

OFFER AN INTERNSHIP
Academic Year 2013 – 2014

Send to Mrs Pr Camproux :

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Name of the head of laboratory or company: Antonio Macchiarulo

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Specialty training : Research Professional

a few key words to describe the subject of training :

The training will be focused on the study of the molecular basis of selectivity of small molecule inhibitors towards IDO1 and IDO2. In this framework, the training will cover the application of homology modeling, docking studies and molecular dynamic simulations, attempting to explain biological data of selected IDO inhibitors from scientific literature and generate new working hypothesis.

Title of internship:

Insights into Structural and Conformational Features Affecting Ligand Selectivity in IDO1 and IDO2.

this subject is a first step towards a thesis: Yes - No

Short texte describing your project

The major route for the catabolism of tryptophan in mammals is the kynurenine pathway (KP). Metabolites generated in this pathway are involved in several disease conditions, including cancer, inflammatory disorders, psychiatric disorders and neurodegenerative diseases. Three enzymes are now known to catalyze the first and rate-limiting step of the KP: tryptophan 2,3-dioxygenase (TDO), indoleamine 2,3-dioxygenase-1 (IDO1), and indoleamine 2,3-dioxygenase-2 (IDO2). A large body of studies, in particular, have pinpointed a role of IDO1 in tumorigenesis and immune responses. However, clear physiological and pathophysiological functions of IDO2 are still elusive, making the design and development of selective IDO inhibitors very important to shed lights on specific functions of these

agreement with available biological data will be selected and submitted to molecular dynamic simulations (MD). The analysis of MD trajectories will allow investigating how different structural and conformational features of the enzymes may affect inhibitor binding selectivity.

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