

Master/ Bachelor Thesis Project

Protein Engineering Group

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PROTEIN SELECTIVITY

Investigation of *HpUrel*s proton rejection mechanism using Yeast Cell Assays

Life Science Center

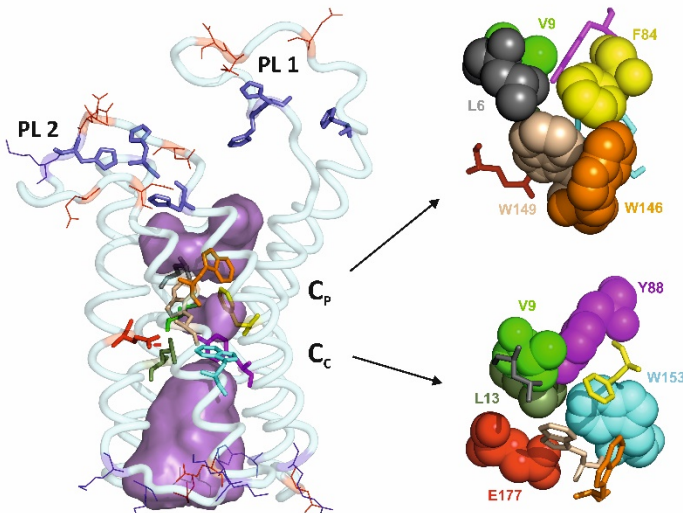
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More than 50% of the world's population is infected with *Helicobacter pylori*, a pathogenic bacterium responsible for numerous gastroduodenal disorders such as chronic gastritis, peptic ulcer disease and gastric cancer. Standard treatment comprises 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, *HpUrel*. 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.



HpUrel monomer; Inner surface representation of *HpUrel* (pdb code: 3UX4) with its two constriction sites (Cp and Cc). Periplasmic loops PL1 and PL2 constitute *HpUrel*'s pH sensor (protonatable His residues are depicted in blue sticks).

The channel manages to conduct and select urea-like molecules, water and potentially ammonia, while it is assumed to exclude protons from the gastric juice. Facilitation of proton transport would be lethal to *H.pylori* since the acidification of the cytoplasm would result in the breakdown of the proton-motive-force across the inner membrane of *HpUrel*.

We plan to investigate *HpUrel*'s proton rejection mechanism using protein mutants 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