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Membrane transporters and receptors in Brain – Nissen laboratory

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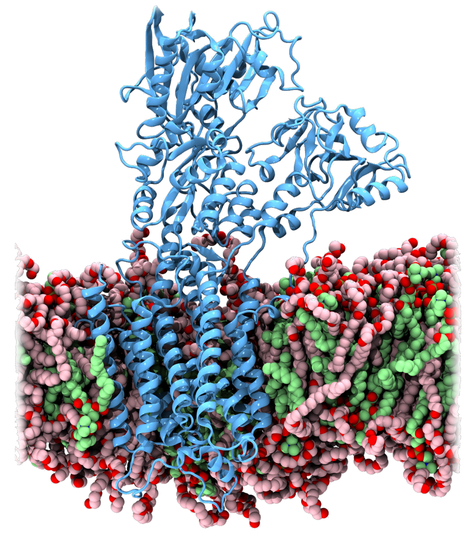
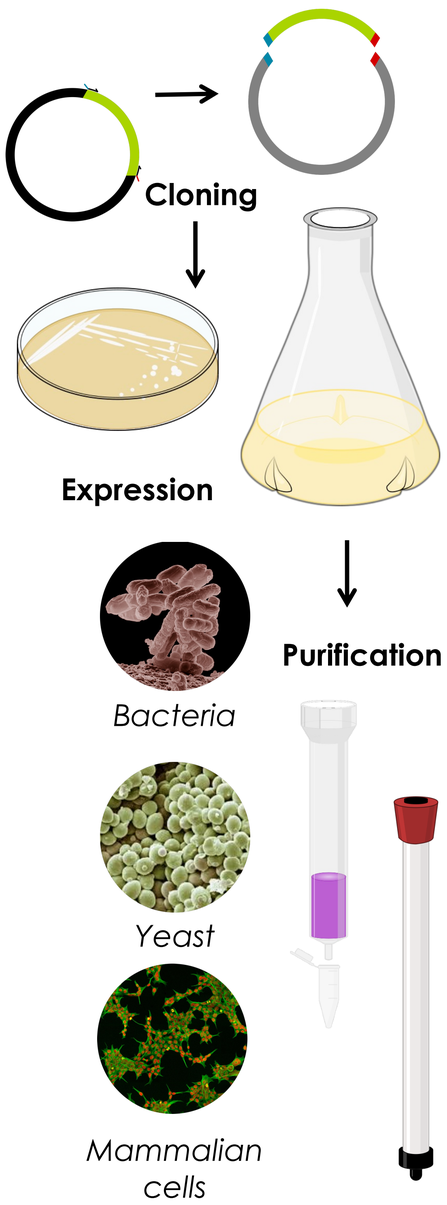
BACKGROUND/OVERVIEW The Nissen group investigates molecular mechanisms of membrane **transport processes** and **biomembrane structure** of importance in **neuroscience**.

Methods: mainly focused on **cryo-electron microscopy (Cryo-EM)**, **biochemistry and biophysics** of protein interactions and dynamics, and **molecular cell biology** using **fluorescence microscopy** and **cryo-electron tomography.** ***Key topics:*** **membrane transporters and receptors** in brain that are affected in neurological and psychiatric disorders, including **P-type ATPases**, **Na^+ dependent neurotransmitter and chloride transporters** (SLCs), **insulin and sortilin receptors**. We study structure, function and mechanisms of regulation, effects of disease causing mutations, and aim also for structure based drug discovery and protein engineering. We also engage in mathematical modelling of molecular networks in brain.

Research Areas: Structural neurobiology, Membrane transport and signalling, Cryo-EM, biochemistry-biophysics, drug discovery, network modelling.



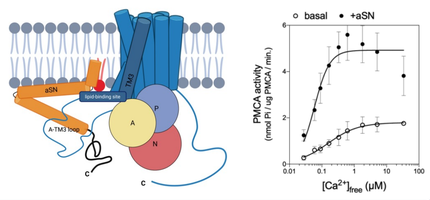
Workflow



Projects

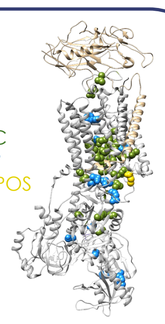
Ca^{2+}-ATPases in neurons – PMCA and SERCA types

- Characterization of isoforms.
- Regulation by lipids, autoinhibition a-synuclein.



