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Technology Offer

Application of novel channelrhodopsins: molecular engineering, site-specific opsin targeting, discovery of new variants and the advancement in optogenetic devise development

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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

Scientists from the Max-Planck-Institute of Biophysics in Frankfurt developed a mutant of ChR2, L132C that upon high-frequency blue light stimulation display excellent spike reliability and accelerated repolarisation in a Ca^{2+} dependent manner. This mutant, termed CatCh i.e. Calcium transporting Channelrhodopsin, shows a four-fold Ca^{2+} permeability compared to wildtype ChR2 and a 70-fold light sensitivity of fast spiking hippocampal neurons. The superior properties of CatCh result from the enhanced Ca^{2+} permeability. Increased $[Ca^{2+}]i$ elevate the internal surface potential, promoting voltage-gated Na+ channels activation and as a consequence increase light sensitivity. Repolarization following light-stimulation is significantly accelerated by Ca^{2+}-dependent big potassium channel activation. Therefore, CatCh induces an increased light sensitivity in neurons with much accelerated response kinetics as a result of increased Ca^{2+} permeability and subsequent consequences on neuronal excitation. Due to its minimal light requirements CatCh spikes can be generated far from its spectral maximum of 474 nm e.g. with green light facilitating tissue penetration. The CatCh expression level is excellent in many different cell types and has already been applied in mice and macaque in the context of vision restoration.

CatCh exemplifies a new principle by which blue light-gated channels can be engineered to increase the light sensitivity of neuronal stimulation. The crucial characteristics of triggering precise and fast action potentials while requiring low light intensities for activation pave the way for gene-therapeutic visual restoration effort and other biological applications such as Ca^{2+} dependencies in cell organelles.

Patent Information

The priority application was filed September 2010 (EP11760432). The patent has been granted in EP, US, AU, CA, CN, IL, JP, MX, RU, SG and KR.

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Literature

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