COURSE DATA

Data Subject	
Code	43105
Name	Biochemical basis of clinical toxicology
Cycle	Master's degree
ECTS Credits	4.5
Academic year	2020 - 2021

Study (s)

Degree	Center	Acad. year	Period
2142 - M.U. en Aproximaciones Moleculares CC Salud 12-V.2	Faculty of Biological Sciences	1	Second term

Subject-matter

Degree	Subject-matter	Character
2142 - M.U. en Aproximaciones Moleculares CC Salud 12-V.2	3 - Biotransformation, metabolism of drugs and xenobiotics	Obligatory

Coordination

Name	Department
CASTELL RIPOLL, JOSE VICENTE	30 - Biochemistry and Molecular Biology
DONATO MARTIN, MARIA TERESA	30 - Biochemistry and Molecular Biology
O'CONNOR BLASCO, JOSE ENRIQUE	30 - Biochemistry and Molecular Biology

SUMMARY

The objective of this course is to provide students with basic knowledge of the general mechanisms involved in the phenomena of xenobiotic-induced toxicity and, in particular, by drugs. Specifically, it describes the nature and implications of interactions between molecules with potential toxic and biological structures and their involvement in cellular functions or processes that may even threaten the survival of the affected cell. In this context the metabolism of drugs and the effects that these interactions cause on the body's homeostasis are studied. Special emphasis is also made on the toxicity of iatrogenic origin, giving examples in the study of drugs that cause organ toxicity. Finally we study how to evaluate the potential toxicity of a new drug for pharmaceutical development

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

There are no specified enrollment restrictions with other subjects of the curriculum.

Other requirements

None

OUTCOMES

2142 - M.U. en Aproximaciones Moleculares CC Salud 12-V.2

- Students should apply acquired knowledge to solve problems in unfamiliar contexts within their field of study, including multidisciplinary scenarios.
- Students should be able to integrate knowledge and address the complexity of making informed judgments based on incomplete or limited information, including reflections on the social and ethical responsibilities associated with the application of their knowledge and judgments.
- Students should communicate conclusions and underlying knowledge clearly and unambiguously to both specialized and non-specialized audiences.
- Students should demonstrate self-directed learning skills for continued academic growth.
- Students should possess and understand foundational knowledge that enables original thinking and research in the field.
- Conocer en profundidad y comprender la organización a nivel molecular de células, sistemas y procesos de relevancia en las Ciencias de la Salud.
- Conocer en profundidad y comprender las bases moleculares de la enfermedad.
- Conocer en profundidad y comprender las metodologías de investigación básica aplicables a las Ciencias de la Salud.
- Tener capacidad de analizar y sintetizar un problema.
- Tener capacidad de comunicación oral y escrita en una segunda lengua científica.
- Tener capacidad de localizar información.
- Tener capacidad de desarrollar un trabajo interdisciplinar.
- Conocer y comprender los conceptos básicos y las aplicaciones en investigación básica y clínica del estudio de las Bases Bioquímicas de la Toxicología Clínica.
- Conocer, comprender y aplicar en la práctica las técnicas de estudio de las Bases Bioquímicas de la Toxicología Clínica en situaciones relacionadas con la investigación básica y clínica.
- Aprender a identificar, manejar y presentar adecuadamente en informes y exposiciones públicas, conocimientos existentes sobre el estudio de las Bases Bioquímicas de la Toxicología Clínica, usando como vehículo la lengua inglesa.

- Aprendizaje, manejo y presentación de informes y trabajos en exposición publica de las aplicaciones biomédicas de los conceptos farmacogenéticos en las distintas terapias actuales, usando como vehículo la lengua inglesa.

LEARNING OUTCOMES

- Identify the toxic phenomenon as an interaction at the biochemical and / or molecular
- Identifying potential toxicity associated with the use of therapeutic drugs.
- Recognize the importance of the molecular and cellular mechanisms involved in toxicity for the design of safer drugs.
- Learn the basics of idiosyncratic toxicity phenomena.

Gain knowledge of biological models and experimental strategies that allow pre-clinical identification of potentially toxic molecules

DESCRIPTION OF CONTENTS

1. Introduction

Basics in Clinical Toxicology.
The importance of Toxicology in the clinical world. The dose-response relationship. Drug safety: accidental toxicity or exaggeration of the pharmacological action. General or tissue-specific toxicity. Molecular and biochemical approach to toxicology

2. The toxic phenomenon and its study

Toxicokinetics. Intrinsic and idiosyncratic toxicity. Latent and bioactivable toxins. Analytical methods for the study and identification of metabolites. Experimental models for the study of the toxic phenomena

3. Molecular interactions as basic mechanisms of toxicity

Consequences of the interaction of xenobiotics with cellular structures and/or functions. Adaptation vs toxicity . Molecular targets of toxic action: Proteins and DNA. Types of interactions and their consequences.