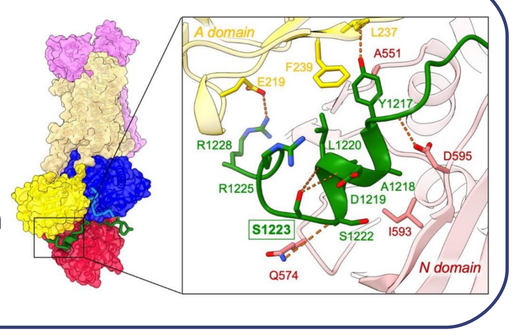
Na^+,K^+-ATPase

- Study of disease variants causing rare neurological disorders (AHC, CAPOS) associated with encephalopathies as well as cognitive and motor disabilities.
- Characterization of isoforms with a focus on specific functions and regulatory pathways.



Phospholipid flippases

- Structural and functional characterization of yeast and mammalian "lipid-pumps".
  - Substrate identification
  - Mechanism of autoinhibition by lipids and termini.
  - Physiological function.

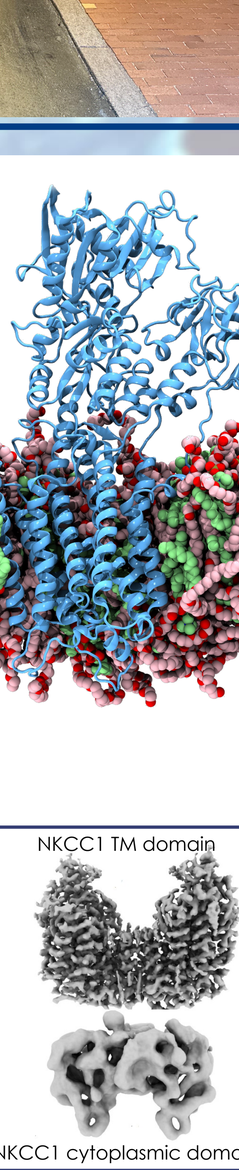


Drug discovery

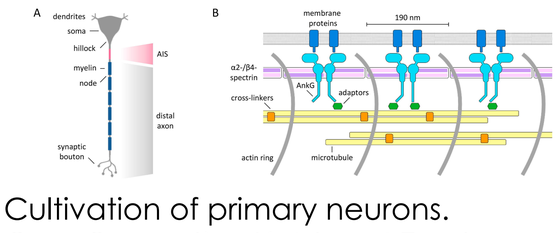
- Compound screening for the inhibition of Cu-ATPase and its disease mutants for the potential treatment of Wilson's disease. A genetic disorder characterized by accumulation of copper in the liver and brain.

Solute carriers (SLC)

- Characterization of secondary active transporters carrying ions, neurotransmitters, amino acids, polyamines and phosphate.



