Universitat Pompeu Fabra Barcelona

Year : 2017/18

3378 - Bachelor's (degree) programme in Biomedical Engineering
22212 - Introduction to Biopharmaceutical Design

Syllabus Information

Academic Course: 2017/18

Academic Center: 337 - Polytechnic School

Study: 3378 - Bachelor's (degree) programme in Biomedical Engineering

Subject: 22212 - Introduction to Biopharmaceutical Design

Credits: 4.0

Course: 4

Teaching languages: Theory: Grupo 1: Pending
Practice: Grupo 101: Pending
Grupo 102: Pending
Seminar: Grupo 101: Pending

Teachers: Sira Defaus Fornaguera, Ismael Zamora Rico, Ferran Sanz Carreras, Abel David Gonzalez Perez, Andres Ozaita Mintegui, Manuel Pastor Maeso, Miguel Angel Mayer Pujadas, Josep Eladi Baños Diez, Jordi Mestres López, Jana Selent

Teaching Period: Quarterly

Presentation

Developing a new drug for a disease or clinical condition is a complex process. In this course we aim to provide the student with an overview ranging from the early stages of the drug discovery to the final product that can be taken to the drug market.

Associated skills

General competences

- A general understanding of the different stages of drug discovery from initial target identification and validation, through assay development, high throughput screening, hit identification, lead optimization, the selection of a candidate molecule for clinical development, phases of clinical trials and final drug approval.

Specific competences

- Understanding the field of application of most common experimental and computational methods within the drug-discovery pipeline
- Understanding the language of other professional (medicinal chemist, pharmacologist) working in the drug discovery and development field

Learning outcomes

Student successfully completing this course:

- Have a general understanding of the drug discovery and development process
- Know and understand different experimental and computational methods in the drug discovery and development process (advantages and limitations). Critically rationalize and interpret data linked to those methods.
- Have the skills to communicate efficiently with other professionals involved in the field of drug discovery and development

Contents

The course content is divided into four Units, starting with a general introduction to the subject (Unit 1) and providing essential background for drug discovery and research (Unit 2) that is required to understand the course and following blocks covering the most common methodologies (Unit 3-4).

Unit 1: Introduction to drug discovery and development

1.1. Drugs/Medicines: definition, social and economical importance, main actors. Medicines versus APIs (active pharmaceutical ingredients), drug administration, treatment

1.2. Overview of the drug R&D "pipeline": target discovery and

validation, hit identification, lead optimization, preclinical drug development, clinical drug development, post-marketing monitoring

Unit 2: Foundations of drug discovery

2.1. Notions of medicinal chemistry: organic molecules, drug-likeness, chirality, charge, identifiers

2.2. General mechanisms of drug action: drug-receptor interaction, targets for drug action, molecular and cellular aspects of drug action, sensitization and desensitization, quantitative aspects of drug-receptor interaction

2.3. Notions of experimental pharmacology: in vitro and in vivo pharmacology, agonist/antagonist, dose-response relationship, potency and efficacy concepts, drug distribution and bioavailability, concepts of IC50, Ki, Kd, LD50, therapeutic index

2.4. Notions of knowledge management in pharmaceutical research: sources of relevant information for pharmaceutical research. Open source vs proprietary sources. Walkthrough by several highly relevant sources (ChEMBL, DrugBank, Open PHACTS, etc..). Open PHACTS API.

2.5. Notions of pharmacokinetics: overview of the physiological processes involved in the Absorption, Distribution, Metabolism and Elimination of drugs. Importance and implication of ADME for the development of new drugs. Experimental and computational tools used for assessing the drugability of candidates from the point of view of their ADME properties.

2.6. Notions of drug safety assessment: strategies for drug safety assessment, non-clinical, preclinical, clinical

Unit 3: Discovery and preclinical drug development

3.1. Identification of potential cancer drug targets using cancer genomics data: Recent advances in DNA sequencing technologies provide unprecedented capacity to comprehensively identify mutations, genes, and pathways involved in the tumorigenic process, raising the hope of extending targeted therapies from a few successful examples to a broader personalized medicine strategy. In the lecture I will explain how to explore cancer genomics data to identify potential new cancer drug targets.

