1-S13-3 Symposium13

Pathological role of astrocytes in neurodegeneration of multiple sclerosis

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Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). MS is characterized by extensive immune cell infiltration leading to inflammation, demyelination, and neurodegeneration. Recently, accumulating evidence has suggested that glial cells may contribute to the development of MS pathology. However, the molecular mechanism underlying the regulation of neuronal degeneration in MS remains largely unknown. N-myc downstream-regulated gene 2 (NDRG2) is a differentiation- and stress-associated molecule, and predominantly expressed in astrocytes in the CNS. In this study, we examined the relevance of NDRG2 in experimental autoimmune encephalomyelitis (EAE), a mouse model of MS. The expression of NDRG2 was enhanced in the acute and chronic phase after induction of EAE. Genetic deletion of NDRG2 ameliorated the clinical course and demyelination after EAE induction. Although the loss of NDRG2 slightly affected the inflammatory response, it significantly reduced neurodegeneration both in the acute and chronic phase. Further analysis revealed that deletion of NDRG2 restored the EAE-related decreases in the expression of astrocytic glutamate transporters. Thus, our findings suggest that NDRG2, expressed in astrocytes, may play a key role in the pathology of MS by modulating neuronal vulnerability to glutamate toxicity.