SANOFI Recherche & Développement

Internship : 6 months, molecular modelling

Titre : Is the specificity of a ligand for its CYP related to its affinity to a particular access channel?

Cytochromes P450 (CYPs) are a large family of hemoproteins widely implicated in drug metabolism. Lots of models have been developed to predict the inhibition and metabolism of CYPs but the driving force for the binding of ligands in CYPs is not yet fully understood.
It is already known that some recognition patterns of substrates are located in the active site and also line putative access channels. Several channels are potential paths for ligand entrance and metabolites way out but no relationship has been established between a ligand and a particular access channel.

The study will use previous results obtained by LSOD team (CEA Saclay). CYPs access channels have been identified by Delaunay's triangulation method and the putative entry points for a given ligand will be used as starting point for simulation of ligand entrance in CYP central cavity by molecular dynamics. Several points will be studied: for instance influence of the membrane on channels accessibility and plasticity, energetic profile of each access channel or dynamics of entrance of several classes of drugs.
The identification of geometrical and energetical profile channel-related or ligand-related should lead to a better understanding of ligand recognition and a better prediction of inhibition and metabolism by CYPs.

The internship is proposed to be done in Sanofi Research Center (Vitry-sur-Seine) with scientific support of Dr. François André (UMR 8221 CNRS, LSOD, CEA Saclay).

Requirements :
Education in computational chemistry and/or structural bioinformatics, with strong interest in protein structure analysis and molecular dynamics.
Computing skills and knowledge of some scripting languages (knime, python, perl) would be a plus.

Please contact:

Claire MINOLETTI-HOCHEPIED
SANOFI - LGCR / SDI / DD-LO
13, Quai Jules Guesde
F - 94 400 Vitry-sur-Seine
Claire.Minoletti@sanofi.com