＜シンポジウム 05―1＞中枢神経の免疫疾患とグリア

Promoting Remyelination by Reducing an Inhibitory Microenvironment

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Remyelination occurs in Multiple Sclerosis although its extent is limited in many patients. Approaches to induce remyelination include increasing trophic support or by overcoming impediments present in the microenvironment. We have examined the expression of extracellular matrix molecules around demyelinating lesions in the dorsal column of the mouse spinal cord. Demyelination was produced by the local deposition of a toxin, lysolecithin. We found that chondroitin sulfate proteoglycans (CSPGs) accumulated early following demyelination while laminins accumulated during the period of remyelination. Microglia/macrophages and reactive astrocytes were sources of CSPGs and laminins, respectively. Significantly, CSPG expression was down-regulated during remyelination, emphasizing that demyelination was correspondent with accumulation of CSPGs while remyelination was concurrent with removal of CSPGs and accumulation of laminins. In vitro, CSPG were a poor substrate for oligodendrocyte adhesion and maturation while laminin facilitated these processes. To further elucidate the relevance of CSPGs in vivo, we utilized xyloside to reduce the production of CSPGs that occur following demyelination. Xyloside treatment reduced the content of CSPGs, increased the number of oligodendrocyte precursor cells, and resulted in enhanced remyelination. These results highlight the extracellular matrix proteins around demyelinating lesions in the regulation of remyelination. In particular, we document the inhibitory roles of CSPGs, the removal of which facilitated repair.

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