MEDICINE AND SURGERY

Course: The Cell: Molecules and Processes

Year: 1st

Period: 2nd semester

Credits: 6 (72 hours)

Objectives

The Cell: Molecules and Processes (CMP) provides ground to understand the relationships between molecular and cell biology, genetics, and medicine. The course will particularly emphasize presentation and critical discussion of the major biological functions at a molecular level, and will provide the foundations for medical genetics, which will be further developed during the second year. The knowledge acquired in the course is necessary to proficiently study other preclinical and clinical sciences, including physiology, general pathology, immunology and microbiology. The course's content is especially propaedeutic to Molecular Medicine & Computational Biology, and Mechanisms of Diseases 1 and 2.

Application of knowledge and understanding:
By the end of the course the student will be able to:

- Describe the main cellular processes, such as cell division, protein sorting to different organelles, cell signaling, and apoptosis
- Describe the main molecular processes leading to replication of DNA, synthesis and processing of RNA, and translation into proteins
- Describe the main mechanisms of DNA mutation and the processes involved in maintaining genome integrity and relate them to human diseases
- Relate the various processes that control cell communication, cell proliferation and death with the development of diseases (e.g. cancer)
- Compare the diverse modes of inheritance, acquire the ability to draw pedigree charts, and describe different methodologies to diagnose genetic diseases.

Making judgements; Communication skills; Learning skills.
By the end of the course students will have improved their ability to communicate and work in team, and acquired advanced learning skills in group studying, knowledge organization, information selection, revision and retention.

Prerequisites

It is expected that the students are already familiar with the general structure and function of a eukaryotic cell and organelles, as covered in the Cytology module, which is part of the Building Bodies course (1st year, 1st semester). Students are also expected to know the structure and properties of water and biomolecules, as described in the course "Principle of the Living Matter" (1st year, 1st semester).

Contents

Topic 1. The origin of life

Content: Prokaryotic and eukaryotic cell organization. From prokaryotic to eukaryotic cells: the endosymbiotic theory.

Teaching method: Lecture

Learning objectives:

- 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 2. How does evolution work?

Content: Darwin, Wallace and the origin of species. Example of application of the evolution theory in medicine.

Teaching method: FLIPPED Classroom, including asynchronous individual work at home (following the instructions on the LMS) and synchronous group activity for activation of knowledge.

Learning objectives:

- Define evolution, natural selection, adaptation, variation, species, selective pressure, vestigial structure
- Discuss the scientific evidence supporting Darwin's theory for evolution
- Explain how evolution works
- Relate evolutionary concepts to medical problems

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.

Teaching method: Lecture

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
- Discuss the differences between allosteric and covalent regulation of protein activity

Topic 4. Structural and functional properties of DNA molecules

Content: DNA as the genetic material. Structure of the genetic material.

Teaching method: Lecture

Learning goals:

- Describe the structure of DNA
- Describe how DNA was demonstrated to be the genetic material
- Discuss the structure-function relationships of DNA molecules

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.

Teaching method: Lecture

Learning goals:

- Illustrate how the genetic material is organized in the cell nucleus
- Describe the levels of chromatin compaction

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.

Teaching method: Lecture

Learning goals:

- 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

Clinical drop: Telomerase and cancer

Topic 7. RNA transcription and metabolism: the transcriptome

Content: Eukaryotic transcription: Eukaryotic transcription factors - general & specific. Complexity of the transcriptome.

Teaching method: Lecture

Learning goals:

- Discuss the flow of genetic information
- Describe the mechanism of RNA synthesis (transcription) in prokaryotes and eukaryotes
- Describe the main classes of RNAs present within cells and their functions

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. The RNA world.

Teaching method: Lecture

Learning goals:

- Describe the RNA processing
- Describe how gene expression is regulated 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.

Teaching method: Lecture

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. Mitosis

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

Teaching method: Lecture

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

Clinical drop: pharmacological agents affecting the function of microtubules

Topic 11. Meiosis

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

Teaching method: Lecture

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 12. How genes are inherited

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

Teaching method: Lecture, Activation of knowledge (individual and team work)

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, expressivity, and pleiotropy concepts
- Discuss how genes and environment can interact in determining genetic traits in humans

Topic 13. 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).

Teaching method: Lecture

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 14. Genetic variation

Content: Polymorphisms and mutations: classification and functional consequences.

Teaching method: Lecture

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 15. Protein folding

Content: How proteins acquire their final conformation and their functional properties after synthesis.

Teaching method: Lecture

Learning goals:

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

Clinical drop: Prion disease

Topics 16. 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.

Teaching method: Lecture

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 ER

Clinical drop: Unfolded protein response in human diseases

Topics 17. 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.

Teaching method: Lecture

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 18. Cell cycle regulation

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

Teaching method: Lecture

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 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.

Teaching method: Lecture

Learning goals:

- Describe developmental, physiological and pathological processes in which apoptosis plays a crucial role
- Define molecular pathway(s) 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.

Teaching method: Lecture, Activation of knowledge (Clinical case)

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. Stem cells and other models

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

Teaching method: Lecture

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

Topic 22. 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.

Teaching method: Lecture

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 23. Genome editing by CRISPR/CAS: medical opportunities and professional dilemma. (Interdisciplinary activity between CMP and BMD. Co-hosted by prof. Soldà and Montagna)

Content: Physiologic role of CRISPR-Cas9 system in bacteria. Genome engineering with CRISPR-Cas9, a breakthrough technology. The case of He Jiankui and the first CRISPR-edited babies.

Teaching method: FLIPPED Classroom, including asynchronous individual work at home (following the instructions on the LMS) and synchronous group activity for activation of knowledge.

Learning goals:

- Describe the basis of CRISPR-Cas9 system in bacteria, and how it has been modified into a genome editing tool
- Compare applications and implications of somatic and germline genome editing
- Reflect on how genome editing holds promise as well as presents many unknowns from the perspectives of human health
- Discuss professionalism and ethical issues concerning the application of novel technologies that permanently modify the genome

Teaching Methods

Lectures: the main purpose of lectures is to transfer knowledge to students by guiding them through the most relevant subjects of the course. Students are encouraged to participate to lectures in a proactive manner and to take notes as part of the learning process. Most lectures will be held synchronously, either in presence or using Teams. Slides of the lectures will be uploaded in the LMS platform, where additional material (video, papers, animations) will be posted.

Few lectures will be held with a flipped classroom approach, which combines asynchronous activities with on-campus synchronous activities (group work, activation of knowledge, etc.).

Group work activities - activation of knowledge: the purpose of these activities is to activate and reinforce knowledge acquired during lectures and independent study, in a collaborative learning setting. They promote the students' ability to communicate, work in teams, organize their knowledge, select and revise information, and make connections between topics. For these activities, students will be divided in groups that will remain the same throughout the semester. Participation is mandatory.

Verification of learning

Students' evaluation will be assessed through a written examination with multiple choice questions. The exam will include 33 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. Each question will score 1 point; no penalties will be applied for wrong answers. The threshold score for passing the exam will be 18 points. Score from 31 to 33 will be graded "30 cum laude".

Practical examples of the questions proposed in the final exam will be provided during the course.

Texts

Alberts B et al. Essential cell biology. 5th edition
Hardin et al. Becker's World of the cell. 9th edition