Technology Offer

New versions of channelrhodpsin 2, ReaChR and VChR1 with improved kinetics and light-sensitivity

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Background

The development of the cation channel channelrhodopsin-2 (ChR2) from *Chlamydomonas reinhardtii* by Prof. Ernst Bamberg and his colleagues and its application to light-induced modulation of neurons paved the way for the field of optogenetics.

Over time the light-gated cation channel channelrhodopsin-2 (ChR2) has become an indispensable tool in neuroscience. Based on the pioneering work on ChR2 new variants have emerged, differing in their spectrum of light absorption, their kinetic properties and the type of electrochemical response. Nowadays light-sensitive opsins are applied to control neural activity not only in the context of research but also in clinical approaches (including neural networks e.g. of the eye, ear, heart, brain).

Technology

ChR2 can be employed for light-induced depolarization, however, there is an ongoing investigation on ChR2 mutants with faster kinetics and increased light-sensitivity for potential clinical applications.

Scientists from the Max-Planck-Institute of Biophysics in Frankfurt constructed faster ChR2 mutants based on the modification at position F219 in helix 6 of the seven transmembrane helix motif. This mutation in wildtype ChR2 accelerates the closing time (off-kinetics) of the channel. Interestingly, in CatCh the modification in helix 6 display a 20-fold increase of Ca^{2+} permeability. The newly discovered effect was verified in ChR2, VChR1 and in the chimera ReaChR. Of note, the considered positions are homologous among different ChRs in helix 6.

The use of these new variants will provide a light stimulation of neurons up to 800 to 1000 Hz. Further, the modification leads to an increase in Ca^{2+} permeability as a tool to influence the Ca^{2+} concentration in the cytosol.

In general, this finding contributes to the development of high-throughput screening platforms and can be applied for stimulating neurons.

Patent Information

A priority application was filed in June 2016 (WO2017207745). Nationalization in EP, CN, US, KR and JP.

Literature

Mager, T., Lopez de la Morena, D., Senn, V. *et al*. High frequency neural spiking and auditory signaling by ultrafast red-shifted optogenetics. *Nat Commun* **9**, 1750 (2018). https://doi.org/10.1038/s41467-018-04146-3

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