

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

<b>Code</b>	43029
<b>Name</b>	Drug-receptor interaction
<b>Cycle</b>	Master's degree
<b>ECTS Credits</b>	4.0
<b>Academic year</b>	2021 - 2022

**Study (s)**

<b>Degree</b>	<b>Center</b>	<b>Acad. year</b>	<b>Period</b>
2138 - M.D. in Research in and Rational Use of Medicines	Faculty of Pharmacy and Food Sciences	1	First term
3103 - Biomedicine and Pharmacy	Doctoral School	0	First term

**Subject-matter**

<b>Degree</b>	<b>Subject-matter</b>	<b>Character</b>
2138 - M.D. in Research in and Rational Use of Medicines	7 - Drug-receptor interaction	Optional
3103 - Biomedicine and Pharmacy	1 - Complementos Formación	Optional

**Coordination**

<b>Name</b>	<b>Department</b>
IVORRA INSA, MARIA DOLORES	135 - Pharmacology
NOGUERA ROMERO, MARIA ANTONIA	135 - Pharmacology

**SUMMARY**

Subject in which, from the basics of drug-receptor interaction, are developed the molecular, biochemical and physiological and mathematical models that allow us to study and to understand the concept of receptor and its pharmacological modulation. Provides a basis for understanding much part of the basic pharmacological mechanisms involving pharmacology research so it is of interest to students to guide their training to research the mechanism of action of drugs, but also for those who need a solid grounding in the molecular mechanisms of signal transduction.



## PREVIOUS KNOWLEDGE

### Relationship to other subjects of the same degree

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

### Other requirements

Previous knowledge of Pharmacology and English is required.

## OUTCOMES

### 2138 - M.D. in Research in and Rational Use of Medicines

- Utilizar adecuadamente las herramientas informáticas, métodos estadísticos y de simulación de datos, aplicando los programas informáticos y la estadística a los problemas biomédicos
- 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.
- To acquire basic skills to develop laboratory work in biomedical research.
- Be able to make quick and effective decisions in professional or research practice.
- Be able to access the information required (databases, scientific articles, etc.) and to interpret and use it sensibly.
- Students should possess and understand foundational knowledge that enables original thinking and research in the field.
- Know how to write and prepare presentations to present and defend them later.
- Be able to access to information tools in other areas of knowledge and use them properly.
- Be able to apply the research experience acquired to professional practice both in private companies and in public organisations.
- Capacidad de seleccionar y gestionar los recursos disponibles (instrumentales y humanos) para optimizar resultados en investigación.
- Dominar el método científico, el planteamiento de protocolos experimentales y la interpretación de resultados en la búsqueda, desarrollo y evaluación de nuevos fármacos.

## LEARNING OUTCOMES



At the end of the teaching-learning process the student should be able to:

1. Familiarize with the concept of receptor and molecular mechanisms of signal transduction, both conceptually and methodologically.
2. Analyze a problem and optimize methodological resources to the resolution of the same
3. Dominate standard laboratory techniques for the study of receptors and how to analyze experimental results.
4. Planning the appropriate organization to perform work as a team and carry it out efficiently.
5. Search and find articles and reviews necessary to propose a research project based, from the methodological point of view, in functional studies of isolated organ and radioligand binding assays.
6. Construct a scientific paper or an oral presentation in a structured and concise manner about ligand-receptor interactions and transduction mechanisms.

## DESCRIPTION OF CONTENTS

### 1. THEORETICAL ASPECTS OF DRUG-RECEPTOR INTERACTION

Development of the concept of signaling through receptors as a primary mechanism for the physiological or pharmacological modulation of cellular processes.

Specification of the contents of the unit:

Receptor concept and its impact on biomedical sciences.

Theory of drug-receptor interaction. Receptor activation models.

Constitutive activity: agonism, inverse agonism, antagonism.

Systems of signal transduction.

Mechanisms of physiological and pharmacological regulation of receptors.

### 2. STUDY TECHNIQUES OF RECEPTORS

Management of the molecular mechanisms of signal transduction, both conceptually and methodologically, including laboratory tests and analysis of the results.

Specification of the contents of the unit:

Specific radioligand binding and fluorescent ligands.

Western blotting, immunoprecipitation, immunofluorescence.

Analysis of receptor expression by RT-PCR quantitative real-time.

Analysis of the functionality of receptors: isolated organ techniques.

Other study techniques: confocal laser microscopy .

**WORKLOAD**

ACTIVITY	Hours	% To be attended
Laboratory practices	15,00	100
Theory classes	10,00	100
Seminars	10,00	100
Group work	5,00	100
Development of group work	25,00	0
Development of individual work	10,00	0
Study and independent work	10,00	0
Readings supplementary material	10,00	0
Preparation of evaluation activities	10,00	0
Preparation of practical classes and problem	10,00	0
Resolution of online questionnaires	10,00	0
<b>TOTAL</b>	<b>125,00</b>	

**TEACHING METHODOLOGY**

During the activities, both theoretical and practical, the applications of the subject contents in relation to the Sustainable Development Goals (SDG) will be indicated. This is intended to provide knowledge, skills and motivation to understand and address these SDGs, while promoting reflection and criticism.

