VNIVERSITAT DE VALÈNCIA

Course Guide
43106 Drug metabolism and biotransformation in the human body

COURSE DATA

Data Subject	
Code	43106
Name	Drug metabolism and biotransformation in the human body
Cycle	Master's degree
ECTS Credits	3.0
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
LOPEZ GARCIA, MARIA PILAR	30 - Biochemistry and Molecular Biology
O'CONNOR BLASCO, JOSE ENRIQUE	30 - Biochemistry and Molecular Biology

SUMMARY

One of the main challenges of biomedical research and present clinical practice on the way to personalized medicine is to optimize the pharmacotherapeutic response, maximizing at the same time safety and effectiveness in the pharmacological treatment of the disease. Current experience shows that drug response varies very significantly between patients: about 1 in 3 does not adequately respond to therapy, either because the drug is not effective, either because it causes unexpected side effects - sometimes very serious. Human variability in drug response is largely determined by interindividual differences in qualitative and quantitative drug processing by our own body, ie in their absorption and distribution to target tissues, metabolism and excretion (ADME). The specific study of these processes is therefore an essential step in the research and development of any new drug.

The subject *Drug metabolism and biotransformation in the human body*, provides a rigorous, comprehensive and integrated view of the biochemical processes that define the ADME of a compound, the key elements (metabolic enzymes and transporters) that mediate these processes, and the biological significance of biotransformation. With a multidisciplinary perspective, we will revised the tissues and systems responsible for drug metabolism and transport, their characteristics and functional requirements, the methods of study, and the mechanisms that modulate drug biotransformation in physiological and pathological conditions. We will analyze the genetic and nongenetic factors that explain, at the molecular level, human intra- and interindividual variability in biotranformación, the clinical consequences of these differences, and its significant impact on biomedical R & D and current clinical practice (development of new drugs and diagnostic methods , clinical trials, etc.).

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

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

Other requirements

Los conocimientos generales o especificos en Bioquímica, Biología Celular y Molecular, Fisiología y Biomedicina que proporcionan las titulaciones de Grado o Licenciatura en el ámbito de las Ciencias de la Salud, Ciencias de la Vida, Ciencias Experimentales y en Tecnologías afines.

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 trabajar en equipo
- Tener capacidad de desarrollar un trabajo interdisciplinar.
- Conocer y comprender los mecanismos y sistemas enzimáticos responsables de la biotransformación de farmacos y otros xenobióticos en el organismo humano, su significado biológico y sus implicaciones clínicas.
- Conocer y comprender el mecanismo molecular subyacente en las interacciones medicamentosas, así como las bases bioquímicas y moleculares de la variabilidad interindividual humana en relación al metabolismo de fármacos, y ser capaz de aplicar estos conceptos en casos prácticos representativos.
- Aprender a identificar, manejar y presentar adecuadamente en informes y exposición pública, los conocimientos existentes (clínicos y/o experimentales) en relación a biotransformación, 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

1. To know and understand the enzymatic mechanisms and systems responsible for the biotransformation of drugs and other xenobiotics in the human organism, its biological significance and its clinical implications.
2. To understand and understand the molecular mechanism underlying drug interactions, as well as the biochemical and molecular bases of human interindividual variability in relation to drug metabolism, and be able to apply these concepts in representative practical cases.
3. To learn to identify, integrate and adequately present in public reports and exhibitions, existing knowledge (clinical and / or experimental) in relation to biotransformation, using the English language as a vehicle.

DESCRIPTION OF CONTENTS

1. INTRODUCTION. Fundamentals, specific terminology and basic concepts

1.1. What determines the pharmacological response: Pharmacokinetics and Pharmacodinamics
1.2. Interindividual differences in drug response: Efficacy, tolerance and ADRs. Phenotypic evidences and study methods of PK and PD variability
1.3. Genetic and nongenetic determinants of pharmacokinetic variability. Implications and biomedical relevance.

