



## **MEDTEC SHOOL**

**Course: CELL BIOLOGY, HISTOLOGY, EMBRYOLOGY (CBHE)**

**Year (1<sup>st</sup>-2<sup>nd</sup>-3<sup>rd</sup>-4<sup>th</sup>-5<sup>th</sup>-6<sup>th</sup>): 1<sup>st</sup>**

**Period (1<sup>st</sup>-2<sup>nd</sup> semester – annual): 1<sup>st</sup>-2<sup>nd</sup> semester**

**Credits: 11 (5 CFU for CB, 6 for H-E), 132 hours**

### **Objectives**

The principal objective of this integrated course is to provide students with an understanding of the structural and functional organization of the human body at the cellular and subcellular levels. The course is divided in three modules: Cell Biology, Histology, and Embryology. The syllabus is here detailed for each module, focusing on the topics that will be the object of one or more lessons. By the end of the Cell Biology module, students will acquire knowledge about the architecture and characteristics of animal cells, the main molecular cellular processes, and the bases of genetics. The Histology module will provide students with the ability to recognize and describe histological preparations, identifying the structure, function and features of the main histological tissues. By the end of the course, students will acquire knowledge about organization of cells and tissue and their relationship with function and dysfunction and will be able to recognize the various tissues by light microscopy using preparations stained with routine histological techniques. In the module of human Embryology, the students will be introduced to the processes of gametogenesis, fertilization, embryonic development in human development. Following a description of the early stages of embryogenesis, some major topics in organogenesis will be introduced as to understand the main morphological events characterizing the development of the body and its various organ systems. Knowledge acquired during this course is fundamental to understand other preclinical and clinical disciplines. At the end of the course students will be able to:

- Identify, describe, and explain the function of the main structures/organelles of an animal cell
- Describe and relate different processes characterizing an animal cell
- Apply genetic laws and hereditary models to solve simple problems
- Identify, describe, and explain the function of the main tissues
- Describe how tissue characteristics reflects their functional role and pathological alterations
- Identify, describe and explain the main events controlling gametogenesis, fertilization and early stages of embryogenesis.
- Recognize the main morphological events characterizing the development of the body and its various organ systems

### **Prerequisites:**

“Chemistry and organic chemistry exam” (1semester 1 academic year) is required to sustain CBHE exam.

## Contents

### Cell biology module

#### Topic 1. Structure and function of human cells

*Content:* Cell membrane and endoplasmic reticulum. The fluid-mosaic model of the cell plasma membrane. Main structural features and functions of membranes. Principles of transmembrane transport. Exocytosis and endocytosis; Lysosomes; Peroxisomes; Mitochondria, Cellular cytoskeleton, structure of the nucleus

*Learning goals:*

- Recognize and illustrate the cell membrane: structure, specialized functions, mechanisms of transport
- Recognize and illustrate the morphology and specific functions of the rough and smooth endoplasmic reticulum
- Illustrate the mechanisms of endocytosis and exocytosis
- Recognize the lysosomes, mitochondria, and peroxisomes
- Illustrate their structure and specific functions
- Illustrate the structure and function of microfilaments, intermediate filaments, and microtubules
- Recognize and illustrate the morphology and function of the nucleus, chromatin arrangement, nuclear envelope, nucleolus, and nuclear pores

*Clinical drop:* Lysosomal storage diseases, pharmacological agents affecting the function of microtubules

#### Topic 2. The origin of life

*Content:* Prokaryotic and eukaryotic cell organization; the endosymbiotic theory; the RNA world

*Learning goals:*

- Illustrate how the cell represents the fundamental unit of life
- Discuss the main structural differences between prokaryotic and eukaryotic cell
- Discuss how eukaryotic cells might have evolved

#### Topic 3. Protein structure

*Content:* the central dogma of molecular biology, protein classification, protein constituents, the peptide bond and its properties, the four levels of protein structure, protein function regulation

*Learning goals:*

- Understand the flow of information within cells
- Illustrate the main functions of proteins
- Describe the classification of amino acids



- Describe the four levels of protein structure

#### **Topic 4. Structural and functional properties of DNA molecules**

*Content:* DNA as the genetic material. Structure of the genetic material, physico-chemical properties of DNA molecules.

