

**COURSE DATA****Data Subject**

Code	43107
Name	Pharmacogenetics
Cycle	Master's degree
ECTS Credits	3.0
Academic year	2022 - 2023

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
O'CONNOR BLASCO, JOSE ENRIQUE	30 - Biochemistry and Molecular Biology

SUMMARY

Thanks to the technology advances of the genomics era, Pharmacogenetics and Pharmacogenomics focus on the study of polymorphisms in DNA sequence, mRNA expression patterns, proteome, metabolome, etc. and the effect of all these factors on drug response in a given individual.

Pharmacogenetics aims to establish and to identify the genetic basis of differences in the response to drugs, as one of the major problems facing current medicine is the great variability both in terms of drug effectiveness and toxicity, so that different patients respond differently to the same medication.

This is due to genetic and nongenetic factors. The gene expression, rather than the genome itself, and gene polymorphisms determines and explains, at least in part, such differences.

Importantly, the inherited determinants which influence response to a drug, generally remain stable throughout the life of a person.



Knowledge of the human genome has provided the basis of the current state of Pharmacogenetics, Pharmacogenomics and the understanding of the molecular basis of disease. All together, they provide new approaches that take into account the characteristics of the genomic sequences, allowing an integrative vision which include interactions between genes. Understanding how the genome and the influence it may have on the effectiveness of certain drugs is believed to be the "key" for creating personalized drugs having high efficacy and minimal side effects. There are tests for molecular diagnostics by which physicians and pharmacists can select drugs and doses for each patient individually. The development of Pharmacogenetics, provides thus one way to make drug prescriptions without the current empiricism and heading toward a more personalized therapy.

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 las bases moleculares del polimorfismo humano, que generan variación interindividual en la administración, distribución, metabolismo y excreción (ADME) de fármacos, así como en las dianas moleculares de acción bioquímica-farmacológica. Conocimiento e identificación del polimorfismo genético de proteínas (enzimas, transportadores, receptores) que participan en estos procesos.
- Comprender la investigación básica y clínica de la medicina personalizada.
- Aprendizaje, manejo y presentación de informes y trabajos en exposición pública de las aplicaciones biomédicas de los conceptos farmacogenéticos en las distintas terapias actuales, usando como vehículo la lengua inglesa.

LEARNING OUTCOMES

1. To know the different genetic polymorphisms of metabolizing enzymes, transporters and drug targets and its application in personalized medicine.
2. To provide the basics for developing a critical mind on the clinical implications of Pharmacogenetics / Pharmacogenomics regarding the efficacy and toxicity of drugs that allow their rational use.
3. To learn to identify, manage and present properly in reports and public presentations, the existing knowledge in clinical applications of the Pharmacogenomic approach to optimized treatment of disease.

DESCRIPTION OF CONTENTS

1. Introduction to Pharmacogenetics and Pharmacogenomics

Pharmacogenetics vs Pharmacogenomics: historical evolution, scope and experimental approach. Specific objectives - clinical perspective and pharmacological R & D.

2. Human genetic variability and Pharmacogenes

Fundamentals of human genetic variability: SNPs, Indels and CNVs. Functional consequences of genetic polymorphism - genotype-phenotype relationships. Most relevant pharmacogenes (PK / PD and ADRs) and databases of interest. The implementation of pharmacogenetics in clinical practice.

3. Methods in Pharmacogenetics

Molecular technologies for genotyping, applicable to the detection of polymorphisms. DNA sequencing: capillary and massive (NGS). Amplicons for detection of SNPs. Multiplexed PCRs. Taqman tests. Biomarkers



4. Pharmacogenetics of drug metabolism (I): Phase 1 drug metabolizing enzymes

Interindividual variability: causes. Molecular basis of CYP2D6, CYP2C9, CYP1A1 and CYP2E1 polymorphism. Other CYPs. Other Phase 1 enzymes.

5. Pharmacogenetics of drug-metabolizing enzymes (II): Phase 2 enzymes

Glutathione-S-transferases. N-acetyltransferases. Methylating enzymes, glucuronic acid conjugation, flavin monooxygenases, and others.

