MS8. Molecular machines and motors

Chairs: Nenad Ban, Leonid Sazanov

MS8-P1 Structural characterization of the STAS domain of prestin

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Prestin is the anion-dependent motor protein responsible for the outer hair cells (OHCs) electromotility, at the basis of the increased sensitivity and frequency selectivity of the hearing process in mammals. Electromotility is the ability to convert changes in the membrane potential into variations in the OHCs cell length, with an amplification of the auditory stimulus. Prestin, member of the SulP/SLC26 family of anion transporters, is an ATP- and Ca^{2+}-independent molecular motor with piezoelectric properties. Prestin function relies on the presence of different monovalent anions. Physiologically the most relevant is chloride that has been proposed to be the extrinsic voltage sensor. While in non-mammals prestin has been shown to be an electrogenic anion transporter, in mammals prestin is considered an incomplete transporter. Topologically, prestin is divided into a large transmembrane domain, a short cytosolic N-term tail and a long cytosolic C-term portion mainly composed by a so-called STAS (Sulphate Transporters and Anti-Sigma factor antagonist) domain, essential for function. The 3D structure of the STAS domain from rat prestin consists of a central β-sheet, composed of 6 β-strands, surrounded by 5 α-helices, a fold conserved from bacteria to mammals (Pasqualetto et al, 2010). Recently, the experimentally validated 3D model of the mammalian TM domain of prestin identified the central anion-binding site in the middle of the domain, along as a possible pathway leading anions from the cytosol (Gorbunov et al, 2014). However, the cytosolic recruitment site for anions has not been identified yet. Here we present crystallographic data revealing the presence of an anion-binding site in the STAS domain of an incomplete-transporter prestin that is absent in a non-mammalian homologue with exchangers properties. This anion-binding site is important for the fine regulation of the electromotile properties of this molecular motor.

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