

# Proteoglycans and injury of the central nervous system.

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## Abstract

Proteoglycan is a family of glycoproteins which carry covalently-linked glycosaminoglycan chains, such as chondroitin sulfate and heparan sulfate. Proteoglycans are believed to play important roles in morphogenesis and maintenance of various tissues including the central nervous system (CNS) through interactions with cell adhesion molecules and growth factors. In the CNS, a significant amount of evidence has been accumulated to show that proteoglycans function as modulators in various cellular events not only in the development, but also in the pathogenesis of neuronal diseases and lesions. When the CNS is injured, several chondroitin sulfate proteoglycans (CSPG) are up-regulated in glial scars formed around the lesion site. The glial scar also contains some molecules inhibitory to axonal growth, such as myelin-associated glycoprotein, Nogo, and Semaphorin. In vitro studies revealed that CSPG largely exert a repulsive effect on axonal regeneration, and a signal from CSPG modulates the actin cytoskeleton of outgrowing neurites through the Rho/ROCK pathway. These findings suggest that CSPG are responsible for unsuccessful axonal regeneration in glial scars. Various attempts to overcome the inhibitory effect of CSPG have been pursued in vivo. Digestion of chondroitin sulfate chains by chondroitinase ABC, suppression of CSPG core protein synthesis by decorin, suppression of glycosaminoglycan chain synthesis by a DNA enzyme, and inhibition of the Rho/ROCK pathway with specific inhibitors were all successful for increasing axonal regeneration. For a clinical application, the most effective combination of these treatments needs to be examined in the future.

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