

DANDRITE Seminar

by visitor **Azadeh Shahsavar**

Thursday 12 June 2014

13.15 - 14.00

Conference room (3130-303)

Gustav Wieds Vej 10 C, 3. floor, 8000 Aarhus C



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Structural Insight into the Gating of a Pentameric Ligand-Gated Ion Channel

Pentameric ligand-gated ion channels mediate fast chemical transmission of nerve signals in the central and peripheral nervous system. X-ray structures of a bacterial proton-gated homolog, GLIC, have been established in the open (active) and locally closed (intermediate) conformations at acidic pH. We have determined its closed resting-state crystal structure at neutral pH, thereby providing the structure of the only missing end-point of the gating mechanism in the same pentameric ligand-gated ion channel. In the extracellular domain (ECD) of the resting-state structure, a marked quaternary change occurs, involving both a twist and a blooming motion, and the pore in the transmembrane domain (TMD) is closed by an upper bend of helix M2 (as in locally closed form) and a kink of helix M1, both helices no longer interacting across adjacent subunits. On the tertiary level, detachment of inner and outer β sheets in the ECD reshapes the orthosteric binding site at the ECD-ECD interface. The structural data, together with site-directed mutagenesis, physiological recordings, and coarse-grained modeling, have been integrated to propose a model of the gating transition pathway.

Host: Core group leader Poul Nissen, DANDRITE