

Title	How a molecular motor works: deciphering the molecular bases of the hearing process in mammals.
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Project description:

Prestin is a protein transporter that belongs to the SLC26 family of anion exchangers, found in the cochlear OHCs (outer hair cells), where it is densely packed in the basolateral membrane. OHCs in mammals have the ability to alter their cell length actively and quickly in response to changes in membrane potential triggered by incoming sound waves. This form of voltage-dependent cell movement, known as “electromotility”, is provided by prestin. OHC electromotility is part of the mechanical sound amplification system responsible for increased hearing sensitivity and frequency selectivity in mammals. Hence prestin is a unique ATP- and Ca²⁺-independent molecular motor with piezoelectric characteristic. We plan to combine structural and functional characterization of mammalian and non-mammalian prestin to provide a solid framework to comprehend electromotility and anion transport at atomic level, and how these events are regulated. To understand how this transporter function dynamically we will apply a modern “integrative structural biology” approach, merging methods that span different resolution scales and time frames, such as Xray crystallography, Bio-SAXS, NMR and SPR. Experimental results will be integrated and finalized by innovative computational approaches.

Publications:

- 1) Lolli G, Pasqualetto E, Costanzi E, Bonetto G, Battistutta R. (2016) The STAS domain of mammalian SLC26A5 prestin harbours an anion-binding site. *Biochem J.* 473, 365-370.
- 2) Gorbunov D, Sturlese, M, Nies, F, Kluge M, Bellanda M, Battistutta, R, Oliver, D. (2014) Molecular architecture and the structural basis for anion interaction in prestin and SLC26 transporters. *Nat Comm*, 5, 3622.
- 3) Lolli G, Ranchio A, Battistutta R. (2014) Active Form of the Protein Kinase CK2 $\alpha 2\beta 2$ Holoenzyme Is a Strong Complex with Symmetric Architecture. *ACS Chem Biol.* 9:366-371
- 4) Lolli G, Pinna LA, Battistutta R (2012) Structural Determinants of Protein Kinase CK2 Regulation by Autoinhibitory Polymerization. *ACS Chem Biol*, 7, 1158-1163.
- 5) Pasqualetto E, Aiello R, Gesiot L, Bonetto G, Bellanda M, Battistutta R. (2010) Structure of the cytosolic portion of the motor protein prestin and functional role of the STAS domain in SLC26/Sulp anion transporters. *J Mol Biol.* 16, 448-462.
- 6) Battistutta, R. (2009) Structural bases of protein kinase CK2 inhibition (Review). *Cell. Mol. Life Sci.* 66, 1868-1889.

Collaborations/Network:

Prof. Dominik Oliver, Department of Neurophysiology of the Philipps University in Marburg (D)
 Prof. Gianluca Lattanzi, Physics Department of the University of Trento (I).
 Dr. Graziano Lolli, Centre for Integrative Biology (CIBIO), University of Trento (I).