Elucidating the structure and mechanism of proton-coupled peptide transporters

J. M. Jensen and O. Mirza

Biostuctural Research Group, Department of Medicinal Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen, Universitetsparken 2, DK-2100 Copenhagen, Denmark

Proton-dependent oligopeptide transporters (POTs) are secondary active symporters that utilize the transmembrane proton gradient to drive the uptake of di- and tripeptides. The human POT, hPepT1, located in the small intestine has shown the ability to translocate di- and tripeptide-like drugs such as -lactam antibiotics in addition to its natural substrates. Due to this potential as a drug uptake facilitator there is an immense interest in exploiting this ability further by designing drugs that can be distributed orally and subsequently be transported into the cell by hPepT1. To gain a better understanding of hPepT1, homologous prokaryotic POTs are examined as model systems. Specifically POTs from Escherichia coli are investigated in order to elucidate their structure by X-ray crystallography and their mechanism by functional studies of POT mutants.