Theoretical classes and participatory lectures

Discussion of items (readings)

Seminars

Laboratory practices and practices in computer room

Project development

Debate or guided discussion

Conference of experts

The course is structured in a series of lectures, which will introduce students to the theoretical concepts of drug-receptor interaction, for, from them, ask the student an experimental problem to be solved. With the knowledge gained and additional literature available in the Virtual Classroom, students must develop an appropriate experimental protocol to solve the problem, run in the laboratory, to obtain experimental results, analyze and develop a written report of all these activities following the outline of a research paper. The course will finish with an oral presentation of the work performed.

To complete face-to-face teaching, students will be able to take online questionnaires, practical exercises or comments on research articles...



As a communication support is used:

Virtual Classroom platform of the University of Valencia that allows teacher-student communication and storage of slides

Other teaching resources that is available to students.

## EVALUATION

### Continuous evaluation:

Class attendance 20%

Active participation 10%

**Evaluation of theory** 10%

**Individual work** (problems and questions) 30%

**Teamwork** 30%

To pass the subject, attendance at 80% of face-to-face sessions and obtaining a qualification greater than or equal to 50% within each evaluated section will be required.

## REFERENCES

### Basic

- WHALEN E.J., RAJAGOPAL S., LEFKOWITZ R.J. Therapeutic potential of b-arrestin- and G protein-biased agonists. Trends in Molecular Medicine (17): 2011.
- RAJAGOPAL S., RAJAGOPAL K., LEFKOWITZ R.J. Teaching old receptors new tricks: biasing seven-transmembrane receptors. Nature Reviews, 9, 2010.
- ZHOU X.E., MELCHER K., XU H.E. Understanding the GPCR biased signaling through G protein and arrestin complex structures. Current Opinion in Structural Biology. 45: 150-159, 2017.
- KENAKIN T. International Union of Basic and Clinical Pharmacology Review. New concepts in pharmacological efficacy at 7TM receptors: IUPHAR. Br. J. Pharmacol. 168: 554-575, 2013.
- SCHARGE R., DE MIN A, HOCHHEISER K, KOSTENIS E., MOHR K. Superagonism at G protein-coupled receptors and beyond. Br.J.Pharmacol. 173: 3018-3027, 2016.
- KENAKIN T. Signaling bias in drug discovery, Expert Opinion on Drug Discovery, 12:4, 321-333, 2017.
- JEAN-ALPHONSE F., HANYALOGU A.C. Regulation of GPCR signal networks via membrane trafficking. Molecular and Cellular Endocrinology 331, 205214, 2011.
- ALEXANDER S.P., MATHIE A., PETERS J.A. Guide to Receptor and Channels, Br J. Pharmacol, 5th edition, (164):S1-S324, 2011.





- Rankovica Z\*, Tarsis F. Brustb, and Laura M. Bohnb,\*"Biased agonism: An emerging paradigm in GPCR drug discovery"

#### **Additional**

- HALL and LANGMEAD. Matching models to data: a receptor pharmacologists guide. British Journal of Pharmacology DOI:10.1111/j.1476-5381.2010.00879.x
- Articulos en revistas especializadas
- SCHEERER P., SOMMER M.E. Structural mechanism of arrestin activation. Current Opinion in Structural Biology. 45: 160-169, 2017
- STODDART L.A., WHITE C.W., NGUYEN K., HILL S.J., PFLEGER K.D.J. Fluorescence- and bioluminescence-based approaches to study GPCR ligand binding. Br. J. Pharmacol. 173: 3028-3037, 2016.<https://webges.uv.es/uvGuiaDocenteWeb/guia#>
- SEGURA V, PÉREZ-ASO M, MONTO F, CARCELLER E, NOGUERA MA, PEDIANI J, MILLIGAN G, MC GRATH J, D'OCÓN MP. "Differences in the Signaling Pathways of  $\alpha 1A$ - and  $\alpha 1B$  Adrenoceptors Are Related to Different Endosomal Targeting" PlosOne 8(5): e64996, 2013.
- MC GRATH J. "Localization of  $\alpha$ -adrenoceptors: JR Vane Medal Lecture" Br. J. Pharmacol. 172: 1179-1194, 2015
- Von Moo E, van Senten JR, Bräuner-Osborne H, Møller TC. Arrestin-dependent and -independent internalization of GPCRs methods, mechanisms and implications on cell signaling. Mol Pharmacol. 2021; 99(4):242-255 DOI: 10.1124/molpharm.120.000192

#### **ADDENDUM COVID-19**

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

##### **1. Contents**

The initially programmed contents are maintained.

##### **2. Workload and temporary planning of teaching**

To teach this, the scheduled schedules are maintained and the student will be given the freedom to carry out the autonomous learning with the materials that are uploaded in the virtual classroom, but maintaining the volume of work that marks the original teaching guide. Theoretical classes will be taught through the BBC. In the case of laboratory practices, the student will be provided with data from other practices that can be analyzed and discussed. Previously they will be shown with the help of videos, powerpoint or computer programs, how the realization of the practice in the laboratory would be.

##### **3. Teaching methodology**

- Uploading materials in the Virtual Classroom

In the case of sessions of theoretical / participatory seminars, taught by external teachers, students will be provided (through the Virtual Classroom) the materials provided in the original guide, adapted and incorporating explanatory annotations so that the student can access them at any time

- BBC synchronous video conferencing



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- Use of the virtual classroom forum and e-mail to answer questions

**4. Evaluation**

It is not necessary to adapt the evaluation process described in the teaching guide.

**5. Bibliography**

The same bibliography recommended in the teaching guide is maintained.

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