

TBI induces a fast influx of Basophils into the spleen, that activate B cells and Dendritic cells via IL-13 signaling

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Introduction: Systemic inflammatory responses have been reported after traumatic brain injury (TBI), with many organs affected. The spleen, one of the most important immune regulatory organs, shows high interaction with the brain, known as the brain-spleen axis. Both brain-derived mediators as well as nerve fibres have been reported to directly affect immune cells in the spleen. We have previously investigated the effects of TBI on splenic immune cells, showing a fast maturation of splenic dendritic cells 3h after an experimental TBI. However, how the signaling and immune response changes to TBI, and possibly DC maturation, remains largely unknown.

Methodology: We have performed large scale phospho-signaling to determine functional immune responses in spleen samples 3h post blunt closed head injury. To identify cell type specific involvement, bio-informatic analysis and immunofluorescence staining were performed. Additionally, cytokine and chemokine arrays, together with ELISA, were employed to assess factors involved in chemotaxis and activation. Finally, fluorescence staining, super-resolution microscopy and in situ hybridization were used to characterize the specific cell type function in vivo.

Results: The large-scale signaling post TBI pointed towards a fast influx of basophil-granulocytes in the spleen, which was further investigated using immunofluorescence staining. Cytokine and chemokine arrays together with ELISA and single mRNA in situ hybridization show CXCL1, expressed by B-cells and DCs, as the main basophil attractant. Immunostaining and super resolution microscopy revealed a direct cell-to-cell interaction between Basophils and DCs/B-cells via IL-13/IL-13Ra1 signaling pathway. Interestingly, this influx was short-lived since basophil levels returned to baseline at 3 days post injury. Furthermore, this phenotype is one of the responses affected by ethanol intoxication, showing no initial basophil increase with ethanol exposure.

Conclusion: We have shown a influx of basophils in the spleen upon TBI, which resulted in a distinct activation of B-cells and DCs, via the IL-13/IL-13Ra1 signaling pathway.