Atomic basis for binding of a novel epilepsy drug

Epilepsy is a highly common neurological disorder, affecting about 1% of the worldwide population. The disease is often caused by mutations in genes encoding for membrane proteins called ion channels. Retigabine, is a *first-in-class* drug targeting voltage-dependent potassium channels by acting as a channel opener. In close collaboration with groups in Canada and the US we have recently established the atomic contributions of the potassium channel to the interaction with retigabine (Kim et al., 2015, Nature Communications). However, it remains unclear which moiety of retigabine is crucial for the interaction with the channel. This project aims to use a series of retigabine analogues to perform a **structure-activity relationship (SAR) study** with regards to retigabine binding to potassium channels. The project will therefore include **pharmacological** components, as well as **basic electrophysiological** aspects and is expected to provide unprecedented insight into the novel and unique mechanism by which retigabine binds to potassium channels.

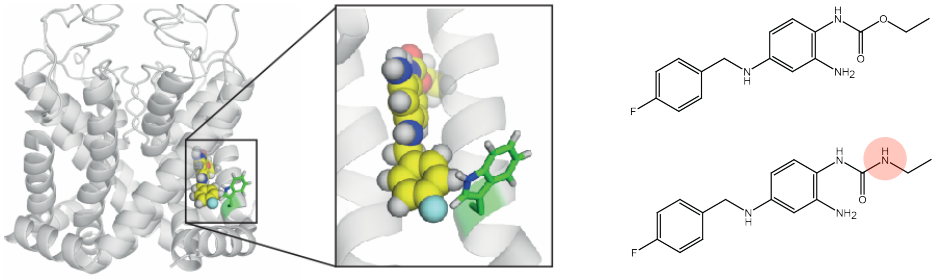

Fig 1: Left: Hypothetical model of the potassium channel bound to retigabine; Right: Retigabine (top) and one of its analogues (bottom) containing a single-atom change (highlighted in red), as an example of a analogue that will be used to determine the atomic details of the drug-channel interaction.

The project will be carried out in the newly-established Center for Biopharmaceuticals, which provides state-of-the-art facilities and a very vibrant and international environment. The project will be supervised by Assoc. Prof. Stephan A. Pless (Stephan.pless@sund.ku.dk). For more information please contact us or visit our website: www.theplesslab.com