CBF

2016|17

MASTER DEGREE

BIOPHARMACEUTICAL

SCIENCES

FACULTY OF PHARMACY | UNIVERSIDADE DE LISBOA

PRESENTATION

This Course enlarges the classical concept of biopharmaceutical sciences by providing scientific, multidisciplinary background on the discovery phase of the drug development process, at advanced level. The program includes the study of molecular mechanisms of disease, potential therapeutic targets and therapeutic strategies, while motivating students to equate and solve problems, in close collaboration with the FCT R&D unit, Research Institute for Medicines (iMed.ULisboa).

OBJECTIVES

The MSc Course in Biopharmaceutical Sciences will train graduates to discover innovative targets and drugs to treat and cure human diseases. Top academic and industry experts will deliver key courses and topics, in line with the preconized research-innovation-education triangle in Europe. This MSc Course has been designed for those targeting a career in research universities and institutes, pharmaceutical industry and biotechs, often providing advanced training toward a PhD degree or a career in pharma and biotechs.

REQUIREMENTS

BSc in areas of Health Sciences, Life Sciences or Biotechnologies, or with adequate curriculum vitae

SELECTION

1) classification of the academic degree, and adequateness to the program; 2) curriculum vitae; 3) interview, if needed. Maximum 16 students will be selected.

APPLICATIONS

July 4 to September 05, 2016
Results – September 9

REGISTRATION

September 12-15, 2016

CALENDAR

From September 19, 2016
Monday through Friday; 17:00 - 20:00 h

TUITION

National students: 3.250,00 € (year 1: 1.500,00 €; year 2: 1.750,00 €)
International students: 7000,00 €
Application: 75,00 € | Registration: 75,00 €
Insurance

STUDY PLAN

4 Semesters | 120 ECTS

Year 1

1st Semester

*Optional:**	ECTS
Metabolic Biochemistry	4
Membrane Transport	4
Molecular Genetics of Bacteria	4
Cellular Microbiology	4
Development and Organization of the Nervous System	4
Brain Barriers in Drug Development	4
Eukaryotic Gene Regulation and Functional Genomics	4
Cell Signalling	4
Biopharmaceutics and Pharmacokinetics	4
Free Curricular Unit I **	4
Mandatory:	
Project I	6

2nd Semester

*Optional:**	ECTS
Oncobiology and Stem Cell Biology	4
Pharmacogenetics	4
Proteostasis Network in Health and Disease	4
Neuropathology and Neuropharmacology	4
Pathophysiology of Neuroinflammation	4
Human Molecular Genetics	4
HIV/AIDS and Associated Infections	4
Research and Development of Biopharmaceuticals	4
Methodologies of Data Analysis	4
Free Curricular Unit II **	4
Mandatory:	
Project II	6

Year 2

3rd and 4th Semester

	ECTS
Dissertation	60

*Optional curricular units — select 24 credits. The 6 curricular units/semester selected by more students will be given in each year.
**Curricular unit within related scientific areas offered by the University of Lisbon.

Biopharmaceutics and Pharmacokinetics

Maria do Rosário Lobato (coordinator)
Paulo Paixão, Nuno Silva

Description and quantitation of factors affecting the absorption, distribution, metabolism and excretion (ADME) of drugs. Development of appropriate dosage regimens and graphical analysis of drug concentration data sets. Bioequivalence and drug product testing. Application of biopharmaceutical and pharmacokinetic theory to clinical problems involved in optimizing and monitoring drug use in patients.

Brain Barriers in Drug Development

Maria Alexandra de Oliveira Silva Braga Pedreira de Brito, Dora Maria Tune de Oliveira Brites (coordinators)
Ana Sofia Iria Azeredo Falcão de Jesus, Ana Rita Mendonça Vaz

Brain barriers are complex and dynamic structures that protect the nervous tissue against the entrance of toxic substances. However, the restricted permeability and selectively limits entry of drugs into the central nervous system (CNS), which constitutes an obstacle to therapy. This course presents the current state of knowledge regarding the following aspects: blood brain barrier (BBB) as a protective interface, its constitution and properties; functional interaction between cells and molecules of the nervous tissue and concept of neurovascular unit; structural and functional changes of the BBB in pathological situations and role of the BBB as a cause or consequence of neurological damage; *in silico*, *in vitro*, *ex vivo* and *in vivo* models to study BBB; *in silico* evaluation of the BBB transposition by drugs; development of drugs for the treatment of CNS disorders and therapeutic strategies to overcome the BBB; other barriers: blood-retinal barrier and blood-cerebro-spinal fluid barrier.

