Fiche UE MU5BIN17

Ouverture en Neurosciences 2

Module : Molecular neuropharmacology : Structure, function and pharmacology of neurotransmitter receptors and transporters

Responsable	**Laetitia Mony**
Co-responsable	

Descriptif	***Parcours type***	***Option***	***Niveau***	***Semestre d'enseignement***	***ECTS***	***Effectif maximal***
	Neurosciences	Neurosciences Cognitives et Comportementales – NCC Neurosciences Cellulaires et Intégrées – NCI-Sciences de la Vision	M2	S3	3	10

Modalités pédagogiques	***Volume horaire Cours***	***Volume horaire TD***	***Volume horaire TP***	***Présentiel/ Distanciel***
	20	3		Présentiel

Objectifs	This module is about neurotransmitter receptors and transporters, which are key actors of neuronal communication. The recent boom in membrane protein structures sheds a new light on our understanding of the function and the regulation mechanisms of these proteins. It also provides an unprecedented structural and conceptual framework to discover and develop new molecules of pharmacological interest.
Thèmes abordés	This module will tackle the molecular and structural organization, as well as the operating mechanisms of the main classes of neurotransmitter receptors and transporters. We will present their activation principles, as well as their interactions with ligands. Emphasis will be put on the allosteric mechanisms and subsequent conformational dynamics. We will also show how malfunction of these proteins can be at the origin of pathologies, making them targets of therapeutic interest. Finally, using concrete cases, this module will introduce students to the development process of new molecules of neurological and psychiatric interest.

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Compétences acquises à l'issue de l'UE (concepts, méthodologie et outils)	1 – G protein coupled receptors (GPCRs) (5h) – Following a general presentation of this very large receptor family, activation of metabotropic glutamate and GABA receptors will be studied in more details (agonist binding, signal transduction and G-protein activation), allowing identification of different pharmacological targets on these receptors (agonist binding site, transmembrane site, …). In addition, modern tools to design and develop new molecules acting on GPCRs will be presented (structure-activity relationship, molecular modeling, docking, pharmacophore modeling, high throughput screening of active molecules, …). 2 – Ionotropic glutamate receptors (iGluRs) (5h) – The course will describe the diversity of iGluRs and the molecular determinants of the functional differences between the different iGluR classes. A focus will be put on the molecular mechanisms at the origin of receptor activation, desensitization and modulation. We will furthermore put an emphasis on the rich pharmacology of iGluRs, especially of NMDARs, and describe the therapeutic potential of the allosteric modulatory sites recently identified in AMPA and NMDA-type iGluRs. 3 – P2X receptors (2h30) - P2X receptors form the third major class of ionotropic receptors. The specificities (molecular architecture, gating, permeation…) of this class of ligand-gated channels will be presented at the molecular level. The functions and therapeutic potential of these receptors will also be addressed. 4 – Pentameric ionotropic receptors (2h30) – The presentation of the molecular organization of the receptors belonging to this family will highlight the similarities but also the divergences between the nicotinic and $5HT_3$ receptors (excitatory) and the $GABA_A$ and glycine receptors (inhibitory). We will analyze in more details the mechanisms of action of clinical drugs targeting these receptors (benzodiazepines, $GABA_A$ receptor allosteric modulators, $5HT_3$ receptor antagonists, …). We will also tackle the pathological consequences of numerous mutations affecting pentameric ionotropic receptors. 6 – Optopharmacology (2h30) – This transversal course will describe photochemical and genetic strategies aimed at rendering neurotransmitter receptors light controllable, and provide an overview of the neurobiological insights gained from such approach. 7 – Finally, this course series will be concluded by a talk from a project leader in the pharmaceutical industry, who will present several aspects of the design and development of a new drug (2h).
Prérequis	Basic knowledge in protein biochemistry (amino acid properties, protein structure, ligand/protein interactions) and pharmacology (what is an agonist, antagonist; notions of competitive and non-competitive inhibition).

Modalités d'évaluation/100	***Ecrit***	***Oral***	***CC***	***Autre***
	60	40		

The date of the written exam is contingent upon the ENS schedule. It will take place the week after the module (jan 10-14 2022)

Langues utilisées	***Dans les cours, TD, TP***	***Dans les documents, supports***
	English	English

Localisation	Ecole Normale Supérieure (ENS)

MAJ 30-07-21