2. BIOTRANSFORMATION: Drug and xenobiotic metabolism in the human body

2.1. Definition, processes and consequences
2.2. Enzyme systems responsible for drug biotransformation. Metabolism enzymes, transport proteins, and steps involved. Tissue distribution and subcellular localization. Study methods.
2.3. Particular features of the biotransfomación enzymes. Genetic polymorphism and its phenotypic expression. Interspecies differences and interethnic.
2.4. Biological significance of biotransformation: An integrated view

3. THE CYTOCHROME P450 GENE SUPERFAMILY

3.1. CYP in the biosphere. Nomenclature and evolutionary relationships.
3.2. Human CYPs. Major isoforms in the metabolism of xenobiotics and the metabolism of endogenous substrates.
3.3. CYP as an enzyme system. Components of the functional CYP, 3D structure, and structure-function relationships. Catalytic cycle and the electron transfer auxiliary systems. Study methods.
The CYP activity as a source of oxidative stress.
3.4. Tne relationships of CYP activity with other metabolic pathways

4. INTERINDIVIDUAL VARIABILITY IN BIOTRANSFORMATION: Molecular bases

4.1. Modulation of the expression level: Mechanisms of enzyme induction.
4.2. Modulation of functional activity: Inhibition, covalent modification and allosteric modulation. Biological significance and applications
4.3. Genetic polymorphism: Variations affecting structure, function or the level of gene expression. Relationship phenotype / genotype

5. CLINICAL CONSEQUENCES OF VARIABILITY IN BIOTRANSFORMATION: Monographic seminars presenting relevant selected examples

5.1. Drug interactions (drug-drug, drug-gene)
5.2. Altered therapeutic effectiveness (on-target).
5.3. Interactions with secondary tissue targets (off-target).
5.4. Drug-food interactions.
5.5. Interaction with endogenous pathways, etc.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	20,00	100
Group work	10,00	100
Study and independent work	10,00	0
Readings supplementary material	10,00	0
Preparation of evaluation activities	15,00	0
Preparing lectures	10,00	0
TOTAL	75,00	

TEACHING METHODOLOGY

English version is not available

EVALUATION

To pass the course will be mandatory attendance at least 80% of classroom activities. A system of continuous assessment of learning is proposed, with the assessment of the following sections:

1. Evaluation skills acquired through a written test, to be held at the end of the semester and will involve 40% of the final grade.

2) Assessment of written work submitted., Attending to their scientific quality, formal presentation, and demonstrated competence in the interpretation and transfer of theoretical concepts to current clinical / biomedical. It represents 30% of the final grade.

3). Interests of the student in the art and their active participation in all the activities proposed, expressed by the continued / regular classroom activities attendance, attitude and contributions to classroom discussions and seminars, and the quality of the individual oral presentation . It represents 30% of the final grade.

REFERENCES

Basic

- Handbook of Drug Metabolism, 2nd edition, P.G Pearson y L.C. Wienkers, Informa Healthcare USA,2008.

- The Biochemistry of Drug Metabolism (2 vols). B. Testa y S. Krämer, Willey, 2010.
- Cytochrome P450. Structure, Mechanism, and Biochemistry 4rd edition. Ed.: P.R. Ortiz de Montellano, Springer, New York, 2015.
- Rapid Review Phaymacology (en especial los capítulos iniciales), 3rd edition. Ed: T.L. Pazdernik y L. Kerecsen, Mosby, 2010.
- Handbook of Drug-Nutrient interactions, 2nd edition, Eds: J.L. Boulloto y U.T. Armenti. Humana Press (Springer), 2010
- Pharmacogenomics. Eds.: W. Karlow, U.A. Meyer y R.F. Tyndale, Taylor & Francis, New York, 2005.

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 done by means of a system of continuous assessment of learning similar to that already proposed in the Teaching Guide is maintained, with the assessment of the following sections:

1. Assessment of the knowledge acquired through a **written test** that will be carried out at the end of the semester by means of a combined objective test (quizz and essay type), using the tools provided by the Virtual Classroom. It will account for 50% of the final grade.

2. Assessment of a **written work presented electronically** by the students, based on its scientific quality, its formal presentation, and demonstrated competence in interpreting and transferring theoretical concepts to current clinical / biomedical practice. It will represent 40% of the final grade.

3. Student interest in the subject and their active participation in all the activities carried out during the course, expressed by the continuous / regular attendance at class, and their attitude and contributions in the tutoring discussions (classroom and virtual classroom forums). It will represent 10% of the final grade.