Chondroitin sulfate

Chondroitin sulfate is a sulfated glycosaminoglycan (GAG) composed of a chain of alternating sugars (N-acetylgalactosamine and glucuronic acid). It is usually found attached to proteins as part of a proteoglycan. A chondroitin chain can have over 100 individual sugars, each of which can be sulfated in variable positions and quantities. Chondroitin sulfate is an important structural component of cartilage and provides much of its resistance to compression.

Along with glucosamine, chondroitin sulfate has become a widely used dietary supplement for treatment of osteoarthritis.

After spinal cord injury (SCI), the disruptive interactions of chondroitin sulfate proteoglycans (CSPGs) produced by reactive astrocytes create glial scars that are major barriers to neural circuit reconnection and functional recovery. Recent work reveals a novel strategy to inhibit an inhibitor of neural regeneration.

Lang et al overcame CSPG-mediated inhibition of Axon regeneration by blocking proteoglycan interactions with PTPRS (receptor-type tyrosine-protein phosphatase sigma) (PTPσ). In vitro studies showed that PTPσ was upregulated in growth cones in a CSPG-rich gradient. Furthermore, although PTPσ is normally distributed throughout neurons when CSPGs were absent, PTPσ levels were increased in the growth cones when CSPGs were present. This marked rise in growth cone PTPσ levels coincided with growth cone overadherence to proteoglycans; the PTPσ-CSPG interaction caused beaded growth cone structure and prevented further axonal growth. These revelations further illuminate the ability of PTPσ to inhibit regeneration of nerve fiber because upregulated PTPσ interacted with the CSPGs to stabilize dystrophic growth cones [1].

This study raises many questions: How is neuroplasticity involved? Why is ISP-mediated PTPσ inhibition correlated with 5-HT fiber regeneration? Is this a backup regenerative pathway in the post-SCI environment? How can ISP work beyond contusive injury models? Answering these and other relevant questions is key for potential translation of this novel ISP strategy beyond animal models to human clinical trials [2].

1)
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2)
Sharma T, Pereira Alves GC, Kuo JS. “Inhibiting the Inhibitors” to Support Axon regeneration. Neurosurgery. 2016 Feb;78(2):N14-6. doi: 10.1227/01.neu.0000479891.17866.c7. PubMed PMID: 26779793.