



MASTER DEGREE
**BIOPHARMACEUTICAL
SCIENCES**

2022 · 23

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 programme includes the study of molecular mechanisms of disease, potential biomarkers, therapeutic targets and strategies, while motivating students to equate and solve problems, in close collaboration with the FCT R&D Unit, Research Institute for Medicines.

OBJECTIVES

The MSc Course in Biopharmaceutical Sciences will train graduates to discover innovative biomarkers, targets and therapeutic strategies to diagnose, treat and cure human diseases. Top academic and industry experts will deliver key practical 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 universities and research institutes, pharmaceutical industry and biotechs, often providing advanced training towards a PhD degree or a career in pharma and biotechs.

Coordinator:

Cecília M. P. Rodrigues

Scientific Committee:

Cecília M. P. Rodrigues

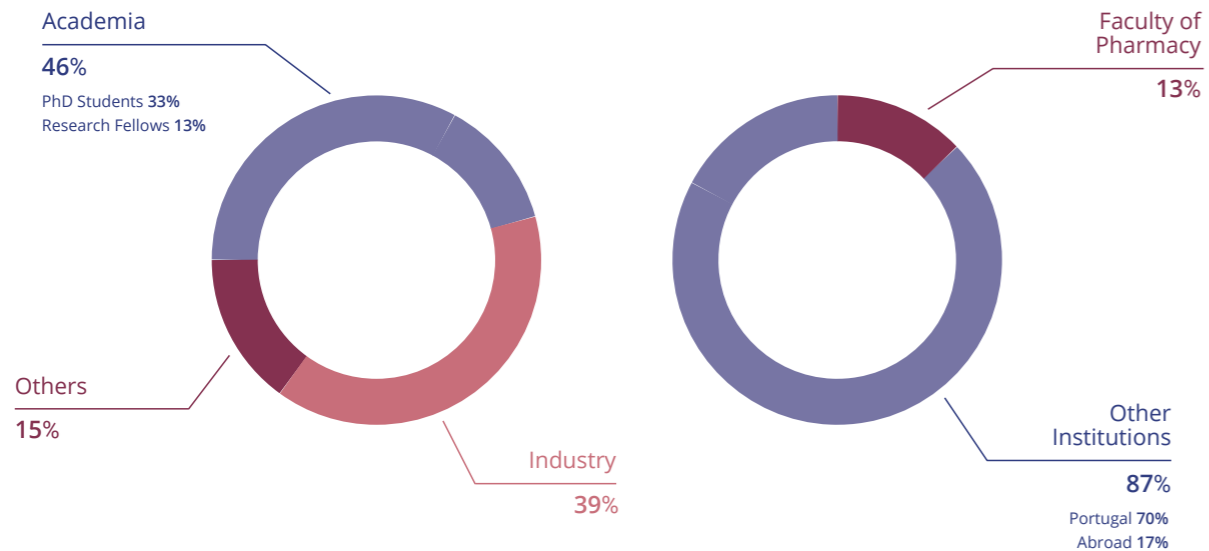
Graça Soveral

Madalena Pimentel

Maria Alexandra Brito

EMPLOYABILITY*

*Data: 2018-21



REQUIREMENTS

Students and professionals with BSc in areas of Health Sciences, Life Sciences or Biotechnologies, or with recognised curriculum vitae.

SELECTION

1) Certificate of BSc or equivalent, with final grade;
2) Curriculum vitae; 3) Motivation letter and interview, if needed.
Maximum 32 students will be selected.

APPLICATIONS

1st call | Application period: 1 June to 15 July 2022
Publication of results: 22 July 2022

2nd call | Application period: 1 August to 1 September 2022
Publication of results: 12 September 2022

REGISTRATION AND ENROLLMENT

25-28 July 2022
15-17 September 2022

CALENDAR

Beginning of classes: 19 September 2022
Monday through Friday, 17h00 – 20h00

TUITION FEES

National students: € 3.250 (year 1: € 1.500; year 2: € 1.750)
International students: € 7.000 (year 1: € 3.250; year 2: € 3.750)
Application: € 75 | Registration: € 75
Insurance

