UNIVERSIDAD AUTÓNOMA DE MADRID

33207 - DRUG DESIGN: FROM CLASSICAL TO IN SILICO

This is a non-sworn translation intended to provide students with information about the course

Information of the subject

Code - Course title: 33207 - DRUG DESIGN: FROM CLASSICAL TO IN SILICO

Degree: 721 - Máster en Investigación Farmacológica (2018)

Faculty: 106 - Facultad de Medicina

Academic year: 2023/24

1. Course details

1.1. Content area

Classical drug design based on homology of molecules with known activity and computer-aided drug design based on the three-dimensional structure of the selected pharmacological targets. Computational methods of interaction calculations and structure selection.

1.2. Course nature

Optional

1.3. Course level

Máster (EQF/MECU 7)

1.4. Year of study

1

1.5. Semester

Second semester

1.6. ECTS Credit allotment

5.0

1.7. Language of instruction

English

1.8. Prerequisites

General concepts of chemistry.

1.9. Recommendations

Students will require to have a good comprehension of English to follow the lectures, to be able to communicate, answer the multiple-choice test and present their review work. This course is addressed to students with basic knowledge in biophysics, molecular biology, bioinformatics and biochemistry.

1.10. Minimum attendance requirement

It will be mandatory to attend at least 80% of the sessions.

1.11. Subject coordinator

Maria Francisca Cano Abad

https://autoservicio.uam.es/paginas-blancas/

1.12. Competences and learning outcomes

1.12.1. Competences

BASIC AND GENERAL

GE1 - Acquire the knowledge, skills and abilities necessary to carry out an innovative quality research in Pharmacology

CB6 - Possess and understand knowledge that provides a basis or opportunity to be original in the development and / or application of ideas, often in a research context

CB7 - Know how to apply the acquired knowledge and their ability to solve problems in new or unfamiliar environments within broader (or multidisciplinary) contexts related to their area of interest

CB9 - That the students know how to communicate their conclusions and their knowledge to specialized and non-specialized publics in a clear and unambiguous way

CB10 - Posses the learning skills that will allow the students to continue studying in a way that will be largely self-directed or autonomous.

TRANSVERSAL

T2 - Ability to carry out effective scientific and technical communication, both in a specialized environment and in more general environments, including the educational.

T1 - Ability to carry out a self-learning plan, perform an autonomous consultation of the bibliography and databases at the scientific, technical or regulatory level.

SPECIFIC

ES-3 - Know the basic aspects about the design and obtaining new drugs, both at a chemical and biotechnological level, as well as the scientific, ethical and regulatory aspects that condition it.

ES-4 - Know the most common therapeutic targets in cardiovascular disease or diseases of the nervous system and assess their physiological significance and their therapeutic projection.

1.12.2. Learning outcomes

Drug Design is a multidisciplinary programme focused on the understanding of the interactions between pharmacologically interesting targets and small molecules using biophysical methods or computational chemistry approaches. Academics from CIVIS partnering universities: National Kapodistrian University of Athens, Aix-Marseille Université, Sapienza University, Universidad Autonoma Madrid, University Tuebingen and University of Bucharest will jointly deliver lectures and laboratory practical sessions that will prepare students with knowledge regarding various scientific approaches applied in each stage of drug design and development process. The main topics addressed include:

- Molecular interactions, thermodynamics in drug discovery, drug discovery process and technologies, fragment-based drug discovery, hit to lead optimization, the molecular drug space selection and optimization,
- Biophysical assays for high throughput screening or characterization of interactions: Microcalorimetry ITC & DSC, nanoDSF, Analytical UltraCentrifugation, Surface Plasmon Resonance, NMR, Xray Crystallography

- Cellular and animal models for preclinical screening and toxicity studies
- Virtual Screening, Pharmacophore modelling, QSAR
- Clinical Trials, Regulatory Affairs, Patent writing and application
- Practical Workshops:
    - DSF in High Throughput Screening
    - Gastroplus ADMET predictor to screen gastro-intestinal absorption and metabolism properties
    - 3D QSAR practical course
    - NMR practical course
    - *In vitro*, *ex vivo* and *in vivo* methods in the hit to lead optimization and mechanism of action determination
    - Analysis and evaluation of antimicrobial activity

1.12.3. Course objectives

The participants will:

- learn and practice in a multi-cultural environment
- understand the current challenges and the main approaches used in modern day drugs design and discovery process
- acquire knowledge and practical skills concerning the in silico and wet lab methods used for drug design and development
- develop specific and transferable skills relevant to a wide variety of scientific and professional careers in medical and pharmaceutical industries

1.13. Course contents

The programme combines virtual courses and on-site lectures and practical sessions.

