Novel Channelrhodopsins for Inhibition of Neuronal Activity

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Optogenetics is rapidly evolving field that provides the ability to control neurons using light-sensitive proteins called channelrhodopsins (ChRs). When genetically expressed in neurons, ChRs have the ability to selectively manipulate neuronal activity in a light-dependent manner. Gene-therapy using ChRs has the exciting potential to be used to treat patients suffering from disorders caused by aberrant neuronal signaling. Dr. John L. Spudich and his research team have disrupted the field of optogenetics through their discovery and development of first of their kind anion channelrhodopsins (ACRs). These ACRs are orders of magnitude more efficient than any other optogenetic tools currently available and have the unprecedented ability to effectively inhibit neuron firing. Development of the ACRs into gene therapy based therapeutics, may potentially open new avenues for treating excessive neuron firing in conditions such as Parkinson's disease, neuropathic pain and epilepsy.

Technology Overview

Dr. John L. Spudich and his research team have discovered a novel family of light-gated anion channel proteins derived from algae, anion channelrhodopsins (ACRs). When genetically expressed in neurons the functional rhodopsin domains of these ACRs induce membrane hyperpolarization, and as a result induce neuronal silencing, in a light-dependent manner.

Stage of Development

The investigators have humanized several ACRs and have successfully expressed the modified proteins in mammalian cells. In addition to discovering new ACRs, the investigators are probing the molecular mechanism of action of identified ACR proteins.

Potential Applications

The rhodopsin domain of these ACRs have the potential to be used as gene therapy based therapeutics for diseases caused by overactive neurons, such as:

- Parkinson's disease
- neuropathic pain
- cardiac disorders
- epilepsy
- ocular disorders

Technology Advantages

The ACRs overcome the inefficiencies of previously available optogenetic tools by providing:

- neuronal inhibition orders of magnitude greater than previously characterized optogenetic silencing proteins (i.e. archaerhodopsin-3 and CholC mutant); and
- extremely high light-sensitivity, absolute anion selectivity (i.e. chloride ions) and rapid kinetics.

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Intellectual Property Status:

- ACR patent applications are pending.
- ACR portfolio is available for licensing.
- Non-ACR patents and patent applications for optogenetic tools are also available for licensing.

Associated Publications

- Science. 2015 Aug 7;349(6248):647-50. PMID:26113638
- Proc. Natl. Acad. Sci. USA. 2015 Nov 17; 112(46):14236-41. PMID:26578767
- Photochem Photobiol. 2015 Dec. PMID: 26686819

About the Investigator

Dr. John L. Spudich is a Professor and Robert A. Welch Distinguished Chair in Chemistry at the University of Texas Health Science Center at Houston, where his research is primarily focused on the mechanisms by which photosensory receptors sense and transmit information concerning the environment.