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

AARHUS UNIVERSITY

DANDRITE Topical Seminar

Wednesday 4 January 2017
at 14.00 – 15.00

Building 1170, room 347, Aarhus University

Michael Habeck

Postdoctoral fellow, Karlish Group,
Dept. of Biomolecular Sciences,
Weizmann Institute of Science,
Rehovot, Israel.

Seminar on "Functional effects of specific lipid binding to Na,K-ATPase"

Activity and structural integrity of membrane proteins can be regulated either by physical properties of the bilayer or by site---specific interactions. For Na,K---ATPase, lipids bound to the transmembrane domain were observed in crystal structures yet effects of specific lipid binding are poorly understood.

We addressed this question by combining site directed mutagenesis, biochemical analyses and native mass spectrometry and studied the effect of lipids on stability and activity of recombinant Na,K---ATPase. Phosphatidylserine (PS) and cholesterol stabilize the Na---pump against thermal and detergent mediated inactivation but do not per se affect activity. ATPase activity is stimulated by polyunsaturated phosphatidylcholine or –ethanolamine (PC/PE), which results from the acceleration of the E1P---E2P conformational transition. Both effects occur in detergent in the absence of a bilayer.

Furthermore, they are independent of each other and can be selectively abrogated by mutation of lysine residues at the cytoplasm---membrane interface. Thus, binding sites for PS and PC/PE were identified. These findings support the idea of functional specific phospholipid---Na,K---ATPase interactions. We show specific lipid binding by native MS, which revealed that one molecule each of PS and PC can bind specifically to the Na--- pump. Functional properties of detergent soluble Na,K---ATPase with PS, cholesterol and PC are remarkably similar to properties of renal enzyme highlighting the importance ofspecific interactions over bulk bilayer interactions.

Host: Group Leader Poul Nissen, DANDRITE, Dept. of Molecular Biology and Genetics, Aarhus University