Decreased Expression of Sodium Channel Isoform Nav1.7 in Mouse Dorsal Root Ganglion Neurons after Infection with a Recombinant Herpes Virus.

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Introduction: Excitable tissues throughout the body employ voltage-gated sodium channels (NaCh) to generate and propagate action potentials. Even though their role appears to be similar in all excitable tissues, at least 9 different NaCh alpha subunit gene products are known to exist. One of several possible explanations for having multiple isoforms performing the same basic function is that different NaCh isoforms may be required for the conduction of different sensory modalities. Our investigation of NaCh isoforms and sensory modalities focused on Nav1.7, a tetrodotoxin-sensitive NaCh suggested to be important in nociception and hyperalgesia by previous studies (Koszowski and Levinson, in preparation; Gould et al, 2000).

Methods: To elucidate further the role of Nav1.7 in sensory modalities in the peripheral nervous system, a unique approach to decreasing dorsal root ganglion (DRG) neuron protein expression was developed. A recombinant non-replicative herpes virus vector was created that encoded anti-sense Nav1.7 mRNA. This virus was then used to infect mouse DRG nociceptors. Changes in Nav1.7 protein expression level in cryo-sectioned DRG neurons were determined with quanitative confocal immunohistochemistry.
Results: Quantitative immunohistochemistry demonstrated a significant decrease in Nav1.7 protein expression in small and medium diameter DRG neurons infected with the anti-sense encoding herpes virus construct.

Discussion: This is the first demonstration of specific and targeted modulation of sodium channel isoform expression in vivo. On-going and future work will concentrate on the electrophysiological and behavioral effects of decreased Nav1.7 protein in normal and in hyperalgesic states. Ultimately, this novel technique for changing protein expression could become an important diagnostic and therapeutic tool for the treatment of neuropathic pain.

References:

Gould, H.J. III, Gould, T.N., England, J.D., Paul, D., Liu, Z.P., and Levinson, S.R. (2000) A possible role for nerve growth factor in the augmentation of sodium channels in models of chronic pain. Brain Research 854:19-29.

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