Analysis of the Ion Channel Gating Mechanism in Solution by Nuclear Magnetic Resonance (NMR) Spectroscopy

Claudia Börger[1,2], Sven Schünke[1, 2], Matthias Stoldt[1,2], Dieter Willbold[1, 2]

[1]*Institute of Physical Biology, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany;* [2]*Institute of Complex Systems, Structural Biochemistry (ICS-6), Research Center Jülich, Jülich, Germany.*

Ion channels activated by cyclic nucleotides play crucial roles in signal transduction pathways. Upon binding of cyclic nucleotides to the intracellular cyclic nucleotide-binding domain (CNBD) of HCN or CNG channels (hyperpolarization-activated and cyclic nucleotide-gated channels or cyclic nucleotide-gated channels) an opening of the membrane pore occurs.

To analyze the underlying gating mechanism highly resolved structures of the cyclic nucleotide-binding domains are necessary. Until now, structures of CNBDs from eukaryotic HCN channels as well as prokaryotic CNG channels are known. However, CNBD crystal structures of the HCN channels reveal no significant differences between apo and holo state[1,2]. In contrast, CNBD structures of the prokaryotic *Mesorhizobium loti* K1 channel, solved by liquid state NMR spectroscopy, show substantial rearrangements upon binding of a cyclic nucleotide[3,4].

Further elucidation of the gating mechanism will be done by structural analysis of an eukaryotic CNBD using liquid state NMR spectroscopy.

REFERENCES:
1. Zagotta W.N., *et al.*, *Nature*, 425, 200-205 (**2003**)
2. Taraska J.W., *et al.*, *Nat. Methods*, 6, 532-537 (**2009**)
3. Schünke S., *et al.*, *EMBO Rep.*, 10, 729-735 (**2009**)
4. Schünke S., *et al.*, *Proc. Natl. Acad. Sci. U S A*, 108, 6121-6126 (**2011**)

Receptor ion channel

Key words: signaling, ion channel, cyclic AMP
Presenting author: C. Börger
Corresponding author: D. Willbold d.willbold@uni-duesseldorf.de