



Technology Offer

## Xenorhodopsin - a new inward-directed proton pump for an alternative optogenetic approach

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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 report inward directed proton pumps of xenorhodopsins from Nanohaloarchaea family of microbial rhodopsins. The structure of a xenorhodopsin from the nanohalosarchaeon *Nanosalina* (NsXeR) revealed the ion translocation pathway to be different to currently known rhodopsins. NsXeR is a powerful pump with a high turnover rate that is able to elicit action potential up to the maximum intrinsic firing frequency. Light-induced depolarizing current by NsXeR was sufficient for the activation of neuronal rat hippocampal cells with high temporal accuracy. Important to note, NsXeR is entirely independent of ion conditions giving rise to an alternative for light-induced control of neurons as well to cation-selective channelrhodopsins.

Altogether these newly discovered inward directed proton pumps are a valuable new optogenetic tool, which is cation independent, pH insensitive and with highly specific activation capacity that can be expressed in a broad spectrum of cells. Xenorhodopsin can be used for the modification of cell organelles as well as for specific biomedical applications where precise subtle effects are needed.

### Patent Information

Priority application was filed in March 2017 (WO2018189247). Nationalization in US, EP, JP, CA, and CN.

### Literature

Shevchenko, Vitaly, et al. "Inward H<sup>+</sup> pump xenorhodopsin: Mechanism and alternative optogenetic approach." *Science advances* 3.9 (2017): e1603187.

Nagel, G., Szellas, T., Huhn, W., Kateriya, S., Adeishvili, N., Berthold, P., Ollig, D., Hegemann, P., & Bamberg, E.: Channelrhodopsin-2, a directly light-gated cation-selective membrane channel. *Proceedings of the National Academy of Sciences of the United States of America*, 100(24), 13940-13945. (2003). <https://doi.org/10.1073/pnas.1936192100>.

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