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Large scale cytokine response in spleen of subacute experimental TBI points towards reduced nerve innervation

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Background: Traumatic Brain Injury (TBI) affects systemic immune responses in many distal organs, with strong effects previously identified in spleen. The brain has been reported to have a strong interaction with the splenic immune system, by both brains derived mediators and nerve innervation. We have previously shown a fast maturation of dendritic cells post moderate blunt injury in the spleen. However, the long-term immune responses of a more severe injury remain uninvestigated.

Methodology: We have performed large scale cytokine array to investigate immune responses in spleen samples 5 days post experimental controlled cortical impact. Bio-informatic analysis was performed to assess the processes involved in the cytokine landscape post injury. Immunofluorescence staining and in situ hybridization were done to get an initial idea about these processes.

Results: Out of 640 cytokines we found 340 cytokines to be differentially expressed, pointing towards a strong immunological involvement in the subacute phases of TBI. Bio-informatic analysis shows involvement of multiple cell types, including dendritic cells, T-cells and granulocytes. A more specific pathway analysis revealed the enrichment of multiple immune related pathways, like Jak-STAT pathway, IL-17 signaling and Toll-like receptor pathway. Interestingly, The Axon guidance pathway shows significant enrichment, with several proteins downregulated that are involved in axon guidance like ROBO3 and SLIT2. Single mRNA in situ hybridization data reveal a strong decrease in the cholinergic receptor Chrm2.

Conclusion: We have shown a strong cytokine response in the subacute phase of TBI, with several proteins involved in decreased axon guidance. This data points towards a decrease of splenic nerve innervation in the subacute phase post severe TBI.