

Myeloid-specific conditional deletion of p38 α MAPK differentially regulates the neuroinflammatory response to traumatic brain injury.

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Traumatic brain injury (TBI) initiates a multitude of cellular responses in the brain following the primary injury. Aberrant neuroinflammatory signaling cascades are one of these hallmark responses. Consistently, dysregulation of neuroinflammation has been linked with propagating neurodegenerative sequelae following TBI. The p38 α mitogen activated protein kinase (MAPK) is a key signaling kinase that drives inflammatory responses in many CNS disorders. Therefore, we are exploring the role of p38 α MAPK in regulating inflammatory-linked responses to TBI. In the current study, we compartmentalized the cell-specific deletion of p38 α by creating two genotypes of mice; p38 α Δ CX3CR1-CreERT2 and p38 α Δ LyzM-Cre bone marrow chimera, which restricted the genetic deletion of p38 α to microglia and circulating myeloid cells, respectively. Focal contusion TBI was generated in the mice using the controlled cortical impact method. Mice were examined at acute (1d post injury) and subacute (7d post injury) timeframes for peripheral macrophage recruitment using flow cytometry and for inflammatory response using multiplex ELISA and qRT-PCR gene expression assays. Collectively, our data demonstrate differential roles of p38 α in regulating both microglia and peripheral macrophage contributions to TBI-induced neuroinflammatory sequelae.