*Learning goals:*

- Describe the structure of DNA
- Discuss the structure-function relationships of DNA molecules
- Discuss the main discovery that led to the definition of DNA as the genetic material

#### **Topic 5. Chromatin and chromosomes**

*Content:* The organization of DNA in the cell nucleus, chromatin structure, histones, how chromatin features are inherited during cell division. The organization of genetic material in bacteria.

*Learning goals:*

- Illustrate how the genetic material is organized in bacteria
- Illustrate how the genetic material is organized in eukaryotic cell nucleus
- Describe the levels of chromatin compaction
- Compare the DNA organization in prokaryotes vs eukaryotes

#### **Topic 6. The mechanism of DNA replication**

*Content:* Semi-discontinuous replication, replication strategies, prokaryotic and eukaryotic DNA polymerases, priming. The problem of the replication of chromosome ends

*Learning goals:*

- Discuss molecular mechanism of DNA replication, considering the molecular machineries involved
- Discuss the problems raised by DNA replication and how the different proteins participating in the process can solve them

*Clinical drop:* Telomerase and cancer

#### **Topic 7. RNA transcription**

*Content:* Transcription in prokaryotes and eukaryotes. Eukaryotic transcription factors - general & specific. Complexity of the transcriptome.

*Learning goals:*

- Discuss the flow of genetic information
- Discuss the complexity of the transcriptome in cells
- Describe the mechanism of RNA synthesis (transcription) in prokaryotes and eukaryotes

#### **Topic 8. RNA processing and gene expression regulation in prokaryotes**



*Content:* How mRNAs are processed in eukaryotes, what is RNA splicing. Gene expression regulation in prokaryotes.

*Learning goals:*

- Describe the RNA processing
- Describe the function of operons in regulating gene expression in prokaryotes

### **Topic 9. The genetic code and protein synthesis**

*Content:* 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 goals:*

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

### **Topic 10. Cell cycle**

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

*Learning goals:*

- 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

### **Topic 11. Mitosis**

*Content:* Overview on mechanisms of cell division. Chromosome behavior during cell division in somatic cells. Role of cytoskeleton during mitosis.

*Learning goals:*

- Describe the morphological aspect of nucleus during mitosis
- Describe the stages of mitosis and explain the significance of each step
- Describe the main cytoskeletal structures involved in cell division

### **Topic 12. Meiosis**

*Content:* Chromosome behavior during cell division in germinal cells. Gametogenesis.

*Learning goals:*

- Describe the function and the events that characterize meiotic division
- Illustrate the mechanism of crossing-over
- Understand how genetic variability is produced during meiosis
- Discuss the differences between mitosis and meiosis

### **Topic 13. How genes are inherited**

*Content:* Mendel laws, the genetic significance of meiosis. Extensions to Mendel's laws. Penetrance, expressivity.

*Learning goals:*

- Describe chromosome dynamics during meiosis, and their consequences at the genetic level
- Describe Mendel's laws in the light of the meiosis process
- Discuss the extensions/exceptions to Mendel's laws
- Describe penetrance, and expressivity concepts

### **Topic 14. Cytogenetics and clinical cytogenetics**

*Content:* Preparation and interpretation of the karyotype. Genomic and chromosomal abnormalities and their importance in the phenotype and reproductive risk. Overview of the main techniques (classical karyotyping, FISH -Fluorescence in Situ Hybridization- and CGH - Comparative Genomic Hybridization-arrays).

*Learning goals:*

- Describe the main methods for chromosome analysis and their application to the diagnosis of genetic disorders
- Describe the human karyotype using the relative nomenclature
- Describe the main numerical and structural chromosome anomalies
- Discuss pro, cons, limits of the cytogenetic analysis

### **Topic 15. Genetic variation**

*Content:* Polymorphisms and mutations: classification and functional consequences.

