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SEMAPHORIN 3E REGULATES MACROPHAGES RESPONSE TO LIPOPOLYSACCHARIDE INDUCED SYSTEMIC INFLAMMATION AND SEPSIS

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Background:

Sepsis is an intricate, systemic immune response to an infection. It is the leading cause of death in intensive care units, especially in children and elders.Semaphorin 3E (Sema3E) is a secreted protein which has been shown to participate in various immune processes. Macrophages are important cells of the innate immune system and play a significant role in systemic inflammation and sepsis. There is evidence that Sema3E regulates macrophage function during inflammation, however, the exact role of Sema3E in macrophage function in lipopolysaccharide (LPS) induced inflammation and sepsis remains unclear. We hypothesized that Sema3E, may play a protective role in sepsis through its ability to regulate macrophage function.

Objective:

Our aim is to study the impact of Sema3E deletion on macrophage function during LPS induced inflammation and sepsis

Methods:

We used in vitro (Western blot, Flow Cytometry) and in vivo in both Sema3E deficient and wildtype mice to test our hypothesis.

Results:

We found that *Sema3e*$^{-/-}$mice were better protected from LPS induced inflammation exemplified by better clinical score and lower change in temperature compared to their *Semae3*$^{+/+}$ littermates. Also, *Sema3e*$^{-/-}$mice had lower iNOS expression, nitric oxide (NO) production TNF and IL-6 as well as reduced phosphorylation of STAT1, STAT3, ERK1/2 compared to the *Sema3e*$^{+/+}$littermates. Furthermore, there was a higher percentage of alternatively activated M2 macrophage macrophages in *Sema3e*$^{-/-}$compared to their *Sema3e*$^{+/+}$littermates. Interestingly, the absence of Sema3E led to reduced phagocytic and antigen processing ability of macrophages. *In vivo*specific deletion of the Sema3E high affinity receptor (PlexinD1) on macrophages led to improvement in clinical disease following exposure to lethal dose of LPS

Conclusion:

Collectively, our data reveals that Sema3E is important during inflammatory response to LPS by regulating macrophage phenotype and function suggesting that the inhibition of Sema3E might be a novel strategy to treat different inflammatory diseases.