Docket #: S08-348

Bistable Neural State Switches

Researchers in the laboratories of Dr. Karl Deisseroth and Dr. Peter Hegemann have engineered mutant ChR2 (Channelrhodopsin-2) proteins with light-sensitivity that is increased by orders of magnitude compared to wild-type ChR2. These proteins can be used for temporally precise, noninvasive control of neural circuitry with prolonged activation using minimal light delivery. Practically, one pulse of light every 15 seconds can induce a similar effect to that of several hundred pulses delivered with conventional ChR2. In clinical applications of optogenetics technology, this feature improves safety because light delivery at high levels may cause heating and damage to tissue. In addition, engineered ChR2 would decrease the power draw necessary for prosthetic devices designed to activate neural circuitry.

Related Technologies
ChR2 (see Stanford Docket S05-170) enables the optical control of the electrical and ionic milieu of neurons and other excitable cells, which might facilitate the modulation of ion channels, signal transduction, neural coding, sensory and motor processing, neuropsychiatric dysfunction and interneuron modulation of circuit dynamics.

The inventors have also developed a technology to optically inhibit neurons (see Stanford Dockets S06-398 and S06-398A). When combined, these inventions form a complete system for multimodal, high-speed, genetically targeted, all optical interrogation of living neural circuits.

Continued Research
The inventors are pursuing studies to further characterize light-sensitive mutants in vivo. They are also engineering other opsin proteins to achieve similarly enhanced inhibitory proteins. The invention will be combined with mutations that alter the ion selectivity of the channel and the absorption maximum of the chromophore.

Applications

- Therapeutic - optically activated prosthetics for neuromodulation
- Screening - high-throughput cell-based screening for drugs that affect signal transduction
- Drug dosing management in the context of diabetes and pain control

Advantages

- Enhanced activity by sensitizing cells to their natural synaptic inputs
- Highly light sensitive:
  - improves safety because decreased light requirements are less likely to damage tissue
  - decreases power draw because fewer light pulses are needed
- Advantages of optotgenetics technology compared to cell stimulation via chemically modified ion channels:
  - millisecond kinetics
  - the expression of the ChR2 channel does not affect membrane integrity and cell health
  - this method does not require synthetic chemical substrates
  - allows genetic targeting so that specific neuron subclasses can be probed

Publications

- Berndt A, Yizhar O, Gunaydin LA, Hegemann P, Deisseroth K. "Bi-stable neural state switches." *Nat Neurosci.* 2008 Dec 8.
- PCT Application: PCT/US2009/064355

Patents

- Published Application: WO2010056970
- Published Application: 20110311489
- Published Application: 20130296406
- Published Application: 20140235826
- Published Application: 20170056467
- Published Application: 20170080050
- Published Application: 20190038705

- Issued: 8,716,447 (USA)
- Issued: 9,309,296 (USA)
- Issued: 9,458,208 (USA)
- Issued: 10,071,132 (USA)
- Issued: 10,064,912 (USA)

Innovators

- Karl Deisseroth
- Ofer Yizhar
- Lisa Gunaydin
- Peter Hegemann
- Andre Berndt

Licensing Contact

Evan Elder

Senior Licensing Associate

Email