COURSES & CONTENTS

STUDY PLAN

4 Semesters | 120 ECTS

YEAR 1	1 st Semester	ECTS	2 nd Semester	ECTS
	Elective:*		Elective:*	
	Brain Barriers in Drug Development	4	Biopharmaceutics and Pharmacokinetics	4
	Cell Signalling	4	Cellular Microbiology	4
	Development and Organization of the Nervous System	4	Emerging Infections of Viral Etiology	4
	Eukaryotic Gene Regulation	4	Methodologies of Data Analysis	4
	Human Molecular Genetics	4	Neuropathology and Neuropharmacology	4
	Membrane Channels and Transporters	4	Oncobiology and Stem Cell Biology	4
	Metabolic Biochemistry	4	Pathophysiology of Neuroinflammation	4
	Molecular Genetics of Bacteria	4	Pharmacogenetics	4
	Proteostasis and Therapeutic Development	4	Research and Development of Biopharmaceuticals	4
	Other Curricular Unit I **	4	Other Curricular Unit II **	4
	Mandatory:		Mandatory:	
	Scientific Writing and Communication	6	Experimental Design in Research and Innovation	6
YEAR 2	3 rd and 4 th Semester	ECTS		
	Dissertation	60		
	Annual Workshop			

* Elective 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 Rosário Brito Correia Lobato (coordinator)

Nuno Miguel Elvas Neves Silva, Paulo Jorge Pereira Alves Paixão

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 (coordinator)

Rui Fernando Marques da Silva (co-coordinator)

Ana Rita Mendonça Vaz Botelho

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)

Marta Bento Afonso (co-coordinator)

André Fernando Anastácio dos Santos, Joana Dias Amaral, Rui Eduardo Mota Castro,
Susana Zeferino Solá da Cruz

The cells of our body integrate signals from multiple stimuli to mount appropriate physiological responses. These signals are transmitted to specific targets within the cell by intracellular signalling pathways. The fidelity of signal transmission by these pathways and the crosstalk between them are tightly controlled. This Unit will cover how key signalling pathways in cells transduce extracellular signals to regulate gene expression and cellular processes such as growth and death. It will also provide an understanding of how disruption of these pathways can lead to diseases such as cancer and neurodegenerative disorders and may inspire biomarker and target identification in diagnosis and drug discovery programmes. The aims are to: **1)** provide an understanding of the mechanisms by which cells communicate; **2)** illustrate the commonalities and differences between mechanisms, using examples of key signalling molecules and pathways; **3)** provide a basis for understanding disease processes in which signal transduction is compromised; **4)** give insight into experimental methods used for studying cell signalling. Students will be able to understand the relevance of cell signalling in a variety of physiological and pathological situations, discuss relevant scientific literature, and develop their critical thinking skills.

CELLULAR MICROBIOLOGY

Elsa Maria Ribeiro dos Santos Anes (coordinator)

Jorge Manuel Barreto Vítor, José Miguel Azevedo Pereira

This course details the host-pathogen cell biology. Cell cytoskeleton and extracellular matrix, cell-cell junctions, cell signalling, endocytosis and cell trafficking 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 adaptive 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 host interaction with microorganisms, as well as potential therapeutic targets to control infection and inflammatory processes.

DEVELOPMENT AND ORGANIZATION OF THE NERVOUS SYSTEM

Rui Fernando Marques da Silva (coordinator)

Maria Alexandra de Oliveira Silva Braga Pedreira de Brito (co-coordinator)

Adelaide Maria Afonso Fernandes Borralho, Ana Rita Mendonça Vaz Botelho,
Andreia Pereira Barateiro Macedo

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 of the 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

Maria João Carlos da Silva Gama (coordinator)

Elsa Margarida Teixeira Rodrigues, Andreia Margarida Gonçalves das Neves Carvalho,
Maria João de Jesus Nunes

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. Functional genomics constitutes the second main theme, including analytical experimental methodology used in transcriptomics.

EXPERIMENTAL DESIGN IN RESEARCH AND INNOVATION

Cecília Maria Pereira Rodrigues (coordinator)

All teaching staff members

This Unit consists of a period of direct contact of the student with scientific areas of interest, within the scope of the program contents of the Master Course in Biopharmaceutical Sciences. This is followed by the design of an experimental research essay, under the supervision of the tutor. The programme includes the study of: **1)** principles and methods of selection of research topics, as well as research processes based on critical and creative thinking; **2)** planning and implementation of research and innovation design; ethics in experimental design; **3)** approaches to collection, analysis and validation of experimental data; and **4)** dissemination and presentation of the experimental design; content organization; standards for writing and editing. It includes theoretical and practical knowledge on how to write a piece of work with emphasis on experimental research, how to apply concepts of experimental design, how to recognise and use advanced research methodologies, always prioritizing the key component of motivating students to equate and solve problems.