6. Pharmacogenetics of drug transporters

Transporters of drugs and xenobiotics. Classification and functions. Mechanisms of drug resistance. Clinical consequences of polymorphisms in drug transporters. Techniques to study drug transporters.

7. Pharmacogenetics of adverse drug reactions (ADRs)

Molecular basis of the different types of ADRs. Genetic predisposition. Strategies for the design of safer drugs

8. Clinical Implications Pharmacogenetics (I): from DNA sequence to Precision Medicine

Future of clinical applications: Allelic imputation, phenotypic imputation, Validation of functional evidences, Validation of associations with adverse drug reactions for clinical practice guidelines. Anticoagulants. Cancer. Antidepressants.

9. Clinical Implications of Pharmacogenetics (II): Recommendations for Implementation in the Clinic

10. Clinical Implications of Pharmacogenetics (III): Pharmacogenetics in Translational Research

**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	5,00	0
Preparation of evaluation activities	15,00	0
Preparing lectures	15,00	0
TOTAL	75,00	

TEACHING METHODOLOGY

The subject is devised to be developed in the form of face and non-face work.

Actual teaching of this subject will be made by the following methodological approaches: lectures, seminars sessions exhibit topics chosen among those proposed by the teacher and / or student's proposal and tutoring assistance.

In the lectures, professor will present an overview of the topic, with special emphasis on the key concepts. At the same meeting professor will indicate the most appropriate resources for a deepening of the subject so that students complete their education in the same

EVALUATION

The evaluation of student learning will be carried out by assessing the following sections:

1. Fulfillment of a series of tasks proposed by the professors of the subject and available in the Virtual Classroom.

The tasks will involve the development of questions of a practical nature or clinical relevance. Students will receive the necessary instructions and bibliography to solve the task, which will be graded at the end of the semester.

From this section you can get up to 90% in the final grade of the subject.

2. Student interest in the subject, expressed as their participation in organized discussions, attendance at personal tutorials and/or any other type of activity carried out by the student in relation to the subject.

Of these concepts you can get up to 10% in the final grade of the subject.



REFERENCES

Basic

- Pharmacogenomics. Eds.: W. Karlow, U.A. Meyer & R.F. Tyndale, Taylor & Francis, New York, 2005
- Rapid Review Pharmacology 3^a ed. Eds.: T.L. Pazdernik & L. Kerecsen, Mosby 2010
- Handbook of drug metabolism. 2^a ed. P.G. Pearson & L.C. Wienkers, Informa Healthcare USA, 2008
- Cytochrome P450. Structure, mechanism and biochemistry. 3^a ed. Ed.: P.R. Ortiz de Montellano, Kluwer Academic/Plenum Press, New York, 2005

Additional

- REVISTAS:

The Pharmacogenomics Journal
<http://www.nature.com/tpj/index.html>

Future Medicine Pharmacogenomics
<http://www.futuremedicine.com/loi/pgs>

American Journal of Pharmacogenomics
<http://www.ingentaconnect.com/content/adis/apg>

Journal of the International Society of Pharmacogenomics
<http://www.pharmacogenomicsociety.org/site/journal.asp>

WEB RELACIONADAS

-Pharmacogenomics Knowledge Base:
<http://www.pharmgkb.org/index.jsp>

-International Society of Pharmacogenomics:
<http://www.pharmacogenomicsociety.org/site/newsletter.asp>

-Pharmacogenetics Research Network:
<http://www.nigms.nih.gov/Initiatives/PGRN/>

-U.S. Food and Drug Administration Genomics:
<http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/default.htm>

-American Medical Association Pharmacogenomics:
<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/genetics-molecular->



[medicine/current-topics/pharmacogenomics.shtml](#)

-The Single Nucleotide Polymorphism (SNP) Database:

<http://www.ncbi.nlm.nih.gov/snp>

-Table of Valid Genomic Biomarkers in the Context of Approved Drug Labels (NIH):

<http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm>