Anti-CD49d Antibody Treatment Improves Survival and Attenuates Neurocognitive Deficits after Traumatic Brain Injury in Aged Mice

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Introduction & Hypothesis
Traumatic brain injury (TBI) afflicts approximately seventy million people worldwide yearly 1. While TBI affects individuals of all ages, the elderly (aged 65 years and older) experience higher mortality and more severe consequences than younger individuals. Recently, studies have found that age introduces T cells into the brain, likely due to the structural and functional alterations of the blood brain barrier (BBB) 2. Previously, we have observed that aged mouse brains showed significant CD8+ T cells two months post-TBI. These T cells were largely effector memory (EM) cells. They were more activated and pro-inflammatory 3. Herein, utilizing anti-CD49d antibody (aCD49d Ab) to reduce the invasion of circulating lymphocytes, we are interested in gaining more insight on the presence and function of these T-cells. We hypothesize that blocking infiltration of peripheral T-cells into the injured brain would improve neurocognitive outcomes in aged mice after TBI.

Methods

Use of aCD49d Ab to reduce the invasion of circulating lymphocytes to the injured brains

Experimental Design. Young (4-month) and aged (18-month) male C57BL/6 mice were subjected to our well-established controlled cortical impact (CCI) model of TBI vs sham injury. 300 µg of aCD49d Ab or isotype control were administered 2 hours post-injury and repeated every 2 weeks. In vivo. Central cell proliferation: 50 mg/kg body weight of 5-ethyl-2'-deoxyuridine (EdU) via intraperitoneal injection for 3 consecutive days. In vivo labeling infiltrating immune cells: 3ug BUdR-CD45 by intravenous injection 2 hours before euthanasia.

Results

Does reducing the invasion of lymphocytes improve survival and neurocognitive outcomes post-TBI?

How’s peripheral inflammation affected by aCD49d Ab?

Does reducing the invasion of lymphocytes change T cell transcriptomes?

Conclusions