TECHNOLOGY

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A Novel Therapeutic Technology for the Treatment of Pain

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Background

Researchers at the University of Calgary have developed a novel therapeutic approach for the treatment of pain. The strategy targets the interaction of a previously unknown member of the pain signaling pathway with the Cav3.2 T-type calcium channel, whose role in pain is well known. The technology effectively reduces Cav3.2 activity and has been shown to decrease both inflammatory and neuropathic pain in rodent models.

Cav3.2 T-type calcium channels are transmembrane proteins that are highly expressed on afferent pain fibers. Absolute Cav3.2 channel activity is directly related to pain intensity and increased channel activity is found in a variety of pathological conditions including nerve injury, diabetic neuropathy, and inflammatory pain. To date, the clinical success of inhibitors targeting T-type channels has been limited. This is due in part to the lack of pharmaceutical specificity for individual T-type channel subtypes, an issue the current technology addresses. In addition, the unique therapeutic approach to antagonize Cav3.2 activity without completely blocking channel function should provide selectivity for pain conditions while preserving normal Cav3.2 function.

Areas of Application

- A novel therapeutic for the treatment of neuropathic and inflammatory pain.

Competitive Advantages

- Novel composition of matter and mechanism of action to treat neuropathic, inflammatory, and potentially other chronic pain conditions by reducing Cav3.2 signaling activity.
- Specific modulation of Cav3.2 activity may decrease off-target effects and toxicity associated with non-specific calcium channel inhibitors.

Stage of Development

- Extensive pre-clinical *in vitro* and *in vivo* experiments have validated the target and mechanism of action to reduce Cav3.2 signaling and pain phenotypes.
- Development of small molecule inhibitors targeting the novel mechanism is currently underway.

Intellectual Property Status

- US and EU national phase filings

Publications

Gadotti, V. M., Caballero, A. G., Berger, N. D., Gladding, C. M., Chen, L., Pfeifer, T. A., & Zamponi, G. W. (2015). Small organic molecule disruptors of Cav3.2 - USP5 interactions reverse inflammatory and neuropathic pain. *Molecular Pain*, *11*(1), 12. doi:10.1186/s12990-015-0011-8

Garcia-Caballero, A., Gadotti, V. M., Stemkowski, P., Weiss, N., Souza, I. A., Hodgkinson, V., … Zamponi, G. W. (2014). The deubiquitinating enzyme USP5 modulates neuropathic and inflammatory pain by enhancing Cav3.2 channel activity. *Neuron*, *83*(5), 1144–1158. doi:10.1016/j.neuron.2014.07.036