Introduction

Traumatic brain injuries (TBI) contribute to about 30% of all injury-related deaths in the United States. There are currently no effective therapies for TBI and supportive care remains the mainstay of treatment. Microglia, the brain's resident innate immune cells, work together with infiltrating monocytes and monocyte-derived macrophages (MDMs) to promote both inflammation and foster wound repair. The environment that is created and the mechanisms that drive it are poorly understood. Understanding these mechanisms will help identify what supports repair and regeneration.

Hypothesis

Our research objective was to assess and compare the transcriptional signature at two different acute-timepoints after TBI. Therefore, we hypothesized that monocytes and MDMs would have markedly different transcriptional signature in early TBI compared to the recovery phase of TBI.

Methods: CCI and SSC Analysis

(A) CCI and Single Cell RNA analysis were used to map out monocytes and MDMs.

(B) UMAP showing populations of monocytes and MDMs found 8 hour (left outline) versus 2 week (right outline) post TBI.

(C) Dim plots showing curated markers that identify each cell type.

Results: Temporal Expression of Ly6c

(A) Scatter plot depicting a higher expression of genes associated with Ly6c\textsuperscript{hi} at 8 hours as compared to 2 weeks post injury.

(B) Scatter plot depicting a higher expression of genes associated with Ly6c\textsuperscript{lo} at 8 hours as compared to 2 weeks post injury.

Results: Cytokines Highly Expressed at 8 hrs

(A) Whole brain cytokines IL-2, CXCL2, CCL3, CCL7 and CCL2 were highly expressed 8 hours post injury in the TBI group.

Results: Unique Presence of Macrophages at 8 hrs

(A) Pathway analysis indicating a unique presence of MDM's in mouse brain 8 hour post TBI.

(B) Volcano plot demonstrating the differentially expressed genes (DEGs) of 8 hour versus 2 week macrophages.

Conclusions: TBI Alters Gene Expression

- Our data demonstrates a shift in the gene expression specifically in monocytes and MDMs between acute versus subacute TBI.

- Identifying the discrete functions of infiltrating monocytes/MDMs and how they may interact with resident microglia will promote a broader view of injury pathogenesis in TBI.

- Understanding the nature of their interaction and deciphering their differential gene activation over the course of injury raises the possibility of developing novel gene-specific therapeutic approaches for the treatment of TBI.

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