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

Methods: We 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.

Results: 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].

1)
Zhang Y, Lan J, Zhao D, Ruan C, Zhou J, Tan H, Bao Y. Netrin-1 upregulates GPX4 and prevents ferroptosis after traumatic brain injury via the UNC5B/Nrf2 signaling pathway. CNS Neurosci Ther. 2022 Dec 5. doi: 10.1111/cns.13997. Epub ahead of print. PMID: 36468399.