Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

ACT001 reduces neuroinflammation after traumatic brain injury

Lin Cai
Qiuyuan Gong
Lin Qi
Tongtong Xu
Qian Suo
Xiang Li
Wei Wang
Yao Jing
Dianxu Yang
Zhiming Xu
Fang Yuan
Yaohui Tang
Guoyuan Yang
Jun Ding
Hao Chen
Hengli Tian

Video Byte

Keywords: ACT001, traumatic brain injury, microglial cells, microglia, neuroinflammation, AKT, protein kinase B, NFκB, nuclear factor kappa B, NLRP3 inflammasome, NLR family pyrin domain-containing 3, TBI, brain damage, controlled cortical impact, motor dysfunction, neurological deficit, nuclear translocation, head injury, cerebral injury, Cell Communication and Signaling

Posted Date: May 18th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1668013/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Abstract

Traumatic brain injury (TBI), or brain damage caused by a sudden blow or jolt to the head, is a leading cause of death and disability worldwide. The mechanisms are complex and differ among patients, making TBI difficult to treat, and anti-inflammatory agents that are effective in animal models have been less promising in human trials, indicating that better treatments are needed. To explore new strategies, a recent study investigated the effect of the anti-inflammatory compound ACT001 on TBI. In mice, ACT001 reduced brain damage and improved motor function after TBI by reducing trauma-induced activation of microglia, which are immune cells of the central nervous system. In vitro, ACT001 also reduced activation of mouse and rat microglia induced by the bacterial toxin lipopolysaccharide (LPS) and downregulated LPS-induced secretion of proinflammatory molecules in a mouse microglial cell line. Moreover, ACT001 decreased apoptosis in mouse neurons and increased blood vessel structure formation in mouse brain endothelial cells. Mechanistic studies revealed that ACT001 elicited its beneficial effects by inhibiting the AKT/NFκB/NLRP3 signaling pathway. Although clinical trials are needed, the results show that ACT001 can alleviate microglia-mediated neuroinflammation and facilitate motor function recovery, suggesting that ACT001 is a promising therapeutic agent for TBI.