The physical component of the programme will consist in one week in which the students will participate to practical sessions covering the following topics:

- 3D QSAR practical course
- Gastroplus ADMET predictor to screen gastro-intestinal absorption and metabolism properties
- New strategies to develop drugs for neurodegenerative diseases
- Tools to monitore Calcium siganling
- Introduction to physiologically-based modelling
- Using physicochemical properties to understand molecule behaviour in environment pertinent to pharmacological activity
- Understanding and Applying Halogen-Bonds in Molecular Design and Lead Discovery -
- TBD (NMR spectroscopy, NMR based Metabolomics, Drug Discovery, Structure-Based Drug Design).
- TBD (biophsyical methods such as ITC and DCS microcalorimetry and nanoDSF, for conventional and non-conventional / clinical uses)
- Analysis and evaluation of antimicrobial activity (antibiotic producing microbial strains; screening of antimicrobial activity of novel compounds (minimum inhibitory concentrations, minimum bactericidal concentration, minimum biofilm eradication/inhibition concentration, FIC/FICI, flow cytometry; cytotoxicity on human cell lines (fluorescence microscopy, cell cycle, MTT/LDH assays etc.), genotoxicity (micronucleus test); quality control of pharmaceutical agents.

- **The virtual component of the programme will be organized during the second semester, three hours once per week, for 12 weeks**.

Spring Semester 2024	
Week 1	Molecular Interactions: Classical (Charges, H-Bonds, v.d.Waals, π-int.)
	Molecular Interactions: Non-Classical (Weak H-Bonds, Orthogonal Multipolar Interactions, Sigma hole I Halogen Bonds)
	Thermodynamics in drug discovery (in Hit2Lead / LeadOpt)
	Prof. Dr. Frank M. Boeckler Lab for Molecular Design & Pharm. Biophysics Chair for Medicinal Chemistr of Pharmacy and Biochemistry Eberhard Karls University Tuebingen
Week 2	Molecular Complexity / Drug, Discovery Process and Technologies - Strategies, Issues, Costs, Outlook.
	Fragment-based Drug Discovery
	Hit-to-Lead optimization, Co-optimizing Ligand Properties, Avoiding late Attrition
	Prof. Dr. Frank M. Boeckler Lab for Molecular Design & Pharm. Biophysics Chair for Medicinal Chemistr of Pharmacy and Biochemistry Eberhard Karls University Tuebingen
Week	Animal models (ethical considerations, experimental design, in vivo analysis of drug effects)

3	*In vitro* cell culture models and evaluation of drug effects
	Neurodegenerative diseases and drug discovery
	Dr. Gratiela Gradisteanu, Research Institute of Bucharest University *Lecturer Dr. Miruna Stan, Bucharest University Faculty of Biology Department of Microbiology and Imm* *Professor Maria Cano-Abad, Facultad de Medicina, Universita Autonoma Madrid*
Week 4	Immunomodulation and drug impact on cytokine production and on the M1/M2 macrophage phenoty
	Evaluation drug-induced responses in cultured cells at specific time points (cell cycle analysis and apop Screening of drug-induced reactive oxygen species production in leukocytes subpopulations in whole b
	Dr. Gratiela Gradisteanu, Research Institute of Bucharest University *Associate prof. Luminita Marutescu Bucharest University Faculty of Biology Department of Microbiolog* *Immunology*
Week 5	Biophysical assays for high throughput screening
	Microcalorimetry ITC, DSC nanoDSF analytical Ultracentrifugation
	SPR
	Prof. Francois Devred, Faculty of Pharmacy Aix-Marseille Université,
Week 6	Introduction to NMR
	NMR screening in drug discovery
	Introduction to NMR based metabolomics
	Prof. Emmanuel Mikros, Faculty of Pharmacy, National Kapodistrian University of Athens
Week 7	Pharmacokinetics
	ADME properties
	Prof. Florence Gattacceca Faculty of Pharmacy Aix-Marseille Université,
Week 8	Facts, and principles in drug discovery and development: the molecular drug space selection and optim
	Prof. Sandrine Alibert Faculty of Pharmacy Aix-Marseille Université,
Week 9	Introduction to ligand-based methods: Pharmacophore modeling, QSAR
	Prof. Rino Ragno Faculty of Pharmacy, La Sapienza University,
Week 10	Introduction to advanced ligand method: 3-D QSAR
	Prof. Rino Ragno Faculty of Pharmacy, La Sapienza University,
Week 11	Key note Speech
	Introduction to epigenetics and related drugs
	Antonello Mai Faculty of Pharmacy, La Sapienza University
Week 12	Clinical Trials
	Prof. Evangelos Terpos, School of Medicine, National Kapodistrian University of Athens
	Regulatory Affairs
	Patent writing and Application

