Membrane transporters in neuroscience and drug discovery – Nissen laboratory

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DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

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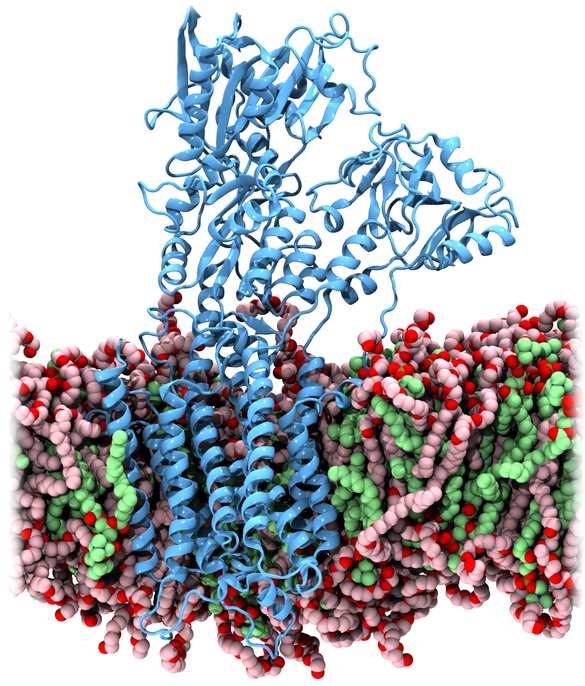
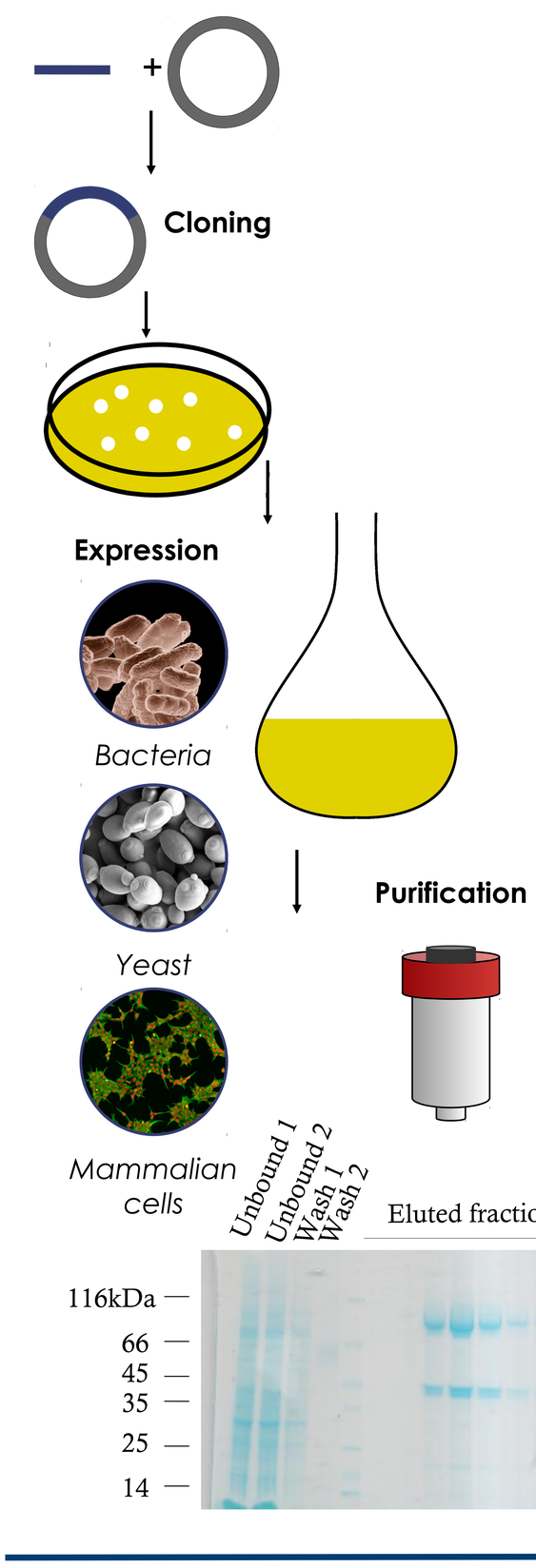
BACKGROUND/OVERVIEW The Nissen group investigates molecular mechanisms of membrane transport processes and biomembrane structure. Activities are mainly focused on cryo-electron microscopy (Cryo-EM), protein crystallography, biochemistry, electrophysiology, and include also small-angle X-ray scattering and cryo-electron tomography. Main subjects of research concern membrane transporters involved with neurological and psychiatric disorders, i.e. P-type ATPase (Na,K-ATPase, Ca-ATPases, lipid flippases) and Na^+ dependent transporters, but include also structure based drug discovery, protein engineering, and biomembrane suprastructures of neurons.