4. Mechanisms involved in the cellular toxicity

Cellular targets. Alterations of the membrane. Mitochondrial dysfunction: key role of mitochondria in the balance of mechanisms of toxicity and cell survival. Disruption of calcium homeostasis. Cell death: necrosis and apoptosis

5. Toxicity of bioactivable molecules (I)

Generation of reactive metabolites: role of biotransformation enzymes. Generation of electrophilic metabolites. Molecular targets. Interaction with DNA and genotoxicity: Examples. Protein adducts: Implications

6. Toxicity of bioactivable molecules (II).

Toxicity of free radicals. ROS generation. Cellular antioxidant defense mechanisms. Oxidative damage to DNA. Oxidative damage to proteins. Lipid peroxidation. Balance bioactivation vs detoxification. Preclinical strategies to identify bioactivable molecules and clinical interest of its possible consequences.

7. Idiosyncratic toxicity

Causes of the emergence of idiosyncratic toxicity. Metabolic idiosyncrasy: causes, consequences and toxicological and / or clinic relevance. Importance of genetic polymorphisms. Toxicity mediated by the immune system: drug allergy. Covalent Binding

8. The toxicity study during new drug development

Principles of regulatory toxicology: drug safety. Preclinical study phases. Models and experimental strategies: in vitro and in vivo studies. Clinical toxicity. Monitoring and follow-up

9. New experimental approaches for toxicity studies

Application of cell cultures to toxic potential screening of new molecules and mechanisms of toxicity study: advantages and limitations. Analysis by high performance imaging: examples. Toxicometabonómica.

This subject will be taught as a theoretical-practical seminar

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	20,00	100
Seminars	15,00	100
Group work	10,00	100
Development of group work	37,50	0
Study and independent work	30,00	0
TOTAL	**112,50**	

TEACHING METHODOLOGY

The development of the course will be structured lectures, seminars and methodological-experimental nature and tutoring assistance.

Teaching in the theory sessions will be mainly of lectures. In these sessions the teacher will present the most relevant content for that topic using the available media. To complement their training, students should prepare a mandatory work on a topic proposed by the teachers. This activity will be conducted in small subgroups (two or three students). Students must attend the necessary literature sources and, under the tutorship of Professor shall prepare such work as a seminar to be presented orally and jointly by all components of the subgroup. Each of the presentations will assist all students of the subject and at least one teacher. After each of the exhibitions will open a round of discussion with the participation of all attendees and in which the study's authors respond to the issues raised.

EVALUATION

Assessment of student learning will consider the knowledge and skills acquired throughout the course, and attendance at various activities and their degree of participation in them. The final numerical grade will be established according to the scores obtained in the following sections:

1.-A final exam will assess the knowledge acquired in the lectures and seminars in methodology. The value of this test will constitute 40% of the final grade for the course.

2.-Evaluation of the work proposed by the professor and his presentation in the form of seminars. The preparation and presentation of this work by the students will be mandatory. It will assess the student's ability to extract information from literature sources available and their ability to organize and develop a team, and the quality and scientific content of the work and the student's ability to present their work publicly and to discuss with peers and teachers different aspects related thereto. The valuation of this section will 50% of the final grade.
In the event that fails and submit this work would be suspended the course, regardless of the grade earned in the other sections.

3. - In the last section of the rating, which will mean 10% of the final grade, teachers assessed students' active participation in educational activities and particularly in discussions and debates that are

established during the seminar sessions .

The final grade for the course will be the sum of all the scores obtained by students in the previous sections

REFERENCES

Basic

- Predictive toxicology in drug safety. Jinghai J. Xu and Laszlo Urban (Eds). Cambridge University Press, 2010
- Mechanistic Toxicology: The Molecular Basis of How Chemicals Disrupt Biological Targets. Urs A. Boelsterli (Ed). CRC Press, 2007
- Adverse Drug Reactions. Uetrecht, Jack (Ed.) Series: Handbook of Experimental Pharmacology, Vol. 196. Springer, 2010.
- Pessayre D, Fromenty B et al. Central role of mitochondria in drug-induced liver injury. Drug Metabolism Reviews, 2012; 44(1): 3487.
- http://www.fda.gov/drugs/drugsafety/default.htm.
- http://www.sabiosciences.com/Apoptosis.php
- http://toxnet.nlm.nih.gov

ADDENDUM COVID-19

This addendum will only be activated if the health situation requires so and with the prior agreement of the Governing Council

In the event that the health situation so requires:

A) Face-to-face teaching will be replaced by online teaching, through synchronous or asynchronous presentations by teachers of the teaching materials, using the tools made available to teachers and students in the Virtual Classroom.

B) The tutorials will be carried out exclusively telematically.

C) The final evaluation of the subject will be carried out by evaluating the following sections:

1) ***Oral presentation of a practical work prepared in a telework group*** by the students on the topics proposed by the teachers of the subject. This part will be worth up to 90% of the final grade. On the agreed date, each student will make their presentation through the BLACKBOARD application available in the Virtual Classroom. The teacher will act as coordinator of the session, giving way to the students who have to present the work, previously loaded (after being authorized as participants). All the other students will connect as "assistants" to see and hear, ask questions and intervene when the teacher passes them by. The teacher will question those who are presenting the topic and all students will be able to participate.

2) ***Interest of the student in the subject***, expressed as their attendance at face-to-face classes, participation in organized discussions, answers to questions from teachers during face-to-face sessions, attendance at personal tutoring and / or any other type of activity carried out by the student in relation to the subject. Up to 10% of these concepts can be achieved in the final grade.