Docket #: S09-300

New Microbial Opsin for Optogenetic Control of Neurons

Researchers in Prof. Karl Deisseroth's lab have discovered and engineered new microbial opsin proteins and cell trafficking tools to enable selective cell-type specific, light-sensitive switches for neuromodulation. These developments expand the existing repertoire of optogenetic proteins that have been developed in the Deisseroth lab since 2005.

The first novel opsin, GtR3, was identified from the cryptophytes Guillardia theta and can inhibit neural activity in response to blue light. When used in combination with NpHR (a yellow light sensing protein), the two opsins can be used to independently modulate two separate populations of cells. The second opsin, DChR1, was identified from Dunaliella salina and is capable of exciting neural activity in response to blue light.

The inventors expanded the versatility of the optogenetic proteins by utilizing motifs for subcellular and transcellular trafficking. With this approach, they have extended optical regulation across the entire visible spectrum, including the far-red/infrared border. In addition, they have increased the potency of optical inhibition are able to target cells with unknown promoters. Together, this generation of light-sensing opsins and trafficking tools can be used regulate the activity of targeted neurons in vivo with exquisite precision and efficiency for either research or therapeutic applications.

Related Technologies
Previous microbial opsin genes discovered in the Deisseroth lab include those described in “Temporally Precise, Genetically Targeted Control of Neural Circuitry” (Stanford Docket S05-170) and “New Light Control Mechanism (NpHR) That Inhibits Neural Activity” (Stanford Docket S06-398,).

Applications

- **Optical control of neural activity** for therapeutic and research purposes

Advantages

- **Tools for full range of visible spectrum**, including:
  - bi-directional (on/off) switching of neurons with either blue or yellow light, depending on opsin used
  - control at far-red/infrared border by using subcellular trafficking
- **Efficient** - increased potency of optical inhibition without increased light power requirement
- **Versatile targeting**, based on:
  - genetic identity
  - morphology and tissue topology

Publications

- Gradinaru V, Zhang, F, Ramakrishnan C, Mattis J, Prakash R, Deister I, Goshen I, Thompson K, Deisseroth K." Molecular and Cellular Approaches for Diversifying and Extending Optogenetics." *Cell* 2010 Epub 2010 March 18.

Patents

- Published Application: WO2011116238
- Published Application: 20160287895
- Published Application: 20170198017
- Issued: 9,079,940 (USA)
- Issued: 9,359,449 (USA)
- Issued: 9,249,234 (USA)
- Issued: 9,604,073 (USA)

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