturated, odd and even carbon fatty acids
- Discuss differences between mitochondrial and peroxisomal oxidation of fatty acids and medical importance of their disorders
- Describe ketogenesis, use of ketone bodies, and recognize clinical significance of ketosis.

There is more to lipids than just being fat

Topics

Overview of lipid functions. Mechanisms and control of cholesterol homeostasis.

Learning Objectives

- Delineate the major metabolic fates of fatty acids and explain their functional roles
- Explain how cells can obtain cholesterol from blood
- Describe inter-organ transport of cholesterol
- Describe biosynthesis of cholesterol and its control
- Recognize cholesterol as precursor of steroid hormones and bile acids
- Explain why cholesterol can be dangerous, and the mechanisms of cholesterol lowering drugs.

Where do amino acids come from?

Topics

Digestion and absorption of proteins. Special roles of aminoacids and important metabolites derived from them.

Learning Objectives

- Explain the different origins of amino acids in humans
- Describe digestion of dietary proteins and absorption mechanisms of amino acids
- Explain how proteolytic enzymes are activated and luminal and cell-surface proteases action
- Describe intestinal mechanism of amino acid and peptide transport
- Define protein turnover and overview mechanism and control of protein catabolism
- Illustrate the major reactions involving amino acids (transamination, deamination, decarboxylation)
- Illustrate mechanism and importance of amino transferases and recognize their use in diagnosis
- Describe precursors, cofactors, and mechanisms of non essential amino acid biosynthesis
- Illustrate normal and abnormal metabolism of phenylalanine (see “Human genetic variation”, in Human and Medical Genetics).

The complex and key potential of cellular amino acids

Topics

Metabolic fates of amino acids and gluconeogenesis.

Learning Objectives

- Describe the role of amino acids as precursors of key nitrogen-containing compounds and illustrate important metabolites derived from them
- Describe energetic fates of amino acids, its cofactor requirement, and differences between glucogenic and ketogenicones
- Define gluconeogenesis, and describe its localization, substrates and energetic
- Illustrate the glucose-lactate cycle and the alanine cycle and recognize their role in homeostasis

- Explain why fatty acids are not substrates of gluconeogenesis and explain consequences
- Describe short- and long-term effects of glucagon and insulin on gluconeogenesis
- Describe regulation of gluconeogenesis and illustrate its coordinated control with glycolysis.

Nitrogen balance, ammonia transport and excretion. Nucleotide metabolism

Topics

Molecular mechanisms of ammonia formation, transport and excretion. Fundamentals of nitrogen balance. Overview of nucleotide metabolism and connections with that of amino acids.

Learning Objectives

- Define nitrogen balance and explain its physiological and pathological variations
- Describe ammonia formation, blood transport, and strategies for elimination
- Overview urea cycle and its regulation, and illustrate reactions that feed nitrogen into it
- Discuss how urea cycle and tricarboxylic acid cycle are connected
- Describe urinary excretion of nitrogen and recognize the existence of urea cycle disorders
- Overview nucleotide metabolism, and explain the role of the involved coenzymes
- Describe the sources of the ring atoms of purines and pyrimidines, and illustrate the role of amino acids in nucleotide metabolism
- Illustrate the final products of nucleotide catabolism, and discuss the medical significance of elevated uric acid production.

Glycogen store

Topics

Glycogen properties and function. Metabolism and regulation of glycogen.

Learning Objectives

- Illustrate the structural features and localization of glycogen
- Differentiate between local and systemic roles of glycogen as glucose store
- Recognize advantages and limits of glycogen as energy storage
- Explain how glycogen can be accumulated and utilized
- Describe molecular processes of glycogen metabolism, and explain how its opposite pathways are counter regulated
- Recognize the medical importance of glycogen storage diseases.

Fat store

Topics

Triacylglycerols properties, location and function. Metabolism of triacylglycerols and its control.

Learning Objectives

- Describe structure, blood transport, and localization of triacylglycerols in humans
- Recognize advantages and limits of triacylglycerols as energy store
- Describe fatty acid biosynthesis, its location, substrates, multi-enzyme complex mechanism, and regulation
- Discuss the role of malonyl-CoA, biotin, and NADPH in fatty acid biosynthesis
- Outline differences betweenβ-oxidation and biosynthesis of fatty acids
- Illustrate the processes of fatty acid chain elongation and desaturation
- Describe triacylglycerol biosynthesis,catabolism, and their hormonal control.

Metabolic interrelationships and cooperation between cells

Topics

Blood glucose homeostasis and effects of its deregulation. Nervous/endocrine control and intercellular cooperation in the fed/fasting cycle and in stress conditions (see “Signal transduction”, in Cell Biology, and “The regulation of gene expression”, in Molecular Biology).

