LACK OF THE NLRP3 INFLAMMASOME IMPROVES MICE RECOVERY FOLLOWING TRAUMATIC BRAIN INJURY.

1)Irrera N. 2)Pizzino G. 3)Pallio G. 4)Mannino F. 5)Arcoraci V. 6)Minutoli L. 7)Squadrito F. 8)Giuliani D. 9)Guarini S. 10)Altavilla D. 11)Bitto A.

University of Messina

Treatment for traumatic brain injury (TBI) remains elusive despite compelling evidence from animal models for a variety of therapeutic targets. The activation of the NLRP3 (Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 3) inflammasome has been proposed as key point in the brain damage associated with TBI (Liu et al., 2013). NLRP3 was tested as potential target for reducing neuronal loss and promoting functional recovery in a mouse model of TBI.

Male NLRP3-/- (n = 20) and wild type (n=27) mice were used. A closed TBI model was performed (Marmarou et al., 1994) and inflammatory and apoptotic markers were evaluated. A group of WT mice also received BAY 11-7082, a NLRP3 inhibitor, to further evaluate the role of this pathway. At 24 hrs following TBI NLRP3-/- animals demonstrated a preserved cognitive function as compared to WT mice, additionally brain damage was less severe and the inflammatory mediators were reduced in brain lysates. The administration of BAY 11-7082 in WT animals subjected to TBI produced overlapping results.

At day 7 histology revealed a more conserved brain structure with reduced neuronal suffering and apoptotic damage in TBI NLRP3-/- animals compared to WT.

Our data indicate that the NLRP3 pathway might be exploited as molecular target for the short-term sequelae of TBI.

Liu et al. (2013). Neurochem Res. 38:2072-83.

Marmarou et al. (1994). J Neurosurg. 80:291-300.