









IL-33 promotes sciatic nerve regeneration in mice by modulating macrophage polarization

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Abstract

Despite the innate regenerative capacity of peripheral nerves, regeneration after a severe injury is insufficient, and sensorimotor recovery is incomplete. As a result, finding alternative methods for improving regeneration and sensorimotor recovery is essential. In this regard, we investigated the effect of IL-33 treatment as a chemokine with neuroprotective properties. IL-33 can facilitate tissue healing by potentiating the type 2 immune response and polarizing macrophages toward the pro-healing M2 phenotype. However, its effects on nerve regeneration remain unclear. Therefore, this research aimed to evaluate the neuroprotective effects of IL-33 on sciatic nerve injury in male C57BL/6 mice. After crushing the left sciatic nerve, the animals were given 10, 25, or 50 µg/kg IL-33 intraperitoneally for seven days. The sensorimotor recovery was then assessed eight weeks after surgery. In addition, immunohistochemistry, ELISA, and real-time PCR were used to assess macrophage polarization, cytokine secretion, and neurotrophic factor expression in the injured nerves. IL-33 at 50 and 25 µg/kg doses could significantly accelerate nerve regeneration and improve sensorimotor recovery when compared to 10 µg/kg IL-33 and control groups. Furthermore, at 50 and 25 µg/kg doses, IL-33 polarized macrophages toward an M2 phenotype and reduced proinflammatory cytokines at the injury site. It also increased the mRNA expression of NGF, VEGF, and BDNF. These findings suggest that a seven-day IL-33 treatment had neuroprotective effects in a mouse sciatic nerve crush model, most likely by inducing macrophage polarization toward M2 and regulating inflammatory microenvironments.