*Learning goals:*

- Describe the different types of point mutations
- Discuss differences between germinal and somatic mutations, and between polymorphisms and mutations
- Describe the functional consequences of the different types of mutation at the RNA and protein levels

### **Topic 16. Protein folding**

*Content:* How proteins acquire their final conformation and their functional properties after synthesis, the role of chaperones and proteasome.

*Learning goals:*

- Understand how proteins acquire their final conformation and their functional properties after synthesis
- Understand the biological role of chaperone proteins
- Describe the function of proteasome
- Describe pathological consequences of protein misfolding and/or aggregation

*Clinical drop:* Prion disease

### **Topics 17. Protein sorting and secretory pathway**

*Content:* Post-translational modifications and fate of proteins after synthesis. Signals and mechanisms of protein sorting to organelles and secretory pathways.

*Learning goals:*

- Describe examples of post-translational modifications and how they might affect protein function
- Discuss general requirements for protein sorting
- Discuss how proteins are guided to the compartments where they function
- Describe the different pathways used to target protein to different cell compartments
- Describe mechanisms controlling proper protein folding during sorting from the ER

*Clinical drop:* Unfolded protein response in human diseases

### **Topics 18. Cell signaling**

*Content:* General principles of cell signaling. Signal transduction. Nuclear receptors. G-protein coupled receptors. Enzyme-coupled receptors. Second messengers. Protein kinases and molecular switches.

*Learning goals:*

- Describe the different types of intercellular communication
- Define the main mechanisms of signal transduction by different types of receptors
- Discuss the central role of protein kinases in regulating this process
- Describe the main pathways of signal transduction by GPCRs
- Understand the role of second messengers

### **Topic 19. Apoptosis**

*Content:* Differences between necrosis and apoptosis. Roles of apoptosis. Molecular regulation of apoptosis. Intrinsic and extrinsic apoptotic pathways. Caspases. The apoptosome. The Bcl-2 family.

*Learning goals:*

- Describe developmental, physiological and pathological processes in which apoptosis plays a crucial role
- Define molecular pathways involved in apoptosis
- Discuss regulator, adaptor and effector molecules in apoptosis
- Discuss signals for elimination of apoptotic cells

**Topics 20. Oncogenes and cancer**

*Content:* General facts and stats about cancer. Cancer as a disease of cell behavior. Hallmarks of cancer. In vitro contact inhibition and in vivo tumor progression. Control of cell proliferation in cancer. Classes of oncogenes. Mechanisms of proto-oncogenes activation. Chromosomal alterations and cancer. Multiple mutations in cancer progression. Tumor suppressor genes.

*Learning goals:*

- Understand genetic and environmental contribution to carcinogenesis
- Understand the altered properties of cancer cells and cancer heterogeneity
- Discuss tumor progression by multiple mutations
- Discuss the differences between oncogenes and tumor suppressors
- Discuss molecular mechanisms of oncogenesis

**Topic 21. Viruses**

*Content:* Classification of viruses: DNA and RNA viruses. Structure of viral particles. Viral tropism. The cycle and the genome organization of retroviruses. Role in human disease. Use of viral vectors for gene therapy.

*Learning goals:*

- Describe the structure of the main classes of animal viruses
- Understand the differences between naked and enveloped viruses (e.g. structure, infection cycle)
- Understand general principles guiding viral replication
- Describe how retroviruses infect and replicate within cells

**Topic 22. Stem cells, iPSc and organoids**

*Content:* Properties and sources of stem cells. Induced pluripotent stem cells. Modelling diseases with iPSCs and organoids.

*Learning goals:*

- Understand the basic properties of stem cells, the concepts of potency, cell fate determination, and reprogramming



- Understand the differences between embryonic stem cells, adult stem cells and induced-pluripotent stem cells (iPSCs), and organoids
- Describe the applications of stem cell research in medicine

Co-hosted by Prof. Paraboschi and Prof. Lodato

### **Topic 23. Genome engineering: new technologies for DNA editing**

*Content:* New technologies to perform genome engineering. CRISPR-Cas9 system. Ethical challenges related to these new technologies.

