# KCa3.1 channel: Computational analysis of three known toxin inhibitors towards new extracellular inhibitors

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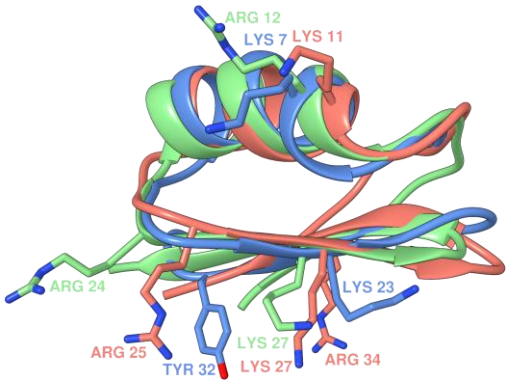


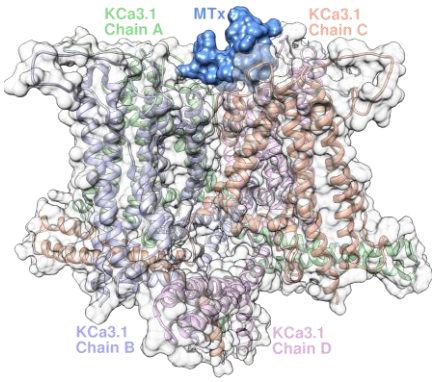


KCa3.1 is an ion channel that is important for immune regulation and the correct function of red blood cells and is associated with certain cancer types. [1]

Three toxins are known to bind to KCa3.1 from the extracellular site and they are called OSK1, Charbydotoxin (ChTx) and Maurotoxin (Mtx). [2] Based on the toxin structures and the available KCa3.1 channel (PDB ID 6cnm), a computational analysis was initiated to model the toxin binding. Initially, a sequence alignment of the three toxins was performed and revealed important conserved residues that are presumably important for binding. The structural alignment can be seen in the picture above and it is based on the available NMR structures of the toxins (PDB IDs 1sco, 2crd and 1txm). In this figure Mtx, ChTx and OSK1 are colored blue, orange and green, respectively. The important residues are shown as sticks.

Based on these results, a flexible peptide-protein docking experiment was performed for the toxins as a starting position for three Molecular Dynamics simulations. The resulting binding pose can be seen in the picture above. This led to a validated binding mode of the toxins that allowed to identify important residues for binding. In the future, a structure-based approach will be performed based on the important interactions identified to discover novel, small molecules by virtual-screening.

[1] B.M. Brown, B. Pressley, H. Wulff, *Curr Neuropharmacol*, **2018**, *16(5)*, 618–626.
[2] R. Chen, S.-H. Chung, *Toxins*, **2015**, *7*, 5194–5211.