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DISSERTATION

“Myeloid Pannexin-1 Mediates Acute Leukocyte Infiltration
And Leads To Worse Outcomes After Brain Trauma”

by
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ABSTRACT

Neuroinflammation is a major component of secondary damage after traumatic brain injury (TBI). We recently reported that pharmacological inhibition of Pannexin-1 (Panx1) channels markedly reduced the inflammatory response after TBI. Panx1 channels have been shown to be important conduits for adenosine 5′-triphosphate (ATP) release and are associated with leukocyte infiltration and pyroptosis. Thus, we decided to examine the specific role of microglia and monocyte Panx1 channels in TBI by generating a myeloid-specific Panx1 conditional knockout (Cx3cr1-Cre::Panx1fl/fl) mice. Using the murine controlled cortical impact (CCI) model of TBI, we report that CCI-injured Cx3cr1-Cre::Panx1fl/fl mice show markedly reduced immune cell infiltration and biomarkers of tissue damage when compared to Panx1fl/fl mice. In line with this, magnetic resonance imaging shows reduced blood brain barrier leakage in CCI-injured Cx3cr1-Cre::Panx1fl/fl mice. There is also a significant improvement in motor and memory function in Cx3cr1-Cre::Panx1fl/fl mice within a week post-CCI injury. Our data demonstrate that CCI-related outcomes correlate with Panx1 channel function in myeloid cells, indicating that activation of Panx1 channels in myeloid cells is a major contributor to acute brain inflammation following TBI. Importantly, myeloid Panx1 channels could serve as an effective therapeutic approach to improve outcome after TBI.