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Research Summary

My research focuses on understanding the mechanisms by which peripheral nervous system (PNS) neurons regenerate to identify potential targets for future therapeutic interventions in the setting of central nervous system (CNS) injury and under conditions of traumatic PNS injuries. We have initially focused on the issue of retrograde injury signaling, or how information about an injury is conveyed from the distantly located lesion site in the axon back to the cell body. We have discovered aspects of this mechanism that include the retrograde transport of organelles bearing the adaptor protein Sunday Driver (syd, also known as JIP3) on their surface and the role of the JNK signaling pathway in injury signaling and axon regeneration. We also demonstrated that following peripheral nerve injury activation of the evolutionarily conserved mammalian Target Of Rapamycin (mTOR) is sufficient to sustain regenerative growth of peripheral nerves. In pursuing our studies on the response of axons to injury, we turned our attention to the microtubule tracks on which vesicles and organelles are transported along axons. These studies led us to discover that injury to peripheral, but not central neurons induces microtubule post-translational modifications, with a decrease in tubulin acetylation. Indeed, we demonstrated that the histone deacetylase HDAC5 is a novel injury-regulated tubulin deacetylase controlling growth cone dynamics and axon regeneration. This work suggests that injury-induced tubulin deacetylation may govern the repair of damaged axon tips and their transformation into growth cones. Recently, we discovered that axon injury induces HDAC5 nuclear export and elicits an epigenetic switch regulating regenerative competence in adult sensory neurons. These findings suggest a role for HDAC5 as a transcriptional switch controlling axon regeneration.

REFERENCES