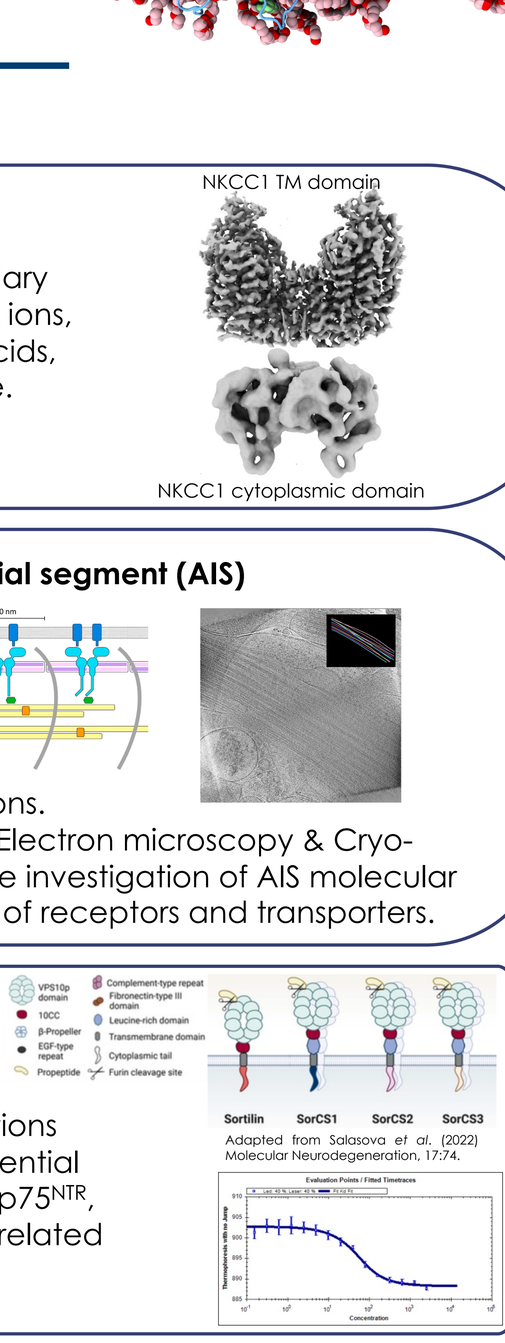
Ultrastructure of the axon initial segment (AIS)



- Cultivation of primary neurons.
- Cryo-Correlative Light and Electron microscopy & Cryo-Electron Tomography for the investigation of AIS molecular structure and identification of receptors and transporters.

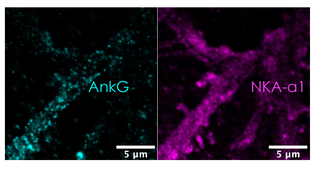
Sortilin receptors

- Structural and biophysical characterization of interactions with neuronal receptors essential for synaptic plasticity (TrkB, $p75^{NTR}$, NMDA), and other disease-related proteins (ApoE).

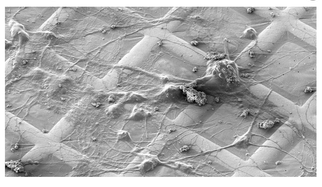


3D reconstruction

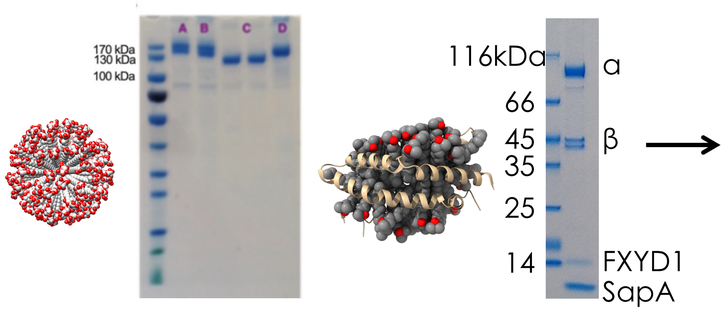
Expansion microscopy



Cryo-electron tomography



Use of membrane mimetics, nanodiscs

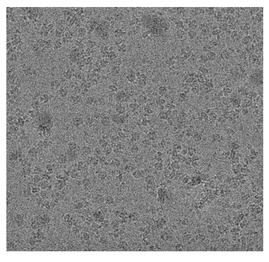


- Detergents, e.g. PMCA variants
- Nanodiscs, e.g. Na^+,K^+-ATPase

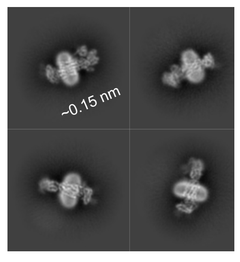
Functional characterization

- Activity assays
- Fluorescence assays
- Proteoliposome assays
- Uptake assays
- Protein interactions
- Protein dynamics/stability

Cryo-EM



Data processing



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Projects
BSc projects
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MSc projects

Educational tracks
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