Netrin-1

Netrin-1 is a protein that in humans is encoded by the NTN1 gene.

Netrin is included in a family of laminin-related secreted proteins. The function of this gene has not yet been defined; however, netrin is thought to be involved in axon guidance and cell migration during development. Mutations and loss of expression of netrin suggest that variation in netrin may be involved in cancer development.

Zhang et al. aimed to investigate the regulatory role of Netrin-1 (NTN1) in ferroptosis after traumatic brain injury (TBI) in mice.

They assessed the expression pattern of NTN1 by RT-PCR, western blot, and immunofluorescence after establishing the TBI model in mice. After treatment with NTN1 shRNA or recombinant NTN1, we determined the biochemical and morphological changes associated with ferroptosis and netrin-1-related pathways. We used Nissl staining to assess lesion volume and the Morris water maze and beam-walking test to evaluate ethological manifestation.

The mRNA and protein levels of NTN1 were upregulated after TBI. The application of NTN1 shRNA increased the number of FJB-positive cells, malondialdehyde (MDA), and reactive oxygen species (ROSs) levels. However, the application of NTN1 recombinant had the opposite effect. Furthermore, knockdown or inhibition of GPX4, Nrf2, and UNC5B counteracted the effects of NTN1 recombinant. Intravenous injection of NTN1 recombinant reduced neuronal loss after CCI and improved motor and cognitive function.

NTN1 had a neuroprotective effect after TBI and inhibited ferroptosis via activating the UNC5B/Nrf2 pathway. These findings may provide potential therapeutic strategies for TBI [1)].

Inhibition of osteoclast activity by alendronate modifies aberrant subchondral bone remodeling and reduces innervation and pain behavior at the early stage of osteoarthritis (OA). These results suggest that intervention of the axonal guidance molecules (e.g., netrin-1) derived from aberrant subchondral bone remodeling may have therapeutic potential for OA pain [2)].

Yung et al. found that Ntn1 accumulates beneath the pial surface separating the CNS from the PNS, with gaps at nerve entry sites. In mice null for Ntn1 or its receptor DCC, hindbrain neurons enter cranial nerves and migrate into the periphery. CNS neurons also escape when Ntn1 is selectively lost from the sub-pial region (SPR), and conversely, expression of Ntn1 throughout the mutant hindbrain can prevent their departure. These findings identify a permissive role for Ntn1 in maintaining the CNS-PNS boundary. We propose that Ntn1 confines rhombic lip-derived neurons by providing a preferred substrate for tangentially migrating neurons in the SPR, preventing their entry into nerve roots [3)].

1)
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2)

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