Cell Signalling

Cecília Maria Pereira Rodrigues (coordinator)
Joana Dias Amaral, Rui Eduardo Mota Castro, Susana Zeferino Solá da Cruz

Cell signalling is an essential part of biological processes. This course includes specific topics, study models and experimental methods, which support current concepts on mechanisms and signaling pathways, with emphasis on proliferation, differentiation and cell death. Interaction and regulation of pathways will be discussed in higher organisms, including the perspective of application in biomedical areas, pharmaceutical and biotechnology, from understanding the pathogenesis of certain diseases, to the development of therapeutic strategies of modulation. The curriculum includes the following modules: 1) features, components and mechanisms of signalling systems; 2) molecular basis of regulation of signalling pathways critical for the survival of living organisms; 3) signalling pathways in (patho)physiological systems and treatment of diseases. In the laboratory, specific cell signalling pathawys will be investigated, from evaluating cell fate in tissues, mammalian cells in culture, and isolated cell organelles, to the identification of the molecular mechanisms underlying signalling.

Cellular Microbiology

Elsa Maria Ribeiro dos Santos Anes (coordinator)
José Miguel Azevedo Pereira, Jorge Manuel Barreto Vítor

This course details the host-pathogen cell biology. Cell cytoskeleton and extracellular matrix, cell-cell junctions, cell signaling, endocytosis and cell traficking and mechanisms of programmed cell death. Mechanisms of bacterial adhesion. Adherence and tropism. Signalling. Mechanisms of bacterial invasion into host. Avoidance of intracellular killing. Interaction of bacteria with the endocytic pathway, membrane trafficking and phagocytosis. Interaction of pathogens with the innate and adaptative Immune system. Manipulation of programmed cell death by pathogens. Bacterial toxins as tools in cell biology. This program will present the tools and methodologies to follow cellular components and study phenomena of interaction with microorganisms; potential therapeutic targets to control infections and inflammatory processes.

Development and Organization of the Nervous System

Rui Fernando Marques da Silva, Maria Alexandra Brito (coordinators)
Dora Maria Tuna de Oliveira Brites, Ana Sofia Iria Azeredo Falcão de Jesus, Adelaide Maria Afonso Fernandes Borralho, Ana Rita Machado Vaz Botelho

Neurogenesis: neurulation, formation of the neural tube, differentiation and cell diversity, cell lineages and genetic dependence, neuronal migration. Neural stem cells: embryonic and adult. Anatomy of the Central Nervous System (CNS): divisions and subdivisions; general structure of the brain and spinal cord; meninges and brain ventricles. Histology CNS: cell types, their structure and functionality. Neurons: structure and function; cell body and neurites; morphological and functional classification; compartments and functional domains, protein synthesis. Cytoskeleton, neuropeptides, classical and unconventional neurotransmitters; axonal transport, motor proteins. Structure and function of glial cells: astrocytes, oligodendrocytes, microglia and ependymal cells. Organization of the central nervous tissues.

Eukaryotic Gene Regulation and Functional Genomics

Maria João Carlos da Silva Gama (coordinator)
Elsa Margarida Teixeira Rodrigues

Studies the molecular mechanisms that regulate eukaryotic gene expression, and whole-genome and global eukaryotic gene expression analyses. Emphasis will be put on transcription/transcription factors as suitable targets for therapeutic drugs. The important interplay between the transcription machinery and chromatin will be addressed in line with the basic principles of epigenetics as an additional layer of transcriptional control. The role of epigenetic mechanisms in normal development and human disease will be explored. Gene regulation by noncoding RNAs will also be addressed. Functional genomics constitutes the second main theme, including analytical experimental methodology used in transcriptomics, proteomics and metabolomics. Finally the sophisticated tools used for generation of genetically modified mice will be presented and the use of novel mouse models humanized for genes in drug metabolism and safety studies will be discussed.

