

Call for applications for a doctoral project as part of the Inlife & IPV Sorbonne université call for projects

Design and development of MétalloPROTACs, an anti-cancer strategy for the targeted degradation of proteins of interest.

Since the 1970s and the discovery of cisplatin, metal compounds have become established in chemotherapy, but their low selectivity limits their development. Sorbonne University's ChemBio team has designed iridium(III) complexes that interact, among other things, with Hsp90, a chaperone protein essential for the folding of oncogenic proteins.

Hsp90 inhibition represents a promising strategy against certain cancers. PROTACs, bifunctional molecules promoting the targeted degradation of pathogenic proteins, have opened up new prospects, although their limitations call for alternatives. HEMTACs, specifically exploiting the interaction of Hsp90 with various E3 ligases, could offer a more effective and selective approach to regulating the stability of proteins involved in tumor progression.

This PhD project aims to design and synthesize iridium-based metalloPROTACs that exploit Hsp90's ability to interact with various E3-ligases and induce the degradation of oncogenic proteins via the proteasome. To validate our concept, we will choose to target and degrade CDK4/6, protein kinases overexpressed in cancer cells and implicated in treatment resistance. This proof of concept will enable us to consider targeting other oncogenic proteins. This project brings together the ChemBio team at IPCM and the TGF- β team at Sorbonne University's CRSA, combining organic and organometallic synthesis and cell biology to develop an innovative approach to the targeted degradation of proteins involved in the mechanisms of carcinogenesis.

We are looking for a motivated candidate for a doctoral research project at the chemistry-biology interface. **The successful candidate will present his/her project at an audition on May 26 and 27 at Sorbonne Université's Pierre et Marie Curie campus.**

Application deadline: send your CV and covering letter before **April 18, 2025** to Candice.botuha@sorbonne-universite.fr

Profile required:

Academic background: Master 2 in molecular chemistry, medicinal chemistry or other relevant field. Dual expertise in chemistry and biology would be an asset. Competence in chemistry and biology: Experience in organic and/or organometallic synthesis, purification and characterization (NMR, MS, chromatography). Interest and/or experience in cell and molecular biology, with cell culture skills appreciated.