EMERGING INFECTIONS OF VIRAL ETIOLOGY

Helena Rebelo de Andrade (coordinator)

José Miguel Azevedo Pereira (co-coordinator)

The number of viral infections that have appeared in recent decades has steadily increased, leading invariably to situations of high morbidity and mortality in the human species. These emerging infections of viral origin are the result of a combination of factors dictated by the characteristics of the infectious agent and its natural host, as well as the transmission mechanisms determined by the way humans and this natural host interact. This Unit intends to explore the strategies to identify and control the emergence of new infections as well as to identify the characteristics inherent to the emerging viruses that allow their adaptation to the human species. In this context, emphasis will be given to the dynamics underlying the change in the interface between human habitats and the natural hosts of the virus.

HUMAN MOLECULAR GENETICS

Isabel Maria Antolin Martins de Carvalho (coordinator)

Jorge 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 CHANNELS AND TRANSPORTERS

Maria da Graça Tavares Rebelo de Soveral Rodrigues (coordinator)

Inês Margarida Vieira da Silva

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

This Unit will focus on the relevance of human metabolism as the basis for the advanced study of disease mechanisms and drug actions. Biochemical processes and homeostasis: fluxes through catabolic and anabolic pathways. Mechanisms of activation/inhibition and enzyme catalysis. Nexus with regulation of gene expression and epigenetics. Metabolic pathways underlying the study of pathogenesis, from rare to common diseases. The inherited metabolic disorders involving amino acid and nitrogen metabolism, fatty acids and carbohydrates. Function and dysfunction of mitochondrial fatty acid beta-oxidation and oxidative phosphorylation in cellular energy metabolism. Mitochondrial alterations in cancer cells. Metabolic interactions and cross-links with xenobiotics and pharmacological or toxicological mechanisms. Therapeutic targets, drug metabolism and drug metabolizing enzymes. Laboratory course content is focused on the application of mass spectrometry-based analytical techniques to specific problems in metabolomics and proteomics. Characterization of biomarkers for the diagnosis and research in health and disease.

METHODOLOGIES OF DATA ANALYSIS

Maria Isabel Calisto Frade Barão (coordinator)

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

Madalena Maria Pimentel (coordinator)
Carlos Jorge Sousa de São-José (co-coordinator)

This Unit is relevant for anyone that will be working in biological sciences. The Unit centers on the most relevant aspects of bacterial genetics, namely on the mechanisms underlying the regulation of gene expression and how gene manipulation leads to the understanding of gene function. The development of novel tools to study gene function or to design new therapies are hallmarks of Bacterial Genetics, leading to applications in microbiology, genetics, biochemistry, bioengineering, medicine, molecular biology and biotechnology. We will cover the following aspects: historical perspective of bacterial molecular genetics and key contributions for the development of Molecular Biology; genetic elements involved in horizontal gene transfer (bacteriophages, plasmids, transposons) and their exploitation as molecular tools; technologies for genetic manipulation (e.g. CRISPR, recombineering, integrative vectors); bioinformatics tools for gene identification and prediction of gene function; molecular genetic analyses; molecular cloning and gene expression vectors; applications in the discovery of new therapeutic targets and agents. Laboratorial teaching includes models of study chosen from ongoing research topics, such as isolation and analysis of mutants, cloning and expression of proteins with therapeutic potential; recombineering; gene functional analysis.

NEUROPATHOLOGY AND NEUROPHARMACOLOGY

Maria Alexandra de Oliveira Silva Braga Pedreira de Brito (coordinator)
Adelaide Maria Afonso Fernandes Borralho (co-coordinator)

Ana Rita Mendonça Vaz Botelho, Rui Fernando Marques da Silva,
Andreia Pereira Barateiro Macedo

Neurological impairment and neurodegeneration in central nervous system disorders. Neurodegeneration mechanisms: role of oxidative stress, excitotoxicity, and cell death pathways. Neuritic development and synaptic plasticity alterations. Susceptibility of various cell types to neurodegeneration induced by various insults. Brain pathology: neurodegenerative diseases and tumours. Behavioural toxicology. Neuromodulation by pharmacological agents. Computational approaches for biomarker discovery, target identification and drug design.

ONCOBIOLOGY AND STEM CELL BIOLOGY

Cecília Maria Pereira Rodrigues (coordinator)

Rui Eduardo Mota Castro (co-coordinator)

André Fernando Anastácio dos Santos, Joana São José Dias Amaral,
Marta Bento Afonso, Susana Zeferino Solá da Cruz

Cell specification, migration, proliferation and death are key cellular and molecular mechanisms underlying cancer onset and development, while also influencing therapy response. Convergence of information from omics technologies, such as genomics, proteomics and metabolomics, and bioinformatics, together with translational state of the art research are shedding light into mechanisms of tumour cell development, evasion, and therapeutic targeting. Based on active research in these areas, this Unit will cover functional aspects of oncogenes, tumour suppressors, apoptotic genes, miRNAs and other relevant players in cancer, involved in gain and loss of function, and principles of therapeutic targeting in cancer. The aims are to: **1)** provide an understanding of the multistep mechanism of cancer cell growth, from cytokines and receptors to multidrug resistance; **2)** explore principles of cancer treatment, from chemotherapy, gene therapy, humoral and cellular immunotherapy to tumour vaccination; and **3)** give insight into experimental methods for diagnosis of cancer. Students will be able to understand how functional systems-biology approaches are being used to identify new therapeutic targets intrinsic to tumor cells or in the microenvironment and to better understand cancer heterogeneity and mechanisms of resistance towards development of the next generation of precision-medicine therapeutics in cancer.

