UE12 MemBioMed
Molecular biology of cellular membranes

Presentation

This course examines cellular membranes, fundamental cell components that play a crucial role in biological processes such as cellular communication, metabolism, and signaling, positioning them as key structures in pharmacology and biomedical science.

Coordinator

Dr. D. Bichet

Courses

40 hours of lectures

Prerequisites

Master the fundamentals of cellular and molecular organization of cells, proteins, and genomes.

Examination methods

1 final exam (analysis of an article) for 70% of the grade; 1 CC (oral presentation of an article) for 30%.

Objectives

Acquire advanced knowledge of the structural and functional organization of cell membranes, understand signaling pathways and the mechanisms governing the assembly and functioning of cell membranes, and be able to interpret literature data in the field.

Why studying biomembranes ?

Cellular membranes are nature's most complex biomolecular systems, acting as semipermeable barriers essential for biogenic processes, energy conversion, information processing, and transport. They impact nearly all aspects of physiology, making membrane-bound molecules prime targets for therapeutics—drugs targeting membrane proteins represent about 60% of the global market. Membranes are dynamic assemblies of proteins and lipids, constantly changing in composition, properties, and shape in response to internal and external signals. Lipids function as solvents, substrates, and regulators of membrane proteins, with overlapping roles that challenge classical molecular biology approaches. As biomembrane research remains crucial in biomedical science, training the next generation of scientists in this field is essential.

Content

1. Cell membrane trafficking and protein biogenesis (Dr. S. Feliciangeli, 4 hrs)

This course provides a comprehensive overview of membrane trafficking and biogenesis, covering the entire lifecycle of membrane proteins. It explores their synthesis and insertion in the endoplasmic reticulum (ER), processing in the Golgi apparatus, and targeting to membranes. Key topics include protein sorting, vesicle formation, cargo selection, and the roles of SNARE proteins and Rab GTPases. The course also addresses vesicular transport mechanisms like endocytosis, exocytosis,

and membrane fusion, and examines the regulation of these processes through endosomal sorting, lysosomal targeting, and autophagy.

2. Membrane lipid composition (Dr. T. Harayama, 4hrs)

This course explores the complex world of lipid bilayer composition, examining how lipid composition adapts to environmental changes, varies between different cell types and undergoes pathological alterations. The course will explore various methodologies for studying lipids, including genetic engineering, metabolic manipulation, synthetic biology, comparative studies and chemical biology. Emphasis will be placed on the analysis of lipids by mass spectrometry-based lipidomics, highlighting its transformative potential to advance medical and biological sciences. By integrating these aspects, the course aims to provide an in-depth understanding of lipid functions and their implications in health and disease.

3. Protein-membrane interactions (Dr. G. Drin, 4 hrs)

Description of how peripheral membrane proteins (PMP) precisely target and associate with organelle membranes of specific lipid composition via structural domains, lipid tail(s), and amphipathic helices according to different modalities (stereospecific, hydrophobic, electrostatic interaction).

4. Lipid dynamics (Dr. G. Drin + Bruno Mesmin, 4 hrs)

This course examines the spontaneous dynamics of lipids, including lateral movement, desorption, and flip-flop, and explores methods to control lipid composition in organelle membranes. It highlights how lipid metabolism, occurring in various organelles, must be coupled with lipid fluxes to maintain metabolic continuity and distribution. The course covers protein families that transport lipids between organelles at contact sites, with a focus on recent in vivo and in vitro approaches. It also addresses the links between cell signaling and lipid transfer, such as ORP5/8 and Nir2 at ER-plasma membrane contact sites, and discusses interorganelle sterol movement related to the SREBP-based sterol sensing system. Additionally, the integration of vesicular and non-vesicular lipid transport will be emphasized.

5. Role of membrane receptors in the Hedgehog signaling pathway (Dr. I. Mus-Veteau 4hrs)

This course focuses on the membrane receptors of the Hedgehog signaling pathway, including the Hedgehog ligands and their interactions with Patched and Smoothened. The course will examine how ligand binding activates these receptors and leads to signaling by transcription factors, affecting gene expression and developmental processes. The course will cover the regulation of this pathway, its roles in development, stem cell regulation and diseases such as cancer and genetic disorders. Experimental techniques for studying these mechanisms and recent advances in therapeutic strategies will also be discussed.

6. Membrane transport mechanisms in excitable cells (Dr. D. Bichet, 4hrs)

This master's course will introduce the fundamentals of bioelectricity, including membrane potential and equilibrium potential. It will delve into ion channels crucial for action potentials, covering their structure, gating mechanisms, and regulation. The course will also explore ligand-gated ion channels and their role in synaptic integration, focusing on how synaptic inputs are integrated, the process of neurotransmission, and mechanisms of synaptic plasticity.

7. Membrane transport mechanisms in non-excitable cells (Dr. C. Duranton, 4 hrs)

This master's course will cover specialized transport mechanisms in non-excitable cells, focusing on ion channels, transporters, exchangers, aquaporins, tight junctions, and nutrient uptake. Key topics include the role of Na^+, K^+, and Cl^- gradients in maintaining osmotic balance and cell volume. The course will also explore dysfunctions in ionic transport, examining how abnormalities in K^+ channels contribute to diabetes, the role of CFTR in cystic fibrosis, and the impact of Cl^- channel dysfunctions in Liddle syndrome.

8. Ion channels regulation by the membrane lipid environment (Dr. F. Chatelain, 4 hrs)

This master's course will explore several key aspects of lipid-channel interactions. It will cover how specific lipids directly bind to ion channels to modulate their activity, such as PIP_2's regulation of K^+ and TRP channels. The course will also examine how lipid bilayer properties—such as membrane tension, curvature, and thickness—affect channel activity, with a focus on mechanosensitive channels like Piezo and TREK1. Additionally, the course will address post-translational lipid modifications of ion channels, including palmitoylation and prenylation. Finally, students will learn methods for studying ion channel activity in various lipid environments, utilizing techniques like patch-clamp electrophysiology and artificial bilayers.

9. Pharmacology targeting ion channels and transporters (Dr. E. Deval, 4 hrs)

Pharmacology is a considerable asset in understanding the physiological and pathophysiological roles of ion channels. Natural or synthetic compounds capable of modulating the activity of these channels are not only powerful tools for fundamental research (molecular aspects), but can also be promising drug candidates, or serve as the basis for the development of new therapeutic strategies.

10. Evolutionary and environmental aspects of biological membranes (Dr. B. Antonny, 4 hrs)

Main evolutionary pressures for making primitive membranes as well as allowing them to adapt to very different environments in terms of pressure, temperature and chemical hazards. These include lipid chemistry - the building blocks - lipid assembly (critical micellar concentration) - membrane permeability to solutes and to ions - membrane fission - ion channels and ion pumps activity. Lipid transporters.