*Learning goals:*

- Learn the systems that can be used to perform genome editing
- Learn the basis of CRISPR-Cas9 technology
- Discuss the application of genome editing in medicine

## **Histology Module**

### **Topic 1: Introduction to histological methods. From tissue sample collection to the observation at the microscope**

**Learning goals:**

- Historical notions of histology
- General aspects of histological specimen processing such as: inclusion, fixation and sectioning
- Introduction to the most commonly used histological and histochemical staining
- Introduction to the main instruments for the morphological analysis and their application in scientific research and medical diagnosis

### **Topic 2: The epithelial tissue: Apical and basolateral specialization of epithelial cells. Cell junctions.**

**Learning goals:**

- Illustrate the morphology and function of the apical and basal domains of epithelial cells
- Illustrate the morphology and function of the specialized structures of the lateral domain: occluding, anchoring and gap junctions

Clinical drop: Epithelial-to-mesenchymal transition in cancer

### **Topic 3: The epithelial tissue: Lining epithelia**

**Learning goals:**

- Recognize the morphological characteristics of the different types of epithelial cells
- Illustrate the classification and localization of the lining epithelia



#### **Topic 4: The epithelial tissue: Secretory epithelia**

##### **Learning goals:**

- Recognize the morphological characteristics of the different types of secretory epithelial cells
- Illustrate the general aspects and functions of exocrine glands
- Illustrate the general aspects and functions of endocrine glands
- Recognize the morphological characteristics and understand the functions of the different types of exocrine and endocrine glands

Clinical drop: Diabetes

#### **Topic 5: The connective tissue: Cellular components and extracellular matrix**

##### **Learning goals:**

- Illustrate the general organization of the connective tissue
- Classify the different cellular components of the connective tissue and recognize their morphological characteristics
- Illustrate the different constituents of the extracellular matrix

Clinical drop: Extracellular matrix remodeling in tumor invasion and fibrosis

#### **Topic 6: The connective tissue: Proper connective tissue**

##### **Learning goals:**

- Illustrate the properties and typical locations of the different connective tissues
- Illustrate the functional roles of the different connective tissues
- Describe the general characteristics of the white and brown adipose tissue

#### **Topic 7: Specialized connective tissues: Cartilage**

##### **Learning goals:**

- Illustrate the cellular and extracellular components of the cartilage and mechanisms of growth
- Understand the functional role of the cartilage
- Describe the main localizations of cartilage in the human body

Clinical drop: Osteoarthritis and cartilage transplant frontiers

#### **Topic 8: Specialized connective tissues: Bone and osteogenesis**

##### **Learning goals:**

- Illustrate the cellular and extracellular components of the bone
- Illustrate the structural characteristics of compact and spongy bones

- Describe the functions of osteoblasts and osteoclasts
- Understand the mechanisms of bone growth, bone remodeling and repair

Clinical drop: Osteoporosis

### **Topic 9: Specialized connective tissues: Blood and hematopoiesis**

#### **Learning goals:**

- Illustrate the cellular and non-cellular components of blood
- Describe the morphological features and the functional roles of erythrocytes, leukocytes and platelets
- Describe the main steps of haematopoiesis: the developmental precursors of erythrocytes, leukocytes and platelets

Clinical drop: Hematopoietic bone marrow transplant

### **Topic 10: Lymphoid organs (lymph nodes, spleen, thymus, tonsils)**

#### **Learning goals:**

- Describe the general features and functions of the lymphoid organs
- Illustrate the structure of the different lymphoid organs: spleen, thymus, lymph nodes and tonsils
- Illustrate the structure and functional organization of the mucosal-associated lymphoid tissue (MALT)

Clinical drop: sentinel lymph node in cancer staging

### **Topic 11: The integumentary system: Epidermis and dermis**

#### **Learning goals:**

- Illustrate the integumentary system
- Recognize the structure of the integumentary system: epidermis and dermis and the morphological and functional characteristics of the different cell types

