

Highlights 2011 – English Version

Using the energy derived from hydrolysis of ATP, P-type ATPases transport essential substrates across cellular membranes. Consisting of a single catalytic subunit they are remarkably simple. High resolutions crystal structures have provided structural snapshots, and combining these with mutagenesis studies and computational modeling, detailed insight into the pumping mechanism have been – and still is – elaborating.

Midterm evaluation

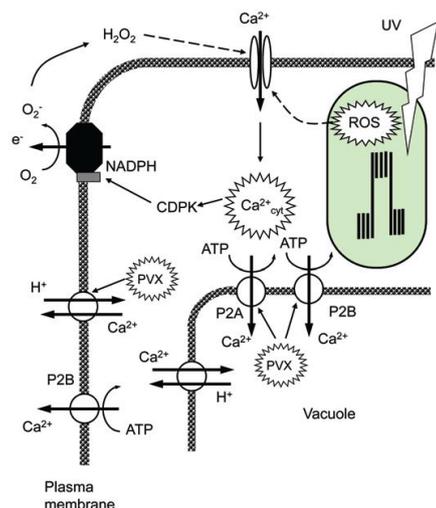
The PUMPKIN Centre is among the very best structural biology Centres in the world, and is without doubt the world leader in research on P-type ATPases. Its influence cannot be understated. A particularly strong feature of the Centre is the strong collaboration between various academic departments at Aarhus and Copenhagen.

Prof. Yvonne Jones (Oxford), Baruch Kanner (Hebrew University), and Stephen White (UC Irvine),
Part of the executive summary from the midterm evaluation

January 10, 2011, the Pumpkin Centre was evaluated with respect to a possible prolongation to a second period; Pumpkin2.0. The midterm evaluation was indeed very positive, and we are happy that our Pumpkin Centre can proceed.

Na^+, K^+ -ATPase

Mutations in brain specific Na^+, K^+ -ATPase isoforms result in two severe neurological diseases (Rapid-Onset Dystonia Parkinsonism, RDP, and Familial Hemiplegic Migraine, FHM). Animal models are used to investigate functions of wild type proteins incl. disease-mutated proteins and knockdown. Combining electrophysiology with docking and molecular dynamics studies allows another angle of studying structure-function relationships.



Role of Ca^{2+} pumps in plant stress tolerance

The role of Ca^{2+} influx channels in oxidative stress signaling and cross-tolerance in plants is well known, yet little is known about the role of active Ca^{2+} efflux systems in this process. We have found that endomembrane Ca^{2+} -ATPases play significant roles in adaptive responses to oxidative stress by removing excessive Ca^{2+} from the cytosol and their function is significantly altered in response to oxidative stress (e.g. UV-light or pathogens).

Post-translational modification of H^+ -ATPases

Phosphorylation is an important posttranslational modification of proteins in living cells and primarily serves regulatory purposes. Using an array of methods we identified 10 different phosphorylation sites in four isoforms of plasma membrane H^+ -ATPases; five of which have not been reported before. The plant protein was phosphorylated at multiple sites when expressed in yeast, and surprisingly, seven out of nine phosphosites identified in one isoform were identical in the plant and fungal systems although none of the sequences in the isoform show homology to proteins of the fungal host.

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Work packages across

To obtain the essential initial crystallization hit and the subsequent optimization remain the major bottlenecks in membrane protein structure determination. We have described an approach to achieve diffraction quality membrane proteins crystals in high concentrations of lipid and detergent (HiLiDe approach). This approach is generally applicable for native and heterologously expressed membrane proteins and is compatible with most crystallization method. It provides a user defined lipidic environment and is in itself not limited to lipids with particular properties, such as lipid-phase crystallization methods.

Comprehensive reviews

During 2011, the Pumpkin Centre across have been invited to write several larger reviews, e.g. Palmgren & Nissen. *P-type ATPases*. Annu Rev Biophys. 2011 40:243-66 as well as Morth et al. *A structural overview of the plasma membrane Na^+, K^+ -ATPase and H^+ -ATPase ion pumps*. Nat Rev Mol Cell Biol. 2011 12:60-70.