HIV/AIDS and Associated Infections

José Moniz Pereira (coordinator)
José Azevedo Pereira, João Gonçalves, Isabel Portugal, Maria Manuel Lopes

HIV/AIDS infection: structure and biology of HIV1 and HIV2; mechanisms of variability and its implications; viral pathogenesis; restraint systems to HIV replication; antivirals; resistance mechanisms; epidemiology and prevention; laboratory diagnosis; treatment; and vaccine strategies. Tuberculosis new challenges: latent tuberculosis and its implications for the epidemic; new forms of tuberculosis associated with HIV infection; multi and extensive drug-resistant tuberculosis; susceptibility and drug resistance. Relevant aspects of opportunistic mycoses associated with HIV/AIDS; factors favoring mycoses; diagnosis of fungal infection; antifungal mode of action and resistance mechanisms; monitoring of prophylaxis and antifungal therapy. Biosafety concepts. Isolation and characterization of microbial pathogens. Methods of susceptibility to antimicrobial agents; methods for microbial typing; laboratory diagnosis: serological, cultural and molecular methods; detection of mutations that confer resistance to antibiotics.

Human Molecular Genetics

Isabel Maria Antolin Martins de Carvalho (coordinator)
Manuel Barreto Vitor

Theoretical lessons include topics such as the human genome: structure, organization and control of gene expression; origin of genetic variation: mechanisms underlying genome alteration and their consequences; patterns of inheritance: mendelian and complex; molecular pathology and genotype-phenotype correlation; molecular diagnosis: genetic tests in individuals and populations; new approaches to treating genetic diseases. Practical classes include analytical strategies for studying different types of pathology; evaluation of gene expression at transcriptional and translational levels; identification of mutations and characterization by sequence analysis; use of bioinformatics tools for experimental design and data interpretation. Laboratory classes will train on isolation and purification of nucleic acids from different types of biological samples; methods for mutation screening; methods for targeted mutation search.

Membrane Transport

Maria da Graça Tavares Rebelo de Soveral Rodrigues (coordinator)

Biologic membranes are essential to cell function. Disorders of membrane structure, dysfunction of membrane proteins and cell compartmentalization may have serious consequences for living cells and have been related with several diseases. Knowledge on structure and function of biological membranes and transport systems is essential for developing new methods for diagnostic, drug design and novel therapeutic approaches.
Subjects to be discussed include: biomembranes, structure and composition; biophysical bases of membrane transport; chemio-osmotic transduction and transport systems – transporters (symport and antiport transport systems), channels and active transport systems (pumps); ABC transporters and multiple drug resistance; transepithelial transport, the kidney as an osmoregulatory organ; intestinal nutrient and drug uptake.

Metabolic Biochemistry

Margarida Maria Fernandes Baptista e Silva (coordinator)
Maria Rita Mouzinho de Albuquerque Azevedo e Castro

Theoretical lectures include topics such as: 1) Metabolism: concepts, importance, major players. Fluxes through catabolic and anabolic pathways: mechanisms of activation/inhibition and enzyme catalysis. Nexus with regulation of gene expression and epigenetics; 2) Inherited Metabolic Diseases of intermediary metabolism and pathophysiology. Major genetic disorders involving amino acid and nitrogen metabolism, fatty acids and carbohydrates: the relationship between genotype and clinical phenotype. Energy metabolism: function and dysfunction on mitochondrial disorders. Mitochondrial fatty acid beta-oxidation and oxidative phosphorylation. The metabolism of homocysteine and B-group vitamins: their connection with cellular methylation reactions, including those of DNA and proteins; 3) Metabolic interactions, therapeutic targets and drug biotransformation. Orphan drugs and therapies for DHM: the example of lysosomal disorders. The biochemical analysis of enzymes and metabolites: characterization of biomarkers in the context of research in DHM. Laboratory classes will train in: 1) Amino acid analysis: its importance and applications in the study of phenylketonuria and amino acidopathies; 2) Bioenergetics and mitochondrial homeostasis: the use of in silico models for the study of mitochondrial diseases; 3) Metabolomics and methods or applications using Mass Spectrometry: organic acids analysis by GC-MS as an example of biomarkers in DHM research. Finally practical classes will include workshops and presentations of scientific publications, giving a context and articulating with the topics taught during lectures and laboratory sessions.

Methodologies of Data Analysis

Maria Isabel Calisto Frade Barão (ccordinator)

Random variables and probability models. Preliminary data analysis. Parametric statistical inference. Analysis of variance and design of experiments. Nonparametric statistics. Regression analysis. Statistical quality control. Special topics: sampling, multivariate data analysis.

