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MEMBRANES
Cross-disciplinary AU centre and network in membrane protein research
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Joint DANDRITE & MEMBRANES Lecture

Thursday 29 January 2015 at 12.15 - 13.00
Aud. 6, building 1170, 3rd floor
Dept. Biomedicine, Aarhus University, Ole Worms Allé 3, 8000 Aarhus

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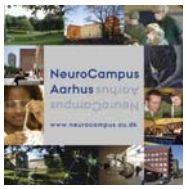
Structural basis for Ca^{2+}-activation in TMEM16 chloride channels and lipid scramblases

The TMEM16 proteins (or Anoctamins) feature a remarkable functional diversity. They contain the long sought-after Ca^{2+}-activated chloride channels but also lipid scramblases.

We have determined the crystal structure of nhTMEM16, a fungal family member that operates as a Ca^{2+}-activated lipid scramblase. Each subunit of the homodimeric protein contains ten transmembrane helices and a hydrophilic membrane-traversing cavity that is exposed to the lipid bilayer as a potential site of catalysis. This cavity harbors a conserved Ca^{2+}-binding site located within the hydrophobic core of the membrane. Mutations of residues involved in Ca^{2+} coordination affect both, lipid scrambling in nhTMEM16 and gating in the Cl^--channel TMEM16A.

The nhTMEM16 structure thus reveals the general architecture of the family and its mode of Ca^{2+}-activation. It also provides insight into potential scrambling mechanisms and serves as a framework to unravel the conduction of ions in certain TMEM16 proteins.

Host: Professor Poul Nissen, DANDRITE, Aarhus University



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