Research Areas: Membrane proteins, Membrane transport, Electron microscopy, Crystallography, Biochemistry, Drug discovery, Tomography



Workflow



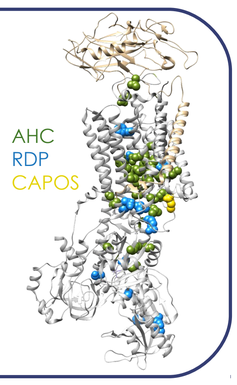
Projects

Ca2+-ATPases – Plasma membrane Ca-ATPase (PMCA) and Sarco/Endoplasmic Reticulum Ca-ATPase (SERCA)

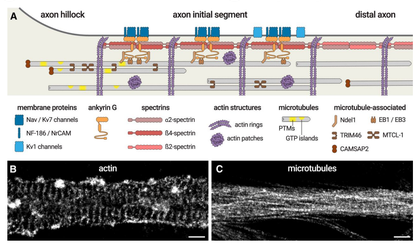
- **SERCA**
  - Neutron crystallography
  - Regulation by histidine rich protein
- **PMCA**
  - Structural and functional characterization of isoforms
  - Regulation by lipids, autoinhibition & a-synuclein

Na,K-ATPase

- Structural and functional studies of mutations causing rare neurological disorders (Alternating hemiplegia of childhood, CAPOS)
- Structural characterization of isoforms



Characterization of the axon initial segment by tomography

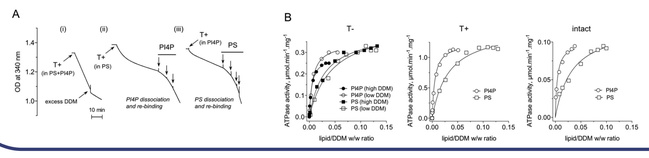


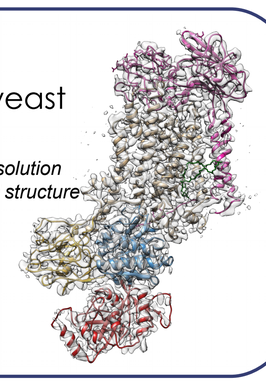
J Neurosci 2018, **38**:2135

Phospholipid flippases

- Structural and functional characterization of yeast and mammalian pumps
  - Substrate identification
  - Mechanism of autoinhibition

3.1 Å resolution cryo-EM structure





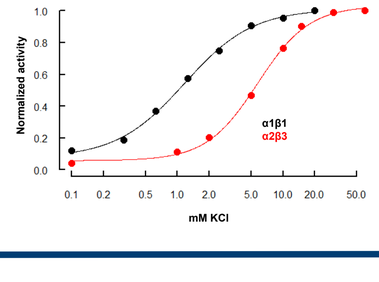
Na-symporters

- Structure determination of Na-K-Cl cotransporters and Na/neurotransmitter symporters

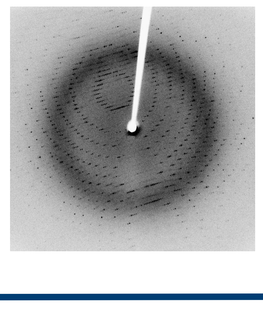
Drug discovery

- Compound screening for the potential treatment of Wilson's disease (Cu-ATPase)

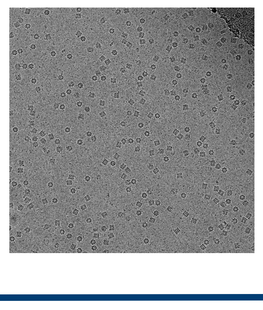
Functional characterization



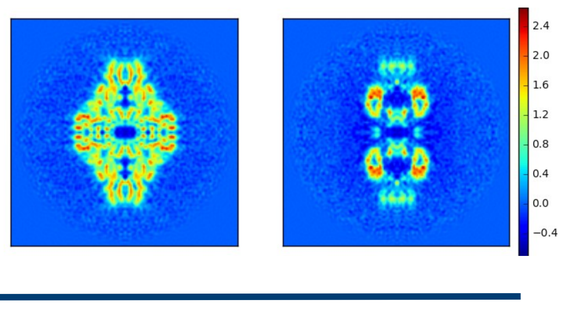
Crystallography



Electron microscopy



Data processing/modelling



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Projects
BSc projects
Course projects
MSc projects

Educational tracks
Molecular Biology
Nanoscience
Medicinical Chemistry
Molecular Medicine
Biology
Bioengineering