Attenuation of Robust Glial Scar Formation after CNC Injury Can Facilitate Functional Recovery

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Disclosures

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Surgical Management of Compressive Neuropathies

• Surgical decompression is often not completely effective in later-stage patients

• How can we optimize functional recovery in this patient population?
CNC Injury as Chronic Wound Healing

Inflammation  Proliferation  Angiogenesis  Remodeling

SCI and Scar Formation

- Glial scar forms by astrocytes/fibroblasts
  - CSPGs (chondroitin sulfate)
  - HSPGs (heparan sulfate)
  - Keratan sulfate proteoglycans
- Schwann cell-rich ECM domains
  - Collagen IV
  - Laminin
  - Fibronectin

SCI and Glial Scar Formation

Reactive astrogliosis by CSPGs has consequences

– Impedes axonal regeneration
– Altered revascularization
– Impaired OPG process outgrowth, differentiation, myelination
– Transduction of extracellular signalling

CSPGs in Peripheral Nerve

Peripheral nerves upregulate CSPGs after crush and transection injuries

Hypotheses

1. CNC injury upregulates ECM proteins and proteoglycans

2. Chondroitinase delivery may attenuate scar formation and improve functional outcomes by improving remyelination and blood flow
Differential CSPG mRNA Expression Profiles after CNC Injury
Aggrecan Upregulation in Early and Late CNC Injury

4 months (EARLY)
40.9-fold upregulation

6 months (LATE)
17.8-fold upregulation

GAPDH

260 kDa
Aggrecan Upregulation in Early and Late CNC Injury
Collagen IV, laminin, and fibronectin are upregulated in epineurium at later timepoints
Vessel

Epineurium

Endoneurium

Perineurium

Axon

Myelin
Scar attenuates after administration of chondroitinase ABC

Figure 2. (A-B) Immunohistochemistry demonstrating no change in decorin levels in compressed nerves at 2 weeks, with (C-D) marked upregulation at 6 weeks and (E-F) attenuated decorin scar after administration of chondroitinase.
Functional improvement occurs after chondroitinase ABC administration.
Conclusions

• CNC injury in peripheral nerve induces scar formation comprised of ECM proteins and proteoglycans

• Chondroitinase attenuates proteoglycan scar formation in the peripheral nerve, and improves functional outcomes
Thank you

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