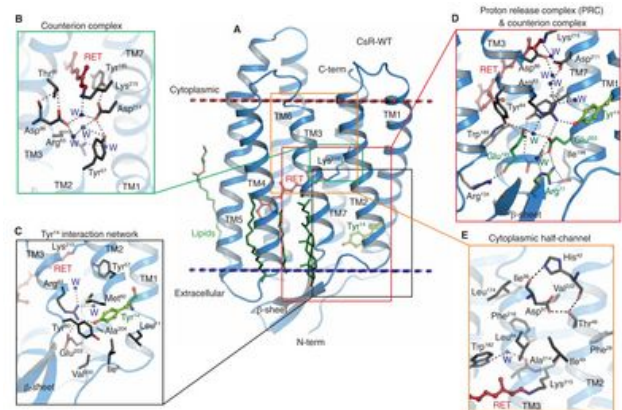


Light-gated ion channels made by structure-based design

Start Time: Wednesday, March 20, 2019

End Time:



A collaborative study of two UniSysCat groups of the principal investigators Patrick Scheerer (Charité-Universitätsmedizin Berlin) and Peter Hegemann (Humboldt-Universität zu Berlin) showed the structure-based design and electrophysiological characterization of a light-gated passive proton channel by genetic engineering of *Coccomyxa subellipsoidea* rhodopsin which is originally a light driven proton pump. The authors suggest a strategy how to develop ion specific transmembrane channels.

“Our study unravels molecular details that differentiate light-driven ion pumps from light-gated ion channels. [...] We conclude that the structural restraints differentiating light-driven pumps from light-gated channels are less notable than anticipated”, wrote the first authors Roman Fudim and Michael Szczepek from the groups of Peter Hegemann (Humboldt-Universität zu Berlin) and Patrick Scheerer (Charité-Universitätsmedizin Berlin), respectively. In this collaborative study the authors designed and characterized a light-gated passive proton channel by structure-based genetic engineering of *Coccomyxa subellipsoidea* rhodopsin (CsR) which is originally a light driven proton pump. They employed electrophysiological and spectroscopic approaches. The authors showed that a specific hydrogen bond between Arg⁸³ and Tyr¹⁴ contributes to the proton transport and the mobility of Arg⁸³ forms a dynamic barrier to prevent passive conductance.

Their solved crystal structure of wild-type CsR at 2.0-Å resolution enabled the authors to identify distinct features that determine ion transport directivity and voltage sensitivity. The authors concluded that substitution of Tyr¹⁴ with a glutamate would increase the attractive force between these two residues, resulting in a different configuration of Arg⁸³. As the Arg⁸³-Glu¹⁴ interaction, necessary for passive conductance which requires deprotonation of

Glu¹⁴, modulates during the photocycle, the passive conductance overlaps with late photocycle steps mainly and is therefore switchable by light. In such way a structure-based approach is presented how to design ion-specific channels from microbial pumps as novel optogenetic tools. Furthermore it was shown that structural changes which are much smaller than generally expected, discriminate pump and channel properties correlated with active and passive ion transport, respectively.

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[Design of a light-gated proton channel based on the crystal structure of Coccomyxa rhodopsin. Science Signaling. 12. 573 \(2019\). DOI: 10.1126/scisignal.aav4203](#)

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