Master « In Silico Drug Design »
2ème année

PROPOSITION DE STAGE
Année Universitaire 2017/2018
A envoyer au Pr Camproux
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HDR : oui ou non

Ecole doctorale de rattachement :

Spécialité du stage : Recherche ☒ Professionnel ☐

Indiquez par quelques mots clés, l'orientation scientifique du sujet :

developement of new routine pipeline using MM/GBSA and Duck methods

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Titre du stage :"In silico methods for prioritising fragment hits against novel disease targets

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

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Description du sujet (quelques lignes):

XChem produces large quantities of highly information-rich data which must be triaged and prioritised using limited down-stream chemistry resource ($1000s / target). We need new tools for rapidly identifying which fragment hits can most efficiently be transformed into chemical probes. As part of this an in-depth understanding of the relative importance of the directional and non-directional interactions between the fragment and the protein and key waters is critically important. This information can be used to prioritise which hits to progress and in what manner, chemically.

The six-month project will be to take novel methods, such as Dynamic Undocking (DUck) [https://www.nature.com/nchem/journal/v9/n3/full/nchem.2660.html] and MM/GBSA [https://www.ncbi.nlm.nih.gov/pubmed/19569205], and help build an infrastructure to perform these analyses on a routine basis within an XChem campaign. We have previously shown that the DUck approach is able to identify complex cooperative interaction behaviours between ligands and proteins and as such expect that it will provide useful information with regards to ranking these interactions. The MM/GBSA approach can be used to assess the importance of key water molecules [e.g.https://www.ncbi.nlm.nih.gov/pubmed/24869780/] that the binding site contains and their relative role in the design of elaborated compounds from the initial hits.

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