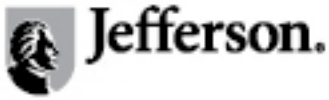

Phase 1

Class of 2022

1-2020

Phosphorylation of a K channel by PKC regulates the excitability of primary sensory neurons and pain signaling

Tyler D. Alexander
Thomas Jefferson University, tyler.alexander@jefferson.edu

Lianteng Zhi, PhD
Thomas Jefferson University, lianteng.zhi@jefferson.edu

Tanziyah Muqeem
Thomas Jefferson University, tanziyah.muqeem@jefferson.edu

Manuel Covarrubias, MD, PhD
Thomas Jefferson University, Manuel.Covarrubias@jefferson.edu

SI/CTR Abstract

Word count: 250 words

Phosphorylation of a K channel by PKC regulates the excitability of primary sensory neurons and pain signaling

Tyler D. Alexander, Lianteng Zhi, PhD, Tanziyah Muqeem, Manuel Covarrubias, MD, PhD*

(*) indicates primary project advisor

Introduction: Voltage-gated potassium channels (Kvs) play an important role in the termination of neuronal action potentials. Kv3.4 is one of many types of Kv channels, found throughout the human body – including in the axon terminals of dorsal root ganglia neurons. Kv3.4 channels are categorized as A-type currents and have prominent fast-inactivation that has been shown to be phosphorylation dependent. It is hypothesized that following spinal cord injury (SCI), Kv3.4 channels become hyperphosphorylated and their expression reduced – leading to an increase in nociceptive signaling.

Methods: We used embryonic DRG neurons, transfected with one of four types of viral AAV6 constructs, to induce expression of Kv3.4 channels. Constructs included EGFP, WT Kv3.4, Kv3.4 A (phosphonull), Kv3.4 D (phosphomimetic), and Kv3.4 dominant negative (DN).

Results: Kv3.4 constructs were differentially trafficked across embryonic DRG neurons, following AAV1 transfection, as seen through immunofluorescence. Peak currents were increased for WT, A, and D mutants, relative to GFP and DN. The sustained current for phosphomimetic was significantly higher than for GFP and phosphonull ($p=0.031$).

G/G_{max} for all traces showed similar activation kinetics. $V_{1/2}$ was relatively unchanged across constructs. The slow inactivating current was measured at t=50 sec and AP duration for the phosphomimetic Kv3.4 channels was shortened compared with GFP ($p=0.018$). The rate of repolarization was increased in phosphomimetic constructs, compared with GFP ($p=0.044$).

Discussion: Phosphorylation of Kv3.4 appears to modulate channel properties and may also play a role in SCI-induced neuropathic pain. Future *in* vivo experiments can assess pain behavior in animals expressing different Kv3.4 constructs.

No citations, tables, figures or appendices allowed.