PATHOPHYSIOLOGY OF NEUROINFLAMMATION

Adelaide Maria Afonso Fernandes Borralho (co-coordinator)

Ana Rita Mendonça Vaz Botelho (co-coordinator)

Andreia Pereira Barateiro Macedo

Neuroscience research advances consider the communication between the immune peripheral system (PNS) and the central nervous system (CNS). Neuroimmune interactions and inflammatory responses are central players in brain function and dysfunction. Their deregulation in brain disorders led to the development of tools to study the underlying pathological processes to find out targets and develop therapeutic strategies. To evaluate and identify the degree and type of neuroinflammation in a specific patient (signature) we use several tools to identify the cellular and molecular mechanisms involved, using biological fluids or patient-derived cells. Isolation and characterization of extracellular vesicles in liquid biopsies may help un disease diagnosis, where their content in microRNAs constitute a promising biomarker. Here, we will focus on the causes, signs, symptoms, and diagnosis of inflammation in the CNS, but also on how leukocytes are recruited and infiltrate the brain, or the communication of peripheral neuronal and glial cells with the CNS. Activation and heterogeneity of microglia and astrocytes in neuro-immune disorders, and changes in myelination/demyelination by dysfunctional oligodendrocytes will be envisaged in a PNS-CNS dialogue perspective.

PHARMACOGENETICS

Elsa Margarida Teixeira Rodrigues (coordinator)

Filipa Duarte Ramos, Hélder Mota-Filipe, Maria João Carlos da Silva Gama

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.

PROTEOSTASIS AND THERAPEUTIC DEVELOPMENT

Ana Paula Peralta Leandro (coordinator)

Maria de Fátima Vieira Ventura

This Unit includes theoretical and practical topics covering cellular events occurring in disturbed protein homeostasis as well as methods for the discovery of compounds aiming to restore the protein balance. Topics include: biologically assisted protein folding; the proteostasis network; conformational diseases and the proteostasis boundary; pharmacological modulation of proteostasis (pharmacologic chaperones, proteostasis regulators and synergistic effects); *in cellulo* and *in vitro* approaches to identify proteostasis checkpoints and modulators of protein folding; identified lead compounds as orphan drugs (Committee for Orphan Medicinal Products and Regulation on Orphan Medicinal Products). Hands-on classes will cover: expression and purification of an eukaryotic enzyme (wild-type and misfolded mutant); protein structural and functional characterization; identification of potential chemical/pharmacological chaperones. The students will also be trained for the use of bioinformatics tools for *in silico* analysis of proteins.

RESEARCH AND DEVELOPMENT OF BIOPHARMACEUTICALS

João Manuel 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 tumour necrosis factor; growth factors; hormones with therapeutic interest; monoclonal and recombinant antibodies; vaccines; gene therapy and siRNA.

SCIENTIFIC WRITING AND COMMUNICATION

Cecília Maria Pereira Rodrigues (coordinator)

All teaching staff members

This Unit consists of a period of direct contact of the student with a scientific area of interest, within the scope of the programme contents of the Master Course in Biopharmaceutical Sciences. This period is followed by the preparation of a review article, under the supervision of the tutor. Included in the programme is the study of: **1)** principles and methods of selection of review topics, according to their current relevance and general interest, based on critical and creative thinking; **2)** planning and implementation of the literature review; tools and methodologies of bibliographic search; information sources; **3)** critical analysis of related literature; **4)** dissemination and presentation of results and conclusions from the literature review; content organization; standards for writing and editing a review article; ethics in literature review; dissemination sites, rules and norms associated with dissemination. It includes theoretical and practical knowledge about how to start a literature review; how to analyse and better select themes and sources of information; how to frame, interpret and critically evaluate available information; and how to present and disseminate results and conclusions of the review.

MASTER DEGREE IN BIOPHARMACEUTICAL SCIENCES

2022/23 · 13th EDITION

Accredited by *Agência de Avaliação e Acreditação do Ensino Superior (A3ES)*

INFORMATION AND SECRETARIAT

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