During the physical mobility component of the programme the students will present their papers assigned during the semester preparatory

** some of the titles may change depending on the professor´s requirements*

1.14. Course bibliography

- **Graham L. Patrick: An introduction to Medicinal Chemisty**: Oxford University press, 4th Edition, 2008.
- **Computational drug design**: Gore, Mohini, Jagtap, Springer, 2018.

2. Teaching-and-learning methodologies and student workload

2.1. Contact hours

The programme proposal consists of two interconnected activities, in which all the CIVIS partners will be involved: an online course to be delivered during second semester , followed by a summer students' week, hosted by the University of CIVIS. The programme virtual component will be delivered by academics with international recognized research experience in the field.

Physical Mobility component
Duration of physical moblility required is 5 Days

Hosting City of the physical activity
CIVIS University

Number of Teaching hours during physical mobility.

A total of 40 hours of practical training and student presentations will be offered, corresponding to 3 ECTS.

Virtual mobility component:

Description of the virtual component program
The Course will consist of online courses organized throughout the second semester, once per week.

A total of 36 contact hours including courses and training, plus 39 hours of online courses will be offered, corresponding to 3 ECTS.

No of the weeks of virtual lessons
12
No of virtual lessons hours per week
3

Total of Student Workload:
Students will have a minimum of 20 hours of individual work for preparing the presentation of their review paper. There will be a minimum of 16 hours of contact hours (guided by professors).

TOTAL HOURS			
		Nº of hours	%
Activities	Lectures	36	50
	Interactive sessions	19	
	Presentations of scientific literature related to the subject	10	
Independent study time	Weekly study (1 hours x 13 weeks)	13	50
	Reading and analysis of scientific papers (2 hours x 13 weeks)	26	
	Preparation of Presentations and interactive sessions	26	
Total student workload: 25 hours x 6 ECTS		**130**	

2.2. List of training activities

Mandatory virtual online session with an optional physical 5-days short stay in another university of the CIVIS Alliance
***[important note]: the second on-site phase may only apply to selected students from the virtual course depending on the slots availability for each participating university; nevertheless, the students not being able to attend the second part on-site will follow most of the contents online except for hands-on sessions.**

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LECTURES: delivered by a professor on the topics included in the program.

SEMINARS/TUTORIAL: exhibition by students of problems and case studies prepared by them and included in the program. It will be followed by group discussions supervised by the tutor.

3. Evaluation procedures and weight of components in the final grade

3.1. Regular assessment

1. Continuous evaluation based on attendance and information obtained through personal tutorials, active participation in classes and seminars and skills and interest shown in class
2. Multiple-choice questions (MCQ) test will be performed at the end of the virtual component program online via the CIVIS platform.
3. Evaluation of the preparation and presentation of specific topics and discussion after their presentation by students in seminars

3.1.1. List of evaluation activities

1. students will be evaluated based on:
   - Attendance to the course (with a mandatory minimum of 80%)
   - Presentation and performance in the sessions of manuscripts discussion and practical tasks
   - Multiple-choice questions (MCQ) test will be performed at the end of the virtual component program online via the CIVIS platform.

   Overall, the evaluation of the virtual part of the program will be based on 3 main items:
   1. MCQ test (40 %) *
   2. Performance during classes and presentations (40%) *
   3. Assistance (20%).

   * 1. and 2. will represent in total 90% of the virtual mobility evaluation.

   Evaluation for the physical program

   Student evaluation in the physical mobility segment, either in another CIVIS university or at UAM, will be based on the performance of each student during the hands-on sessions, as well as on the results of a test with MCQ that will be performed at the end of the physical segment.

   Evaluation will be performed using 2 main items:

   4. MCQ test (40%),

5. Manuscript presentations (40%) – for those students not attending on-site the presentation will take place at their university of origin (UAM).
6. Assistance (20%).
* 1. and 2. will represent in total 90% of the physical mobility evaluation.

3.2. Resit

The same as for the regular assessment.

3.2.1. List of evaluation activities

Multiple choice tests (MCQ) 40
Practical continuous assessment 40
Assistance 20

4. Proposed workplan

Timetable and workplan will be indicated in the website