Spautin-1

Spautin-1 is a small molecule inhibitor that is being studied for its potential use in the treatment of cancer. It is thought to target the ubiquitin-proteasome system, which is involved in the degradation of proteins within cells. By inhibiting this system, Spautin-1 may block the growth and survival of cancer cells. Currently, Spautin-1 is in preclinical and early-phase clinical trials for the treatment of various types of cancer, including solid tumors and hematological malignancies. Further research is needed to determine the safety and efficacy of Spautin-1 as a treatment for cancer.

The potent anti-tumor effects of Spautin-1, a novel autophagy inhibitor, have been documented in malignant melanoma; moreover, the inhibition of autophagy is reported to mitigate anxiety disorders. However, little is known about the ability of spautin-1 to alleviate anxiety. In this study, we sought to investigate whether spautin-1 could alleviate anxiety-like behaviors post-TBI by reducing the loss of PNNs in the LHA. A mild TBI was established in mice through Feeney's weight-drop model. Then, Spautin-1 (20 mmol/2 μl) was immediately administered into the left lateral ventricle. Behavioral and pathological changes were assessed at 24 h, 7 days, 30 days, 31 days and 32 days after TBI by the neurological severity scores (NSS), open field test (OFT), elevated plus-maze (EPM) test, western blot, immunofluorescence assays and electron microscopy. Spautin-1 significantly reversed TBI-induced decreased time in the central zone during OFT and in the open-arm during the EPM test. Spautin-1 also increased PNNs around GABAergic neurons indicated by WFA- plus GAD2- positive A2-type astrocytes and attenuated M1-type microglia in the LHA 32 days after TBI compared to TBI alone. Moreover, compared to mice that only underwent TBI, spautin-1 downregulated autophagic vacuoles, abnormal organelles, the expression of Beclin 1, USP13, phospho-TBK1, and phospho-IRF3 and upregulated the levels of cleaved caspase-3, -7 and -9, but failed to increase TUNEL-positive cells in the LHA at 24 h. Spautin-1 alleviated anxiety-like behavior in mice exposed to mild TBI; this protective mechanism may be associated with decreased PNNs loss around GABAergic neurons via immunologically silent apoptosis induced by the caspase cascade [1)].

1)
Miao HT, Song RX, Xin Y, Wang LY, Lv JM, Liu NN, Wu ZY, Zhang W, Li Y, Zhang DX, Zhang LM. Spautin-1 Protects Against Mild TBI-Induced Anxiety-Like Behavior in Mice via Immunologically Silent Apoptosis. Neuromolecular Med. 2023 Feb 6. doi: 10.1007/s12017-023-08737-2. Epub ahead of print. PMID: 36745326.