Photocontrol of Alpha 7 Nicotinic Acetylcholine Receptors

This PhD project aims to develop molecular tools to study and manipulate alpha7 nicotinic acetylcholine receptors (α7 nAChRs), which are involved in neurodegenerative and inflammatory disorders such as Alzheimer's disease, schizophrenia, and Parkinson's disease. The focus is on the design, synthesis, and characterization of highly selective photoswitchable agonists for α7 nAChRs, enabling rapid, reversible control of receptor activity by light for precise spatiotemporal modulation. This innovative approach will facilitate the study of receptor conformational dynamics in live cells. Existing photoswitchable ligands, such as azocholine, have limitations. This project aims to overcome these challenges by designing new photoswitchable ligands. Molecular docking studies will be based on the recently published cryo-EM structure of α7 nAChR, which will help in selecting promising candidate molecules. The project is divided into five key tasks: 1) Molecular docking ; 2) Synthesis of photoswitchable ligands ; 3) Photophysical and photochemical characterization of these ligands; 4) Electrophysiological characterization ; 5) Nanobody conjugation. The expected outcome of this project is the development of novel tools for the precise control of α7 nAChR activity, advancing our understanding of receptor function and dynamics.

This PhD project will be carried out in collaboration between two research laboratories:

- **CiTCoM UMR CNRS 8038, Inserm U1268** (Pr. Ludovic Jean) – Expertise in medicinal chemistry, docking, organic synthesis, and photoswitchable compounds.
- **Institut Pasteur, Neurosciences Department** (Dr. Pierre-Jean Corringer) – Expertise in the biochemistry and biophysics of nAChRs, including protein engineering, structural analysis, and electrophysiology.

Keywords : Photopharmacology; Nicotinic Receptors; Medicinal Chemistry; Electrophysiology; Molecular Docking

References :

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Angew. Chem. Int. Ed. **2016**, *55*, 10978-10999 DOI: 10.1002/anie.201601931
Chem. Eur. J. **2025**, e202500803 DOI: 10.1002/chem.202500803
Chem Eur. J. **2023**, *29*, e202301160 DOI : 10.1002/chem.202301160
Nat. Commun. **2023**, *14*, 5964 DOI: 10.1038/s41467-023-41734-4

Location :

- CiTCoM UMR 8038, 4 Avenue de l'Observatoire, F-75006 Paris (Pr. Ludovic Jean)
- Neurosciences Department, UMR 3571, Institut Pasteur, 25 rue du Dr. Roux, F-75015 Paris (Dr. Pierre-Jean Corringer)

Candidate Profile :

We are looking for a **PhD candidate** with the following qualifications:

- A solid background in **organic chemistry** with strong expertise in **synthesis** and **characterization of organic compounds** (NMR, MS, etc.).
- A strong interest in **biology**, especially in understanding receptor dynamics and pharmacology.

- The ability to **take initiative** in research, contribute innovative ideas, and work independently.
- **Excellent communication skills** to present research findings clearly and effectively.

Application Process

Interested candidates should send their application to **Pr. Ludovic Jean** (ludovic.jean1@u-paris.fr) and **Dr. Lucas Pagès** (lucas.pages@u-paris.fr)

Applications should include the following documents:
- A detailed CV
- A cover letter
- Grades (M1 and M2)
- Two recommendation letters (or references for potential referees)