Clinical drop: Skin repair and stem cell-based approaches

### **Topic 12: The muscle tissue: Skeletal and cardiac muscle tissues**

#### **Learning goals:**

- Illustrate the general overview and function of the striated muscle tissue
- Illustrate the structure of the skeletal muscle and its components
- Illustrate the neuro-muscular junction and understand basic knowledge of striated muscle contraction
- Recognize the morphological criteria to distinguish skeletal and cardiac muscle in histological preparations

Clinical drop: Duchenne muscular dystrophy



**Topic 13: The muscle tissue: Smooth muscle tissue.**

**Learning goals:**

- Describe the general features of smooth muscle tissues and differences with skeletal muscle
- Illustrate the main localizations of smooth muscle tissue and general principles of smooth muscle contraction
- Recognize the morphological criteria to distinguish cardiac and smooth muscle in histological preparations

**Topic 14: The nervous tissue: Neurons. Nerve fibers**

**Learning goals:**

- Illustrate the structure, morphological features and general function of neurons
- Recognize the axon, myelin sheath, node of Ranvier, Schmidt-Lantermann clefts
- Illustrate the structure of peripheral nerves, distinction of the endoneurium, perineurium and epineurium
- Illustrate the functional role of Schwann cells in the process of myelination

Clinical drop: Multiple sclerosis

**Topic 15: The nervous tissue: Synapses. Neuroglia. Peripheral nerve terminals**

**Learning goals:**

- Illustrate the structure of the neural synapse and its role in nerve impulse transmission
- Classify the different glial cells: morphology, general functions and relationship with neurons
- Illustrate the structure and function of the blood-brain barrier

**Topic 16: The nervous tissue: Synapses. Neuroglia. Peripheral nerve terminals**

**Learning goals:**

- Illustrate the structure of the neural synapse and its role in nerve impulse transmission
- Classify the different glial cells: morphology, general functions and relationship with neurons
- Illustrate the structure and function of the blood-brain barrier

**Embryology Module**

**Topic 1. Principles of gametes production and maturation.**

**Learning goals:**

- To describe the main phases of gametogenesis:

- origin and migration of germ cells
- increase in their number, reduction in chromosomal numbers
- structural and functional maturation of gametes

## **Topic 2. Female gametogenesis and overview of the related changes in the female genital tract and hormonal control.**

### **Learning goals:**

- To describe the structural aspects of the ovary
- To describe the main features of oogenesis and ovulation: the ovarian cycle
- To outline the intrinsic and extrinsic hormonal guidance of the ovarian cycle
- To illustrate the changes in the ovaries during the ageing process.
- To outline the general structure of the uterus and uterine tube and of their cyclic changes
- To give an overview of some of the molecules involved in embryonic development: Transcription factors, Signaling molecules

Clinical drops: Mittelschmerz (abdominal pain) and ovulation

## **Topic 3. Male gametogenesis and overview of the male genital system.**

### **Learning goals:**

- To outline the components of the male genital system and the general structure of the testis and epididymis.
- To describe the histological features of the seminiferous epithelium
- To illustrate the relevance of the “blood-testis” barrier
- To describe the process that leads from spermatogonia to spermatozoa: spermatogenesis and spermiogenesis
- To understand the role of Sertoli cells
- To describe the general aspect of the spermatogenic cycle and spermatogenic wave
- To outline the intrinsic and extrinsic hormonal guidance of male spermatogenesis

Clinical drops: Male infertility, abnormal gametogenesis

## **Topic 4. Fertilization.**

### **Learning goals:**

- To describe the transport of the egg and sperm
- To describe the process of fertilization



- To describe the cleavage process of the zygote and the relevance of the different components of the early embryo: inner cell mass, trophoblast, zona pellucida, blastocele
- To describe the embryo transport to the uterus

#### **Topic 5. Early stages of the embryo development**

##### **Learning goals:**

- To describe the process of implantation into the uterine lining: formation of the trophoblastic plate and placental villi
- To describe the transformation of the inner cell mass into the embryonic shield (disc): becoming bilaminar
- To describe the formation of the amniotic cavity, of the primary and secondary yolk sacs and of the extraembryonic mesoderm

Clinical drop: Ectopic pregnancy

#### **Topic 6: Gastrulation. Becoming trilaminar. 3rd week of Human Development**

##### **Learning goals:**

- To describe the role of primitive streak and primitive node and the formation of the body axes

Clinical drop: situs inversus and Kartagener syndrome

- To describe the formation of the three primitive layers
- To describe the notochord and its role.
- To describe the formation of the neural plate and neural tube.

