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New opsin variants for stable and potent optogenetic control

Researchers in Prof. Karl Deisseroth's laboratory have developed a portfolio of microbial opsin proteins that can be used for precise and modular photosensitization components that enable optical control of specific cellular processes. This technology describes new variants of hyperpolarizing opsins that are engineered for improved membrane trafficking. These new features improve the expression level of active protein to enable more potent inhibition. These novel opsin genes can be used to control neural activity for therapeutic and screening applications.

Stage of Research
The inventors have engineered the variants eMac2.0, eMac3.0, eArch2.0, eArch3.0 with endoplasmic reticulum (ER) export sequences and/or trafficking sequences that direct proteins to the cell membrane. They have demonstrated opsin activity in vitro.

Continued Research
The inventors are continuing studies to test function in vivo.

Applications

- **Optogenetics** - control of neural activity for therapeutic and screening
- **Therapeutic** - optically activated prosthetics for neural inhibition as a potential alternative to tissue ablation or surgery
- **Drug screening** - for agents that affect hyperpolarization-activated channels

Advantages

- **Improved activity** - with better ER trafficking and neurite trafficking there are reduced accumulations and blebbing which in turn leads to better overall performance compared to wild type opsins

Publications

- Zhang F, Vierock J, Yizhar O, Fenno LE, Tsunoda S, Kianianmomeni A, Prigge M, Berndt A, Cushman J, Polle J, Magnuson J, Hegemann P, Deisseroth K. The Microbial Opsin Family of Optogenetic Tools. Cell. 2011 Dec 23;147(7):1446-57.
- Mattis J, Tye KM, Ferenczi EA, Ramakrishnan C, O'Shea DJ, Prakash R, Gunaydin LA, Hyun M, Fenno LE, Gradinaru V, Yizhar O, Deisseroth K. Principles for applying optogenetic tools derived from direct comparative analysis of microbial opsins. Nature Methods. 2011 Dec 18.
- patent application PCT/US2012/069133: Opsin polypeptides and methods of use thereof

Patents

- Published Application: WO2013090356
- Published Application: 20150072394
- Published Application: 20160222073
- Published Application: 20170066806
- Published Application: 20180044388
- Published Application: 20180244737
- Published Application: 20190071476

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