Gene Transfer to Improve Functional Recovery after Plexus Injury

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Injuries to the plexus that result in root avulsion are difficult to treat because even when physical continuity can be reestablished, motor regeneration is poor when the injury is very close to the cell body, and regeneration of sensory axons is inhibited at entry to the spinal cord (dorsal root entry zone, DREZ) by inhibitory molecules expressed on central myelin. These inhibitory molecules exert their effects by activating RhoA in the injured axon; a downstream mediator that can be inhibited by C3 transferase (C3t). We have developed a series of gene transfer vectors based on a non-replicating herpes simplex virus (HSV) recombinant to transfer genes to neurons in vivo. Subcutaneous injection of an HSV-based vector expressing C3t to transduce DRG neurons after proximal root injury supports extension of regenerating fibers through the DREZ and rostrally into the dorsal column. Completed phase 1 and 2a clinical trials of a related HSV-based vector for the treatment of pain support the safety and feasibility of this approach; one that may be applicable to patients with avulsion injury affecting roots of the brachial plexus.

REFERENCES