

Project: Development of Molecular Degraders (Protacs) for Understudied Protein Kinases

Short description: Kinases are one of the most important human protein families and are directly or indirectly involved in all cellular biochemical pathways. Since early 2000's, 88 kinase inhibitors have entered in the clinics, representing a remarkable success story in drug development. However, there is still large number of unexplored kinases which have a strong genetic link to disease but poorly biology understood (see <https://doi.org/10.1021/acs.jmedchem.1c00980>). In addition to the classical pharmacology based on occupancy-driven effect, that has enabled us to develop drugs to treat hundreds of diseases, we are now in a new era in Drug Discovery. PROTACs is a new modality of molecular degraders based on a proximity-driven effect. They are heterobifunctional small-molecules constituted by a ligand to bind the protein of interest, a moiety to recruit a E3 ubiquitin ligase, and a linker connecting both parts. This molecule hijacks the ubiquitin-proteasome pathway to induce the degradation of the desired target protein. Currently, the first Protacs are entering in late-stage of clinical trials as well as many others in early-stage pipeline, which demonstrate a promising therapeutic application.

Objective: We are looking for very motivated students to work in a synthetic organic chemistry lab to design and synthesize molecular degraders (Protacs) for understudied protein kinases. If you want to participate of this "New Era" in Drug Discovery with partners worldwide, just send an email!

Technical skills: Fundamental practical knowledge in synthetic organic chemistry and structural characterization of small-molecules (NMR, MS, HPLC, TLC...).

Openings offered: 1 Master thesis

Language: English

Director MS thesis: *Prof. Dr. Ricardo A. M. Serafim* (ricardo.serafim@iqs.url.edu)

Location: *IQS Synthesis Laboratory*