

Neutrophil accumulation in the DRG contributes to the mechanical allodynia during the preclinical phase of EAE through a TLR4/CXCL1 pathway in the DRG

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(多発性硬化症モデル動物で生じるDRGへの好中球の集積および機械的アロディニアはDRGニューロンにおけるTLR4-CXCL1経路によって生じる)

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論 文 内 容 の 要 旨

Multiple sclerosis (MS) is a potentially disabling disease of the central nervous system. Approximately half of the patients with MS experience severe pain; however, currently available therapeutics provide only insufficient relief. The mechanisms underlying the generation of neuropathic pain in patients with MS are not fully understood. Recently, we found that neutrophil elastase from accumulated neutrophils in the dorsal root ganglion (DRG) sensitizes DRG neurons and induces mechanical allodynia in a mouse model of experimental autoimmune encephalomyelitis (EAE). However, the mechanism underlying neutrophil accumulation in the DRG after myelin oligodendrocyte glycoprotein (MOG₃₅₋₅₅, immunogenic peptide) immunization remains unclear. Here, we found that C-X-C motif ligand 1 (CXCL1) was upregulated in DRG neurons after MOG₃₅₋₅₅ immunization. Increased expression of CXCL1 protein was also observed in primary cultured DRG neurons treated with MOG₃₅₋₅₅, which was mediated through toll-like receptor 4 (TLR4). Gene silencing of TLR4 or CXCL1 in DRG neurons significantly attenuated neutrophil accumulation in the DRG and mechanical allodynia during the preclinical phase of EAE (around day 5 after immunization). Our results thus suggest that a TLR4-CXCL1 pathway in DRG neurons triggers neutrophil recruitment in the DRG and subsequent mechanical allodynia in response to MOG₃₅₋₅₅.