Learning Objectives

- Describe the prompt and long-lasting stores of energy (circulating and tissue stores)
- Explain the importance of blood glucose regulation and discuss the role of inter-tissue glucose sensing and communication
- Demonstrate ability to relate the effects of hypoglycemia to alterations of cellular metabolism and energy management
- Describe the endocrine control of glycemia (insulin and counter regulatory hormones)
- Illustrate structure, secretion, and action mechanism of insulin and glucagon
- Outline metabolic adaptations and regulation in the fed and fasting state and in stress conditions
- Explain the concept of metabolic cooperation among different cells as the key to healthy survival.

Human and Medical Genetics

Overview

This module is focused on the application of genetic principles in the practice of medicine. HMG covers on the basic principles of classical and molecular genetics, exploring the inheritance of diseases in families, pathogenesis of inherited disorders, cytogenetics and molecular diagnosis of genetic diseases and provision of genetic counselling for families. Starting from the learning objectives of the Molecular Biology module, focused on the molecular basis of genetics (including such topics as replication, expression, translation and mutation), HMG module is designed to understand how genetic problems may lead to disease or lethality and provide a conceptual framework for future reference.
Considering that genetics represents a true integration between basic and clinical sciences, some clinical aspects of medical genetics will be addressed in the following years.

Prerequisites

It is assumed that students have a good understanding of basic genetics. The self-study programme includes the following topics: Mendelian genetics: Mendel's Laws of Heredity, probability of inheritance and Punnett Squares, alleles and genes, dominant and recessive alleles, homozygous and heterozygous definitions. The basic rules of probability: the Sum and Product.
If students would like to brush up on genetics terminology, we suggest visiting the websites http://www.genome.gov/Education/(National Human Genome Research Institute) and http://biology.about.com/od/basicgenetics/a/aa071705a.htm, or consulting the book 'Essential Genetics' by P. Russell., Cummings Ed.
Students are encouraged to perform a self-examination test (multiple choice) before the course to check whether their basic knowledge in genetics is sufficient to successfully meet the course programme.

Mitosis, meiosis and ploidy cycles

Topics

Chromosome behaviour during cell cycle in somatic and germinal cells.

Learning Objectives

- Describe the stages of mitosis and meiosis and the cell cycle, and explain the significance of each.
- Differentiate between genome inheritance in somatic cells (Mitosis) and gametes (Meiosis).
- Define haploid and diploid chromosome content during meiosis and mitosis.
- Explain the recombination and crossing-over events.
- Discuss how a mistake in meiosis can result in chromosomal syndromes such as Down syndrome.

Mechanisms of inheritance

Topics

How genetic traits are inherited. The applications of Mendelian laws in monogenic inherited diseases.

Learning Objectives

- List the Mendel's basic principles of heredity applied in humans inherited traits.
- Describe the difference between genotype and phenotype, locus and allele.
- Describe the concept of Multiple-allele Series, and list the ABO blood groups.
- Discuss the patterns and describe the characteristics of single gene inheritance.
- Recognise typical pedigree patterns.
- Calculate the recurrence risks for single gene disorders and to solve problems and complete pedigrees.
- Explain the occurrence of X-linked recessive traits.
- Discuss the difference between expression and penetrance of a disorder.
- Discuss the multiple explanations for variable expressivity of single gene disorders.
- Illustrate the notion of "complex diseases" and describe the importance of the environmental influence on disease predisposition.

Human genetic variation and dynamic mutations

Topics

Relationship between mutation/ polymorphisms and phenotype.

Learning Objectives

- Differentiate between mutation and polymorphism of DNA
- Describe the role of mutations in evolution.
- Discuss the types of mutation that can occur including substitution (missense, nonsense), insertion/deletion (in-frame, frameshift), splice-site, amplification of repeated sequences, genomic instability, and regulatory.
- Describe the potential consequences (on gene expression) of the different types of mutation.
- Discuss the concept that whether a mutation causes disease, is benign or beneficial depends on the precise nature of the change and where and when it occurs.
- Describe examples of human disease caused by different types of mutation.
- Describe the concept of triplet repeat diseases and the correlation between earlier manifestations of clinical symptoms ('anticipation') and molecular pattern.

Population genetics

Topics

Genetic variability in a population: genotypic and allele frequencies. A simplified description of allele assortment at reproduction: the gene pool. The Hardy-Weinberg law (HWL) of allelic and genotypic frequencies, the Hardy-Weinberg equilibrium (HWE), and the conditions for their validity. Factors causing evolution of a population (changes of allelic frequencies over generations) equal to violations of the Hardy-Weinberg postulates.

Learning Objectives

- Be familiar with the lexicon of population genetics: population, gene pool, allele frequencies and genotype frequencies
- Describe the HWL equation and state the HWE principle
- Calculate the allele and/or genotypic frequencies of genes of interest in human genetics, by applying the HWL
- List the factors (inbreeding, genetic drift, mutation, migration, selection) that violate HWE and alter allele frequencies, and describe how they change the HWL .

