Master « Sciences, Technologie, Santé »
Mention « In Silico Drug Design »
2ème année

PROPOSITION DE STAGE
Année Universitaire 2014 –2015

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Nom du Responsable du Laboratoire ou de l'Entreprise:

Affiliation administrative (CNRS, INSERM,…) et Numéro d'affiliation de l'unité : CNRS-UPMC UMR7590

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Nom du Responsable de l'équipe d'accueil (EA) : Catherine-Vénien-Bryan
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HDR : oui

Ecole doctorale de rattachement : 515

Spécialité du stage : Recherche ☐ oui Professionnel ☐ non

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

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Titre du stage :

Etudes dynamiques d'un mutant d'un canal potassium impliqué dans des pathologies cardiaques

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

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Description du sujet (quelques lignes):

Molecular dynamics on a potassium channel KirBac3.1The Inwardly Rectifying Potassium (Kir) channels are a family of potassium channels which play a key role in K+ transport and the regulation of membrane electrical excitability in many cell types1. Kir channels are found in the membrane of almost every cell in the body and control such diverse processes as heart rate, vascular tone, insulin secretion and salt/fluid balance. Their physiological importance is highlighted by the fact that genetically-inheriteddefects in Kir channels are responsible for a number of human diseases (channelopathies).
Recently, Catherine Vénien-Bryan's team has solved the structure of a functionally active engineered mutant of KirBac3.1 (S129R) in which the gate is in an open conformation. A gating model was proposed based on an intricate network of intra- and intersubunit contacts. Comparison with a closed structure has shown that the transition between the closed and open forms depends on the twist conformation of the cytoplasmic domain (CTD). Additionally, this study also highlights how the C-linker, linking the transmembrane domain 2 (TM2) and CTD could couple CTD twist movement to pore opening to stabilize the open state. In parallel, we have also identified Important mutants causing diseases such as KirBac3.1 W46R, for which we have solved the 3D structure. In order to provide crucial molecular dynamics information on how the wild type and mutant channel open/close, we have already started to analyse the normal mode motions for these channels using a new pioneering method developed in David Perahia's group: Molecular Dynamics with Excited Normal Mode (MDeNM). The simulation of the protein being performed in lipidic bilayer. We have already

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