MS8-P5 **Crystal structure of Acid-sensing ion channel 1 in complex with the gating modifier Psalmotoxin 1.**

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Venom-derived peptide toxins, that modify the gating characteristics of ion channels without directly blocking the ion permeation pathway, were important tools for understanding ion channel function. However how these toxins interact with the channels and their exact molecular mechanism is still unknown. We solved the crystal structure of the trimeric chicken Acid-sensing ion channel 1 (ASIC1) in complex with the highly selective gating modifier Psalmotoxin 1 (PcTx1) at 3.0 Å resolution. The structure shows three toxin molecules binding at the proton-sensitive acidic pockets of the ASIC1-trimer and details the molecular interactions that convey the toxins high potency and selectivity. PcTx1 binding locks two separate regulatory regions on the channel in their relative, desensitized-like arrangement. Consequently electron density is observed, that is consistent with a cation trapped above the ion pathway in the channel's central vestibule. A hydrophobic patch and a basic cluster are the key surface motifs of PcTx1 used for interacting with ASIC1. Because these motifs are also present on other gating modifier toxins, our results provide a general concept for gating modifier toxin mechanism.

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MS8-P6 **Glycosylation increases the thermostability of human aquaporin 10**

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Water transport in the human body is vital for our wellbeing. Almost 20 years has passed since the discovery of aquaporins, integral membrane proteins that facilitate passive diffusion of water across the cellular membranes. There are 13 human aquaporins known to date with different tissue specificity as well as transport preferences.

Human aquaporin 10 (hAQP10) is one of the most recently discovered aquaporins and it has been shown to be classified as an aquaglyceroporin since it transports glycerol in addition to water. Notably, no human aquaglyceroporin structure has yet been solved which makes hAQP10 a very interesting target for structural studies . When compared to all human aquaporins, this member gives rise to the highest yield when recombinantly produced in the host *Pichia pastoris*[1] which heavily assists further isolation and characterization of this interesting target. Moreover, the functional characterization made in this study further enhances the interest in this aquaglyceroporin from the human intestine.

We show that about 30% of the hAQP10 purified from *P. pastoris* is posttranslationally modified by glycosylation at one specific residue in loop C. This glycosylation does not alter the transport specificity of the protein, but makes it more stable when subjected to heat. With circular dichroism (CD) we show that the thermostability of hAQP10 is increased by 3-6°C when modified. Since only one third of the protein population is glycosylated, we suggest that the presence of one glycosylated monomer in the hAQP10 tetramer is enough to have a stabilizing effect on the functional aquaporin unit

[1] Öberg, F., Sjöhamn, J. et al, Insight into factors directing high production of eukaryotic membrane proteins; production of 13 human AQPs in *Pichia pastoris*, Mol. Membr. Biol. **26** (2009), pp. 215–227

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