Cytogenetics and clinical cytogenetics

Topics

The Karyotype description.The chromosomal abnormalities and their importance in the phenotype and reproductive risk.

Learning Objectives

- List the basic structure and function of chromosomes, the karyotype and how they relate to medicine.
- Describe the different types of cytogenetic abnormalities that can occur.
- Differentiate among the different techniques (classical karyotyping, FISH -Fluorescence in Situ Hybridisation- and CGH -Comparative Genomic Hybridisation)-arrays) useful to detect microscopic and sub-microscopic rearrangements.
- Describe the recurrence risks in pregnancy for the principal types of cytogenetic abnormality (trisomies and translocations).
- Describe the pre- and post-natal applications of cytogenetic investigation.

Sex determination and X-linked gene dosage compensation

Topics

The genetics of sex determination and the more frequent genetic anomalies associated with incomplete sexual differentiation. How do male and female compensate X-linked gene dosage?

Learning Objectives

- Describe the genetic influence in development of the gonads (see "The Urogenital System", Human Body course)
- Describe the importance of the SRY gene in male sex differentiation.
- Describe some sex determination disorders related to genetic defects.
- Discuss the importance of X chromosome inactivation in females related to gene dosage ("Structure of the genetic material and its organization in the cell nucleus" and "Regulation of gene expression", Molecular Biology).
- Describe the mechanism leading to X-linked gene silencing related to XIST.
- Describe the difference between random and preferential inactivation in presence of chromosome alterations involving X.
- Discuss the concept that a few X-linked genes escape X inactivation process and the relationship with Turner syndrome.

Non-Mendelian disorders

Topics

A non-Mendelian inheritance pattern of genetic diseases: defects of genomic imprinting.Uniparentaldisomies (UPD) and imprinting diseases: PraderWilli/Angelman syndromes and Silver Russell/Beckwith-Weidemann syndromes.

Learning Objectives

- Consider the importance of epigenetic changes in human disease (see "Structure of the genetic material and its organization in the cell nucleus" and "Regulation of gene expression", in Molecular Biology).
- Explain the chromosomal mechanisms leading to UPD.
- List the UPD with a phenotypic effect in humans.
- Discuss the meaning of imprinting in mammals and the epigenetic mechanisms leading to silencing of the imprinted allele.

Gene testing and genetic counselling

Topics

The main classes of gene testing and methods to perform them. The importance of genetic counselling in genetic testing procedures

Learning Objectives

- Illustrate the workings and importance of major molecular genetics techniques for gene testing.
- List the main applications of gene testing: carrier screening, pre-symptomatic testing for predicting adult-onset disorders such as Huntington's disease, diagnosis confirmation of a symptomatic individual.

Inherited cancers

Topics

Cancer occurrence may be an inherited trait. Pattern of mutations of the main class of genes involved in Inherited cancers: the tumor-suppressor genes.

Learning Objectives

- Define sporadic and inherited cancers.
- List some examples and pattern of inheritance of syndromic and non-syndromic hereditary cancer conditions (Retinoblastoma, Breast and ovarian inherited cancers, Colon cancer).
- Describe 'The two hit hypothesis' - tumour suppressor gene mutation in sporadic and inherited cancer, the example of the Retionoblastoma gene (RB).

4. FACULTY

ISABELLA BARAJON, MD. isabella.barajon@unimi.it Professor of Human Anatomy of the Faculty of Medicine and Surgery, University of Milan, since 1998. She teaches medical students in specialist Schools and medical biotechnology students. Her main research interests are related to the field of Neuroscience and Embryology and her current research topics deal with the expression of immunological molecules and cancer testis antigens during embryonic development. She has spent research periods in neurophysiology, medical physiology and anatomy laboratories of the Panum Institute of the Faculty of Health Sciences at the University of Copenhagen and collaborates with the Division of Haematology and Oncology, Texas Tech University Health Sciences Center.

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PF's activity is mainly focused on the genetic and genomic analysis of rare genetic syndrome characterized by intellectual disabilities and/or autism. She is head of a research team, working in the Center of Biomedical Research and Technology, IRCCS Istituto Auxologico Italiano, specialized in Molecular Cytogenetics, Cytogenomics & Molecular Genetics. She is currently involved in the followings research projects: genetics of mental retardation and autism; identification of the genetic cause of syndromes associated with an abnormal karyotype; search of novel genes and mechanisms underlying Cornelia de Lange, Beckwith-Wiedemann and Silver-Russell syndromes by whole-genome approaches; study of patients with clinical diagnosis of Smith-Magenis syndrome without typical deletion in 17p11.2 and identification of new or

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She is involved in research projects that study innovative healthcare training, medical humanities and patients' illness experience. She participated, as group facilitator, in the first workshop on narrative medicine held in Italy by the Columbia University. She has lectured and published on the ways in which narrative training and reflective writing helps to increase empathy and reflection in healthcare students and professionals.