Accepted Manuscript

Review

Changing channels in pain and epilepsy: Exploiting ion channel gene therapy for disorders of neuronal hyperexcitability

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PII: S0014-5793(15)00357-9
DOI: http://dx.doi.org/10.1016/j.febslet.2015.05.004
Reference: FEBS 37160

To appear in: *FEBS Letters*

Received Date: 30 March 2015
Revised Date: 29 April 2015
Accepted Date: 2 May 2015

Please cite this article as: Snowball, A., Schorge, S., Changing channels in pain and epilepsy: Exploiting ion channel gene therapy for disorders of neuronal hyperexcitability, *FEBS Letters* (2015), doi: http://dx.doi.org/10.1016/j.febslet.2015.05.004

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Title

Changing channels in pain and epilepsy: Exploiting ion channel gene therapy for disorders of neuronal hyperexcitability

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Key Words

Gene therapy; ion channels; hyperexcitability; epilepsy; chronic pain; chemogenetics; optogenetics.

Highlights

- Chronic pain and epilepsy affect hundreds of millions worldwide, yet many patients remain resistant to traditional pharmacotherapy.
- Both disorders are characterised by neuronal hyperexcitability, and gene therapy has emerged as a promising tool to counteract this via the manipulation of ion channel expression.
- Optogenetics, chemogenetics, and the up- or down-regulation of endogenous channels have all been shown to suppress excitability in a therapeutically efficacious manner.
- We review the key experimental successes of each approach and discuss the challenges facing their clinical translation.

Abstract

Chronic pain and epilepsy together affect hundreds of millions of people worldwide. While traditional pharmacotherapy provides essential relief to the majority of patients, a large proportion remains resistant, and surgical intervention is only possible for a select few. As both disorders are characterised by neuronal hyperexcitability, manipulating the expression of the most direct modulators of excitability – ion channels – represents an attractive common treatment strategy. A number of viral gene therapy approaches have been explored to achieve this. These range from the up- or down-regulation of channels that control excitability endogenously, to the delivery of exogenous channels that permit manipulation of excitability via optical or chemical means. In this review we highlight the key experimental successes of each approach and discuss the challenges facing their clinical translation.

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