Molecular Genetics of Bacteria

José Moniz-Pereira, Madalena Pimentel (coordinators)
Carlos Jorge Sousa de São-José

Lectures provide a historical prespective of bacterial molecular genetics; relevance of mobile genetic elements in horizontal genetic transfer; bacteriophages plasmids, transposons, its structure and properties; recombinant DNA technology; cloning and gene expression vectors; recombineering; control of transcription in bacteria; bacterial genomics; bioinformatic tools to forecast genes identification and function; development and analysis of bacterial mutant libraries by mutagenic transposition; identification, structure and function of genes; examples of molecular genetic analyses; virulence factors; biogenesis of bacterial cell wall; bacterial resistance to antibiotics; application in the search of new therapeutic targets. Laboratorial teaching includes thematic calsses. Study models are chosen from among ongoing research topics, such as solation and analysis of mutants, cloning and gene expression; recombineering; gene functional analysis.

Neuropathology and Neuropharmacology

Maria Alexandra Brito, Ana Sofia Falcão (coordinators)
Dora Maria Tuna de Oliveira Brites, Rui Fernando Marques da Silva, Adelaide Maria Afonso Fernandes Borralho, Ana Rita Machado Vaz Botelho

Neurological impairment and neurodegeneration; neurodegeneration mechanisms: role of oxidative stress, excitotoxicity and cell death pathways; susceptibility of various cell types to neurodegeneration induced by various insults; neurodegenerative diseases such as Alzheimer's disease and amyotrophic lateral sclerosis; neuromodulation by pharmacological agents and neuroprotection through natural products; brain tumors and valuation of glioma cell susceptibility to a drug; computational drug design.

Oncobiology and Stem Cell Biology

Cecília Maria Pereira Rodrigues, Rui Eduardo Mota Castro (coordinators)
Susana Zeferino Solá da Cruz, Joana São José Dias Amaral

Cell proliferation and death, cell specification and determination, and cell migration, are key mechanisms underlying cancer development, progression and therapy response. Convergence of information from genomics, proteomics, RNAomics and bioinformatics, together with translational state of the art research, are shedding light into how tumor cells overcome regulatory pathways, or how stem cells may be used therapeutically. Based on active research in these areas, this course will cover functional aspects of oncogenes, tumor suppressors, apoptotic genes, microRNAs and other relevant players, their expression and function in cancer, and their modulation as therapeutic approaches. In parallel, the molecular mechanisms that regulate development will also be studied, from pathways by which different cell types and tissues arise during development, to how its misregulation may lead to human diseases. Finally, attention will be given to emerging areas of drug development and systems biology.

Pathophysiology of Neuroinflammation

Dora Maria Tuna de Oliveira Brites, Adelaide Maria Afonso Fernandes Borralho (coordinators)
Ana Sofia Falcão, Ana Rita Machado Vaz Botelho

One of the most recent advances in neuroscience research is the understanding that there is an extensive communication between the immune peripheral system and the central nervous system (CNS). Although an effective inflammatory response is produced to prevent injury, persistent inflammation has been linked to several brain disorders and their progression. This course covers from causes, signs, symptoms and diagnosis of CNS inflammation to the interaction with the innate and adaptive immunity through the recruitment and brain infiltration of leucocytes, namely lymphocytes. Microglia reactivity to insults and infections, the role of macrophages in the CNS and the activation of astrocytes (e.g. NF-kB, inflammasome, phagocytosis and chemotaxis) are dissected. It is elucidated the role of inflammation in autoimmune disorders, relevance of systemic inflammation in white matter lesions, and microglia priming in the vulnerabilities face to a second insult, to ageing and onset of neurodegenerative disorders. The laboratory explores therapeutics targeting inflammation, using up-to-date methodologies to assess neuroinflammatory pathways with *in vitro* and *ex vivo* approaches.

Pharmacogenetics

Elsa Margarida Teixeira Rodrigues (coordinator)
Maria João Carlos da Silva Gama, Hélder Mota-Filipe, Filipa Duarte Ramos

This course provides students with an overview of the current knowledge in Pharmacogenetics. Key areas covered by this course are: 1) Basic principles of human genetics; 2) Human genome and web accessible databases; 3) Methods to identify mutations and to study their functionality; 4) Basis of molecular epidemiology; 5) Genetic polymorphism of drug metabolizing enzymes and drug transporters (characterization and clinical importance); 6) Genetic polymorphism of genes responsible for the drug mechanism of action (characterization and clinical importance); 7) Importance of Pharmacogenetics for therapy of different types of diseases; 8) Association between certain HLA alleles and adverse drug reactions; 9) Useful Pharmacogenetic biomarkers for prediction of adverse reactions/ efficacy; 10) Personalized medicine in the future.

