

OFFER AN INTERNSHIP
Academic Year 2016/2017

Send to Mrs Pr Camproux

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Specialty training : Research Professional

a few key words to describe the subject of training: protein-protein interactions, peptidomimetics, structure-based design, docking, molecular dynamics, cancer

Title of internship: Computational design of novel peptidomimetic inhibitors of cadherin homophilic interactions

this subject is a first step towards a thesis: No

Short text describing your project

The internship will focus on the application of various computational techniques for the design of new peptidomimetics targeting protein-protein interactions. In particular, cadherin-cadherin interactions will be investigated during the training.

As part of an ongoing investigation into the cellular adhesion process mediated by members of the large cadherin family of proteins, we have designed and synthesized small peptidomimetic molecules aimed at providing partial or total inhibition of the cadherin-cadherin interaction. Homophilic cell adhesion is induced by the interaction ("dimerization") of the N-terminal extracellular domains of cadherin molecules from opposing cells. Targeting E- and N-cadherin, that play an emerging role in a number of solid tumors, we have obtained a first set of peptidomimetic ligands mimicking the adhesive interface identified by recent crystallographic structures, i.e., the conserved N-terminal tetrapeptide sequence Asp-Trp-Val-Ile (Org. Biomol. Chem., 2015,13, 2570).

Aim of the training will be the design of second-generation peptidomimetics by using virtual screening protocols to improve the affinity of our ligands for either E- or N-cadherin, or both, and to increase their efficacy on cells. In addition, we intend to improve our structural understanding of the binding of our peptidomimetic ligands to the extracellular domains of the cadherins by molecular

dynamics simulations combined with NMR and/or crystallographic studies (*J. Med. Chem.*, 2010, 53, 5089).

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