System and methods for optogenetic stimulation and inhibition of pain

Title: System and methods for optogenetic stimulation and inhibition of pain

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Abstract: These gene delivery methods lead to nociceptor-specific expression of targeted genes. Nociceptor expression of the opsin proteins used in optogenetics allows for modulation of nociceptor excitability, either activation or inhibition, using non-invasive delivery of light through the skin.

Applications:

*In pharmacological screening, to serve as a pain model with which to test various experimental pain therapeutics.

*In medicine, to treat various pain conditions through inhibition of nociceptors.

Advantages:

*Neural effects are nociceptor specific and do not affect the functioning of other sensory neurons or motor neurons.

*Ongoing modulation is non-invasive with transdermal light delivery.

*Use as pharmacological screening tool can be implemented easily with mouse model.

*Delivery of targeted genes requires a simple surgical procedure without the need to access, and risk damaging, the central nervous system directly.

*Expandable to include other genes of interest to be expressed specifically in nociceptors.

Applications

- 1. Use by companies currently attempting to translate optogenetics to clinical use (Eos Neuroscience, Circuit Therapeutics, Medtronic etc.) to achieve control over the complex experience of pain perception. The methods described in this disclosure will likely underlie any successful use of optogenetics to treat chronic pain, and provide a valuable proof-of-concept of the capabilities provided by such a technique. The method here applies through control of primary nociceptors at the dorsal root ganglion level, but could also be applied to control of pain through control of elements of the spinal cord nociceptive circuit.
- 2. Use as a method to reliably and temporally reversibly induce localized pain through activation of a broad spectrum of unmyelinated nociceptors, without requiring a) tissue damage b) global pain c) application of chemicals with many potential effects. This could potentially aid in rapid screening of drugs and help in the development of novel pharmaceuticals that act to inhibit nociceptor activity.

Advantages

 Prior methods to induce pain are typically based on tissue damage, broad spectrum chemicals/drugs or electrical stimulation that is non-specific. Our approach is readily temporally reversible, acts solely on action potential transmission without inflammatory or tissue damage confounds, and acts specifically on a broad spectrum of nociceptors that are likely activated in chronic pain, doing so without the need for any implants.

Patents

- Published Application: <u>WO2015023782</u>
- Published Application: 20160199663
- Published Application: 20200121942
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