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P8 Membrane Channels, Pumps and Transporters

P8.1

A potassium "transporter" regulated by the ATP/ADP ratio

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The KtrAB potassium "transporter" plays an important role in adaptation to osmotic shock in bacteria. This membrane protein complex is composed by two polypeptides: KtrB is the membrane protein involved in potassium and sodium permeation and KtrA is the cytosolic protein involved in regulation of transporter activity. KtrA binds ATP and/or ADP. We have determined the structure of the KtrAB complex in the ATP bound state and have been performing biochemical and structural studies to unravel the mechanism of regulation of this complex by the ATP/ADP ratio.

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P8.2

Functional and structural dynamics of NhaA, a prototype for Na^+ and H^+ antiporters, which are responsible for Na^+ and H^+ homeostasis in cells

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The crystal structure of the down regulated NhaA crystallized at acidic pH 4 [1] has provided the first structural and functional insights into the antiport mechanism and pH regulation of an Na^+/H^+ antiporter (reviewed in [2]). NhaA is organized into two functional regions: (i) a cluster of amino acids responsible for pH regulation, and (ii) a catalytic region at the middle of the TM IV/XI assembly, containing unique antiparallel unfolded regions that cross each other, forming a delicate electrostatic balance in the middle of the membrane. This unique structure contributes to the cation-binding site and facilitates the rapid conformational changes expected for NhaA. Although extended chains interrupting helices have since emerged as a common feature for ion-binding in transporters, the NhaA fold, shared by ASBTNM [3] and NapA [4] is unique among the three structural folds that comprise the secondary transporters e.g., MFS, LeuT and NhaA [5]. Computational and electrophysiological methods (reviewed in [2]) have been used to develop intriguing models for the mechanism of NhaA. However, the dynamics of the conformational changes and how energy is transduced in this "nano-machine" are still unknown. Ultimately, interdisciplinary integrative results will shed light on the mechanism of activity and pH regulation of NhaA, a prototype of the CPA2 family of transporters.

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P8.3

Mitochondrial machinery for import and assembly of proteins

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Mitochondria contain more than 1000 different proteins, most of which are synthesized as precursor proteins on cytosolic ribosomes. Mitochondrial outer and inner membranes possess translocases that import the precursor proteins. The translocase of the outer mitochondrial membrane (TOM) initially recognizes and transports the large majority of precursor proteins across the outer membrane. Subsequently, at least four different pathways sort the precursor proteins to their intramitochondrial destinations [1]. Presequence-carrying preproteins are translocated by the presequence translocase of the inner membrane (TIM23) and the associated import motor PAM [2]. Metabolite carriers are transferred through the intermembrane space by the small TIM chaperones and are inserted into the inner membrane by the carrier translocase (TIM22) [3]. The mitochondrial intermembrane space import and assembly machinery (MIA) mediates the import of cysteine-rich proteins in a redox-regulated manner [4]. Beta-barrel proteins use small TIM chaperones and the sorting and assembly machinery (SAM) of the outer membrane. Additionally, some alpha-helical outer membrane proteins bypass the TOM channel and are inserted into the outer membrane by the MIM machinery. The mitochondrial contact site and cristae organizing system (MICOS), located at crista junctions between inner boundary membrane and cristae, plays a dual role. MICOS is required for maintaining the characteristic inner membrane morphology and interacts with TOM and SAM of the outer membrane, thus promoting protein biogenesis.

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P9 General Bioenergetics

P9.1

Toward the biogenesis of manmade oxidoreductases working in cells

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