Project I

Cecília Maria Pereira Rodrigues (coordinator)
All teaching staff members

This course consists of a period of direct contact with a specific scientific area, within the general program of the master course in Biopharmaceutical Sciences. This is followed by the preparation of a review article searching the literature on a specific topic, selected by the student together with the tutor. Overall, the program includes the study of molecular mechanisms of disease, potential therapeutic targets and therapeutic strategies, always prioritizing a key component of motivating students to equate and solve problems.

Project II

Cecília Maria Pereira Rodrigues (coordinatior)
All teaching staff members

This course consists of a second period of direct contact with a specific scientific area, within the general program of the master course in Biopharmaceutical Sciences. This is followed by the preparation of a research project on a specific scientific topic, selected by the student together with the tutor. Overall, the program includes the study of molecular mechanisms of disease, potential therapeutic targets and therapeutic strategies, always prioritizing a key component of motivating students to equate and solve problems.

Proteostasis Network in Health and Disease

Ana Paula Leandro (coordinator)
João Leandro, Fátima Ventura

Lectures include topics such as: 1) Proteins: structural organization and stabilizing interactions; post-translational modifications; folding *in vitro* (thermodynamic and kinetic basis; folding models); 2) Protein synthesis and processing: folding *in vitro*/*in vivo*; the ribosome; co- and post-translational folding; folding in the different cellular compartments; 3) Protein degradation: protein half-life; ubiquitin/proteasome and lysosomal systems; endoplasmic reticulum (ER) and mitochondrial associated degradation; ER and cytoplasm protein quality control systems; 4) conformational disorders: genetic diseases and missense mutations; fate of protein aggregates; molecular chaperones and refolding; gain- and loss-of-function diseases; small molecule modulators of intracellular folding (chemical and pharmacological chaperones; proteostasis regulators); 5) orphan drugs: rare diseases; orphan drug designation; regulation and incentive; orphan drugs committee. Pratical classes discuss: 1) Protein expression and purification (recombinant DNA technology and purification methods); 2) Functional and structural characterization: *in vitro* (biochemical and biophysical) and in cellulo methods; 3) Identification of small molecules modulators of protein folding and proteostasis: high-throughput screening; compound libraries; screening of compound (random/oriented search; *in vitro*/*in cellulo*) and targets for proteostasis regulators; 4) Analysis of laboratory data. Finally, laboratory classes include experimentation such as: 1) Transformation of competent cells; overnight preparation; cellular Lysis; 2) Purification of recombinant proteins by affinity and size exclusion chromatographies; Protein quantification; 3) Determination of enzymatic activities; thermal inactivation assays; SDS-PAGE analysis; 4) Tm evaluation by DSF; limited proteolysis; 5) Bioinformatics tools for *in silico* analysis of proteins.

Research and Development of Biopharmaceuticals

João Braz Gonçalves (coordinator)

Traditional biopharmaceuticals obtained by molecular engineering; strategies of biopharmaceutical discovery using molecular methods like proteomics, genomics and metabolomics; strategies of developing biopharmaceuticals using biomolecular technologies of bacterial and mammalian manipulation; methods of discovering and developing therapeutic proteins by direct evolution; direct mutagenesis aiming to improve interaction and stability of therapeutic proteins; development strategies of therapeutic antibodies; patent procedures and international protection; strategies of biopharmaceutical production using microbiological processes and mammalian cell culture; quality control of biopharmaceuticals. Case studies will be covered in several aspects of biopharmaceutical R&D: interferons, interleukins and tumor necrosis factor; growth factors; hormones with therapeutic interest; monoclonal and recombinant antibodies; vaccines; gene therapy and siRNA.

MASTER DEGREE IN BIOPHARMACEUTICAL SCIENCES
2016/18 | 7th EDITION

Coordinator:
Cecília M. P. Rodrigues

Scientific Committee:
Cecília M. P. Rodrigues
José Moniz-Pereira
Dora Brites
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