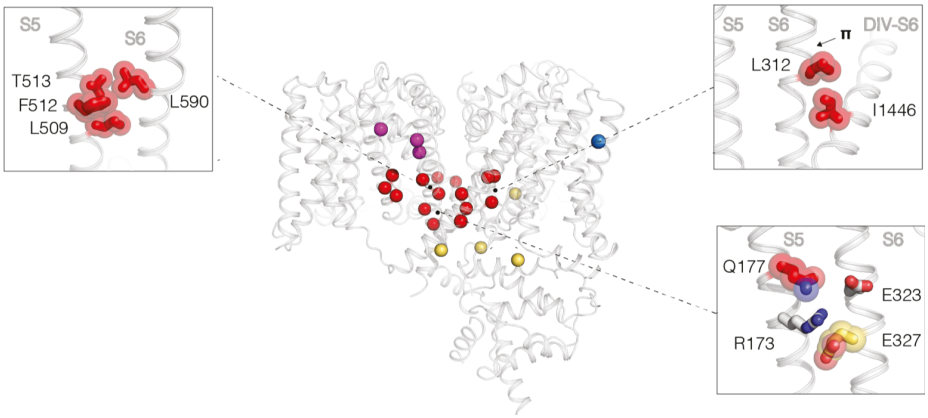
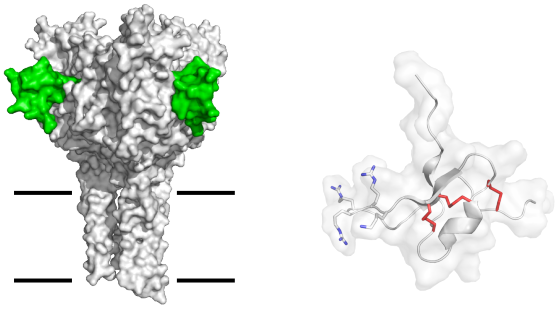


Project 1: Plugging the leak – finding a cure for the incurable

Background: Mutations in a recently discovered protein cause devastating clinical phenotypes in humans. We recently determined the function and 3D of this ion channel (Chua et al, *Science Adv*, 2020 & Kschonsak et al, *Nature*, 2020), but not a single compound is known to inhibit, activate or even modulate the protein. This complete lack of pharmacology is highly problematic, both for the patients, as well as basic research.

Project aim: To functionally characterise human patient mutations and identify the first ever inhibitor by screening peptides and small molecule compounds.

Methodology and approach: Molecular biology, electrophysiology.



Project 2: Targeting pain & stroke using animal venom and neuropeptides

Background: Together, pain and stroke create affect well over 20% of the population, yet the molecular basis for them is poorly understood. Acid-sensing ion channels (ASICs) are emerging as a major player in the initiation of pain, as well as neurotoxicity during stroke. Recent work by our group (Borg & Braun et al, *PNAS*, 2020) shows how endogenous neuropeptides can modulate ASICs with high affinity, thus serving as a potential starting point to develop novel therapeutics.

Project aim: Define the molecular basis for how neuropeptides and animal-derived venom toxins interact with ASICs in order to target pain and stroke.

Methodology and approach: Molecular biology, electrophysiology.

More information:

Web: www.theplesslab.com

Email: Prof Stephan A Pless (Stephan.pless@sund.ku.dk)