Optogenetic tool elucidated: Researchers explain channelrhodopsin

February 28 2012

Controlling nerve cells with the aid of light: this is made possible by optogenetics. It enables, for example, the investigation of neurobiological processes with unprecedented spatial and temporal precision. The key tool of optogenetics is the light-activated protein channelrhodopsin. Biophysicists from Bochum and Berlin have now succeeded in explaining the switching mechanism through an interdisciplinary approach. The researchers report on their findings in the *Journal of Biological Chemistry*.

Until now, little has been known about the mechanism of the protein - especially about how the channel opens. However, deeper understanding is a prerequisite in order to be able to use the light-controlled protein specifically for neurobiological applications. In a new, multi-disciplinary approach, the Bochum scientists led by Prof. Dr. Klaus Gerwert (Department of Biophysics at the RUB) and their cooperation partners in Berlin have been able to shed light on the switching mechanism. The result: the light-induced change in the charge state of amino acid glutamate 90 (E90) triggers an increased penetration of water molecules, so that the protein can now purposefully conduct ions through the cell membrane.

Using time-resolved infrared spectroscopy, the RUB biophysicists Jens Kuhne and Dr. Erik Freier have been able to show for the first time that the channel is opened through the deprotonation of the amino acid glutamate 90 (E90). In addition, the electrophysiological experiments of the researchers in Berlin confirm that a mutation of the amino acid leads

to a change in the ion permeability of the protein. Instead of using safety goggles and lab coats, the two biophysicists Kirstin Eisenhauer and Dr. Steffen Wolf at the Department of Biophysics used supercomputers to simulate how the protonation change of the glutamate opens the channel and allows water molecules to penetrate.

The work has attained particular distinction right now, because shortly after the Bochum pre-publication on the Internet, Japanese researchers published the three-dimensional structure of a channelrhodopsin online in "Nature". "The structure work impressively confirms our biomolecular simulations and the key role played by the amino acid E90 in the switching of the channel", says Prof. Klaus Gerwert. "We are therefore particularly proud to have been preeminent in this internationally competitive field." In 2010, optogenetics was distinguished by "Nature Methods" as the "Method of the Year". Using this method, researchers have succeeded, for example, in restoring the eyesight of blind mice.

More information: K. Eisenhauer, J. Kuhne, E. Ritter, A. Berndt, S. Wolf, E. Freier, F. Bartl, P. Hegemann, K. Gerwert,: In channelrhodopsin-2 E90 is crucial for ion selectivity and is deprotonated during the photocycle, *Journal of Biological Chemistry*, Vol. 287, Issue 9, 6904-6911, 2012, DOI: 10.1074/jbc.M111.327700

Provided by Ruhr-University Bochum