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Master/ Bachelor Thesis Project
Protein Engineering Group
Department of Molecular Biophysics and Membrane Biophysics

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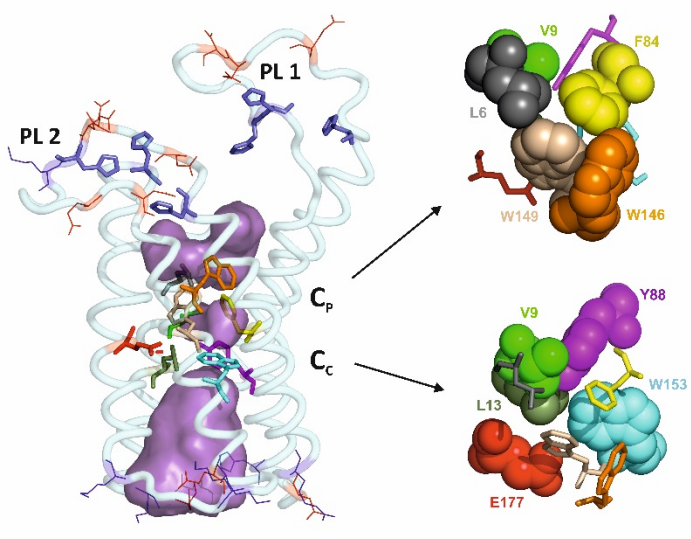
PROTEIN GATING

Investigation of *Hp*UreIs gating mechanism using Yeast Cell Assays

More than 50% of the world's population is infected with *Helicobactor pylori*, a pathogenic bacterium responsible for numerous gastroduodenal disorders such as chronic gastritis, peptic ulcer disease and gastric cancer. Standard treatment comprises the use of a proton-pump-inhibitor in combination with two antibiotics but struggles with increasing therapy failures. A different therapeutic toehold might pose *H. pylori*'s life insurance, a small proton-gated inner membrane channel, *Hp*UreI. It ensures survival in the acidic gastric juice, by means of urea transport from the periplasm to the cytoplasm, where urea is hydrolyzed by urease. The hydrolysis products, ammonia and carbon dioxide, in turn presumably buffer the cytoplasm to a neutral pH and the periplasm to pH 6.1.



HpUreI monomer; Inner surface representation of HpUreI (pdb code: 3UX4) with its two constriction sites (Cp and Cc).

Periplasmic loops PL1 and PL2 constiute HpUreIs pH sensor with their protonatable His residues (blue sticks). Loop movement causes subtle structural rearrangements causing channel closer and opening.

The periplasmic surface of HpUreI is a perfect drug target as potential substances only have to pass the porous outer membrane of H. pylori. However, even after recent cryoEM structures in the open and closed state the mechanism of channel gating is still elusive.

We plan to investigate *Hp*UreIs gating mechanism using protein mutants and chimeras with homologues UreI proteins and yeast growth assays.

We are looking for highly motivated students, with a background in biochemistry, biophysics or molecular biology to join our group.

Tasks to be performed by the student:

- *Literature Research*
- *Site-directed mutagenesis*
- *Transformation*
- *Yeast Assays*
- *Western Blot*
- *ddPCR, qPCR*
- *Data analysis & interpretation*