Clinical drop: sirenomyelia

- To describe the destiny of the neural crest

Clinical drops: epithelio-mesenchymal transition

#### **Topic 7. The 4th week: establishing the body plan.**

##### **Learning goals:**

- To illustrate the concept of organogenesis
- To describe the destiny of the three embryonic layers
- To illustrate the concept of segmentation
- To describe the outcome of the folding of the embryo: formation of the intestinal tube, formation of the body cavities, formation of the body wall

Clinical drop: gastroschisis and omphalocele

#### **Topic 8. The 4th week: Embryonic circulation and principal aspect of body organization.**



### **Learning goals:**

- To describe the formation and general organization of the embryonic circulation

### Clinical drops: vasculogenesis and angiogenesis

- To explain some basic molecular aspects characterizing the establishment of the body plan
- To relate the developmental aspects of the body plan to the adult body organization

### **Topic 9. The maternal-fetal relationship**

### **Learning goals:**

- To understand the exacting requirements of the relationship between the embryo and the mother
- To describe the structure and functional role of the tissue derived from the trophoblast that composes the fetal-maternal interface: placenta and chorion
- To describe the structure and functional role of the extraembryonic membranes derived from the inner cell mass: amnion, yolk sac, allantois, extraembryonic mesoderm
- To describe the formation of the umbilical cord
- To outline the most important aspects of placental circulation and physiology.

### Cinical drop: Maternal immune activation

## **Teaching Methods**

The described topics will be explained during **lectures**, that will be held synchronously, either in presence or with streaming platforms. Students are expected to participate in a proactive manner. Lectures will be integrated by scheduled contributions of internationally renowned experts on specific course topics, organized in “**Meet the expert session**”, where students will have the opportunity to directly interact with scientists/medical doctors and prepare compelling questions to pose to the experts in the Q/A discussion. During the course, students will also be asked to carry out and present to the class a **group project** on topics discussed during lectures, to activate, integrate and solidify the knowledge acquired in class in an interdisciplinary manner. Peers’ assessments of the project will be part of the activity. Teachers will evaluate the group activity and integrate the score with the end of semester exam (ESE).

## **Verification of learning**

ESE will consist of questions from material covered in lectures. Learning goals and objectives presented at the start of each lecture will serve as a study guide for the final exam at the end of the semester. The ESE will be composed of 66 questions, proportionally distributed among the course modules, to be answered in 60 minutes. In detail: 30 for Cell Biology, 24 for Histology, and 12 for Embryology. Questions may include: Multiple choice questions, Drag and drop onto a background image, Drag and drop into text, Matching, Select missing words, Short answers. To pass the test, the student needs to answer correctly to 36/66 questions (grade: 18/30), and to reach a minimum of 50% correct answers in each module. ESE with more than 62 correct questions will be graded “30 cum laude”. Practical examples of the questions proposed in



the ESE will be provided during the course and a practical test of the ESE will be offered (not mandatory) to students to familiarize with the exam platform and assessment modality prior to the ESE.

## **Texts**

Cell Biology:

- Alberts B et al. Essential cell biology. 5th edition
- Hardin et al. Becker's World of the cell. 9<sup>th</sup> edition

Histology:

- Ross and Pawlina, Histology A Text and Atlas - With Correlated Cell and Molecular Biology, 7th International Edition.
- Barbara Young et al. Wheater's Functional Histology: A Text and Colour Atlas, 6th edition. Churchill

Embryology:

- Bruce M. Carlson, Human Embryology and Developmental Biology, 5th edition, Elsevier, 2013
- Gary C. Schoenwolf et al. Larsen's Human Embryology, 5th Edition.
- Kevin L. Moore, T.V.N Persaud, Mark G.Torchia, The developing human. Clinically oriented embryology, 10th edition.