Docket #: S15-285

bReaCh-ES: An optogenetic tool for stimulating neurons with red light

Researchers in Dr. Karl Deisseroth's lab have engineered a channelrhodopsin variant that can be stimulated by red light and has fast stimulation frequencies. In neurons, channelrhodopsins are light activated protein channels that induce action potential firing. Action potentials are the fundamental signal used by neurons to process sensory inputs and induce behavioral responses. As such channelrhodopsins have become a powerful tool to manipulate neuronal activity by light. The inventors have created a channelrhodopsin variant knows as bReaCh-ES. It can be stimulated by red light (wavelengths beyond 600nm) and reliably evokes action potentials at frequencies of up to 20 Hz. The bReaCh-ES tool can be used to interrogate functional connections between neurons of different brain areas or within local neuronal microcircuits.

Stage of research
The inventors have used bReaCh-ES in behavioral experiments in combination with GCaMP (a fluorescent sensor that allows for optical readouts of neuronal activity) for *in vitro* and *in vivo* imaging.

Applications

- Research- map functional connections between brain regions:
    - Map neuronal connections in specific behavioral contexts
    - Investigations into peripheral and central nervous system disorders
- Therapeutic development:
    - Screening new pharmaceutical agents
- Potential for use directly as a therapeutic for neuronal disorders

Advantages

- Allows stimulation with red light (wavelengths between 600nm and 650nm), which:
  - Allows manipulation of larger brain volumes as red light provides higher penetration depth than blue light in biological tissues
  - Is less damaging to genomic DNA- results in lower cell toxicity
  - Allows imaging in combination with GCaMP
- Allows activation of specific connections
- 13 times faster channel closure than its predecessor
- Allows for action potential generation in neurons at frequencies up to 20 Hz
- Can stimulate neurons over a wide range of naturally occurring action potential frequencies
- Can be combined with various promoters and fluorescent proteins to target specific neuronal cell populations in mammalian brains

Publications

- U.S. Published Patent Application 20180250402, "LIGHT-RESPONSIVE POLYPEPTIDES AND METHODS OF USE THEREOF".
- Rajasethupathy P, Sankaran S, Marshel JH, Kim CK, Ferenczi E, Lee SY, Berndt A, Ramakrishnan C, Jaffe A, Lo M, Liston C, Deisseroth K. Projections from neocortex mediate top-down control of memory retrieval. Nature. 2015 Oct 5. doi: 10.1038/nature15389.

Patents

- Published Application: WO2017048808
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