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

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## SI/CTR Abstract

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

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**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.**