Peripheral macrophages are viable therapeutic targets in traumatic brain injury

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Each year in the United States, approximately two million people suffer from traumatic brain injury (TBI). An estimated five million people live with the long-term physical, cognitive, and psychological health disabilities of TBI, with annual healthcare costs estimated at over $60 billion. It is now being recognized that TBI is a process, not merely a single event. Emerging evidence suggests that this process can lead to multiple neurodegenerative disorders. Clinically, TBI is one of the greatest risk factors for the development of dementia and Alzheimer's disease.

Problematically, there is currently no molecular mechanism known for this association or a viable therapeutic strategy.

As a consequence of the primary mechanical disruption, TBI triggers a cascade of molecular and cellular events that are attributed to the degeneration of primarily unaffected neurons adjacent to the impact zone. Of principle interest is the initiation of multiple innate immune effector systems following TBI, specifically microglia and macrophages. In the current study we examine the efficacy of using clinical-grade CCR2 and CCR5 antagonists in both young and aged animal

models of TBI. The effect of these therapeutic strategies was examined in the context of mitigating peripheral macrophage recruitment to the injured brain, altering inflammatory response to injury, and hippocampal-dependent cognitive function. Cumulatively, these data demonstrate that circulating monocytes/macrophages are a viable therapeutic target for the mitigation of TBI-induced neuroinflammatory sequelae.