3.2. Drug target validation: druggable target, pharmacological approaches, genetic approaches (antisense oligonucleotides, RNAi, transgenic animals), caveats: splice variants, multimeric receptors, one gene>one protein>one drug target.

3.3. High throughput screening in drug discovery: compound libraries (natural compounds, corporate compounds), in silico screening, rational drug design, combinatorial chemistry, physical substrates in HTS, biochemical based assays and cell-based assays.

3.4. Structure-based approaches in drug discovery I: generation of 3D models, geometry optimization, ligand docking, de-novo drug design, fragment-based approaches

3.5. Structure-based approaches in drug discovery II: docking, chemoisosterism, target profiling

3.6. In silico prediction of drug properties: in silico prediction of drug properties, concept of molecular similarity and bioisosterism, concept of QSAR, applications of in silico prediction in drug development: structural alerts, read across, QSAR and QSPR

3.7. Integrative knowledge management: exploitation in drug discovery and development, including multi-level and multi-scale modelling and simulation.

Unit 4: Clinical Development

4.1. Testing drugs in humans: an introduction to clinical trials: This lecture will be devoted to explain the main reasons that justify the research in humans during the process of drug development. It will introduce the concept of clinical trial, their different types and its sequential use along the development of new and old drugs.

4. 2. The basis of clinical trial methodology: This lecture will introduce the attendees to the main characteristics of the methodological approach of clinical trials. Special focus will be on the process of randomization, blinding procedures, definition of outcomes, experimental biases and data analysis.

4. 3. Ethical compromises in clinical trials: This lecture will include a historical analysis of how human research was carried out in the past, which justified the definition of bioethical principles applied to such situations. A short review of the current legal status of clinical trials will also be considered.

4.4. Taking drugs to the market: Overview of the steps required for registering a NCI and obtaining the approval of the main international drug regulators (FDA, EMA). Marketing considerations.

4.5. Pharmacovigilance: Follow-up of marketed drugs by the health authorities. Declaration of human adverse effects. Potential implications and reasons for drug market withdrawal.

Teaching Methods

Approach and general organization of the subject

Drug discovery is a complex and multi-disciplinary process. The subject is introduced with an overview which is followed by an introduction to important elements of several disciplines that are essential for understanding the rest of the course: medicinal chemistry, molecular pharmacology, pharmacokinetics, drug safety assessments. After the establishment of basic knowledge, the course will present to the attendees the two main blocks of preclinical drug development and clinical development.

Training activities*

Teaching activities use one of the following formats:

- *Theoretical lessons*. Explanation of the topics by an expert with the support of Power Point presentations. All the material used in theoretical lessons is uploaded beforehand into the course intranet.
- *Hands-on*. Guided practical work on diverse computational methods. The work is individual, guided by a step-by-step protocol, and is carried out at the classroom with the individualized support of a teacher. The results of the hands- on sessions are reported in a document that is used for evaluation.
- *Seminars*. Students work in small groups to prepare a presentation on selected topics, using the material provided or any other that they obtain on their own. The topic is presented orally in front of all the class, under the supervision of a teacher that acts as moderator, and discussed in deep. The quality of the seminars (presentation and general discussion) is evaluated for grading the class.

Attendance to all teaching activities is compulsory.

Evaluation

The students are evaluated using two instruments

1. Evaluation of their participation in seminars and hands-on sessions.
2. A written exercise, including short questions focussed on the most important contents of the course, simple practical problems (choosing methods, interpret results, solve a practical problem) or critical analysis of a given situation.

Students not reaching the overall pass grade will be allowed to retake a written exercise in July, that will be evaluated using the same criteria applied to the first one and descrived below (Grading system)

Grading system

The relative weight of these two above instruments in the final mark is

40% for A (the seminars and hands-on) and 60% for B (the written exercise).

Final marks will range from 0.0 to 10.0. A minimum grade of 5.0 is required to pass the course.

Bibliography and information resources

Bibliography and information resources will be provided by teachers for individual subjects.