antiCD49d Ab treatment ameliorates age-associated inflammatory response and mitigates CD8+ T-cell cytotoxicity after traumatic brain injury

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Introduction

Traumatic brain injury (TBI) affects approximately sixty-nine 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 with similar injury severity. Recently, studies have found that age introduces an uninvited guest in the brains—the T cells likely due to the structural and functional alterations of the blood brain barrier (BBB), which leads to the pass of T cells. Infiltrated T cells can interact with microglia, the gatekeepers in the central nervous system and the main antigen-presenting cell in the brain, in age-associated neurodegenerative diseases.2 Previously, we have observed that aged mouse brains showed significant T cells two months post-TBI. These T cells were largely CD8+ effector memory (EM) cells. They were more activated and inflammatory. Microglia from these aged, injured mouse brains were also activated and upregulated genes involved in leukocyte chemotaxis, partially explaining the significant presence of T cells in the brains.

Previously Published Findings and Hypothesis

Previously, we utilized anti-CD49d antibody (aCD49d Ab), an FDA approved drug for treating multiple sclerosis and Crohn disease (also known as Natalizumab), to reduce the invasion of circulating lymphocytes. We found that aCD49d Ab treatment 1) significantly improved survival, neurocognition and motor function in aged but not young TBI mice, and 2) specifically reduced cytotoxic CD8+ T cells within the brains of aged mice.3 To study the underlying mechanism, we hypothesized that aCD49d Ab treatment would mitigate age-associated T cell functional decline after TBI in aged mice.

Methods

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

- **Ex vivo stimulation**
  - **CD49d**
  - **CD8**

- **Cytokine analysis in aged and young mice at 2 months post-injury:**
  - **A:** Levels of cytokines in the ipsilateral brain tissue homogenates including IL-10, IL-17, IL-22, and TNF-α. Levels of cytokines in the contralateral brain tissue homogenates including IL-10, IL-17, IL-22, and TNF-α. IL-10, IL-17, IL-22, and TNF-α. Levels of cytokines in the contralateral brain tissue homogenates including IL-10, IL-17, IL-22, and TNF-α. Levels of cytokines in the contralateral brain tissue homogenates including IL-10, IL-17, IL-22, and TNF-α.

Results

**aCD49d Ab treatment functions through suppression of age-associated activated cytokine/chemokine response during acute TBI**

**Blood**

- **IL10**
- **IL17A**

**Brain**

- **IL10**
- **IL17A**

**aCD49d Ab treatment leads to fewer clonally expanded CD8+ T cells in aged brains with chronic TBI**

Conclusions

**References**

Acknowledgement