Docket #: S14-125

Structure-guided transformation of channelrhodopsin into a light-activated chloride channel

Researchers in Dr. Karl Deisseroth's lab have created inhibitory channelrhodopsins (ChRs) that allow fast, reversible inhibition of electrical signals in neurons. Optogenetics is a technique used to understand normal and pathological neural circuitry. It uses light to control and monitor the activities of neurons in living tissues, including freely moving animals. A major goal of optogenetics has been to use light to silence electrical activity in targeted neurons. Direct light-triggered inhibition of neuronal activity is possible; however the existing tools are inefficient in neural systems. To overcome this limitation, the inventors have designed a family of ChRs that reversibly and specifically block neural communication in response to light. These inhibitory ChRs provide critical tools for the interrogation and control of neuronal circuits and single neurons.

Stage of Research
The inventors have designed a family of inhibitory ChRs and shown that upon optical activation the inhibitory ChRs can inhibit action potentials without depolarizing neurons.

Applications

- Neuroscience research:
    - Investigate neuronal networks in a variety of behavioral contexts
    - Create and investigate disease models
- Drug development:
    - Screen to test impact of new drugs on nervous system function
- Therapeutic development:
    - Potential neuronal modulation tool to treat a variety diseases

Advantages

- Fast optical inhibition of action potentials
- May be engineered to display step-function kinetics for stable inhibition outlasting light pulses
- Order-of-magnitude greater light sensitivity
- More physiological, efficient and sensitive optogenetic inhibition

Publications

- PCT Patent Application WO/2015/148974 , "ENGINEERED LIGHT-ACTIVATED ANION CHANNEL PROTEINS AND METHODS OF USE THEREOF".

Patents

- Published Application: WO2015148974
- Published Application: 20170095556
- Published Application: 20180344851
- Published Application: 20200030446
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