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YOU ARE INVITED TO ATTEND THE DEFENSE OF THE DOCTORAL DISSERTATION

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

by
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Cell Biology, Neuroscience and Physiology
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Thursday, March 19th, 2019
12:30 P.M.
Cancer Center G1196

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*::Panx1*$^{fl/fl}$) mice. Using the murine controlled cortical impact (CCI) model of TBI, we report that CCI-injured *Cx3cr1*-Cre*::Panx1*$^{fl/fl}$ mice show markedly reduced immune cell infiltration and biomarkers of tissue damage when compared to *Panx1*$^{fl/fl}$ mice. In line with this, magnetic resonance imaging shows reduced blood brain barrier leakage in CCI-injured *Cx3cr1*-Cre*::Panx1*$^{fl/fl}$ mice. There is also a significant improvement in motor and memory function in *Cx3cr1*-Cre*::Panx1*$^{fl/fl}$ 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.