Master « In Silico Drug Design »
2ème année

PROPOSITION DE STAGE
Année Universitaire 2015/2016
A envoyer à Mme Pr Camproux
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Ecole doctorale de rattachement : ED393

Spécialité du stage : Recherche X Professionnel ☐

Indiquez par quelques mots clés, l'orientation scientifique du sujet : biologie structurale et caractérisation des structures protéiques, docking et analyse de données.

Titre du stage : Etude comparative des protéases de VIH-1 et VIH-2

Ce sujet constitue-t-il un premier pas vers un travail de thèse : Non

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Description du sujet (quelques lignes):

HIV-2 is a retrovirus discovered a few years after HIV-1. HIV-2 infections are restricted mainly to West Africa, including Guinea-Bissau, Gambia, Senegal, and Guinea. Some European countries are also concerned with HIV-2 infection, which represents 5% of HIV infection in a series of patients in Portugal [1] and 2% of the new HIV infections in France [2]. The HIV-1 and HIV-2 genomes differ by about 50 to 60% at the nucleotide level. Such differences may be correlated with differential responses to some antiretrovirals, as observed with the natural resistance of HIV-2 to non nucleoside reverse transcriptase inhibitors [3,4].

The first step of this project will focus on the comparison of proteases of VIH-1 (PR-1) and VIH-2 (PR-2) to understand the specificities of PR-2 against inhibitors. This comparison will be performed at the level of amino-acid sequences, tri-dimensional structures, protein pockets, ligand interaction, dimerization zone and H2O molecules using free tools (multiple alignment sequences, superimposition of structures, motifs extraction, MOE) or using softwares and methods developed in MTi (structural alphabet HMM-SA [5], SA-Mot [6], pocket and ligand descriptors [7, 8]). We will used a set of holo forms of PR1 and PR2 available in the Protein Data Bank: 31 PR1 complexed with 9 drugs and 3 PR2 complexed with 3 drugs. To increase the number of holo PR2 structures, the second step of this project will consist in building models of PR2 structures complexed with 6 other drugs using docking procedure (using autodock program). These modelled complexes will then be compared to PR1 structures complexed with identical drugs, using the same comparison protocol used to compare X-ray PR1 and PR2 holo forms.

This project is funded by the ANRS.

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