

Harnessing innate immune training (innate immune memory) to improve sepsis management

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Abstract:

Sepsis affects 49 million people and is accountable for one in five deaths per year worldwide. Unfortunately, all sepsis-directed immunotherapies have failed to improve patient's outcome. We are currently applying precision-medicine approaches in proof-of-concept clinical trials of personalized immunotherapy in sepsis. A highly promising complementary approach to precision-medicine to fight sepsis is trained immunity. Trained immunity refers to the capacity of the innate immune system to recall and adapt to an initial challenge to mount an improved response to a secondary challenge. We recently reported that trained immunity confers broad-spectrum protection against bacterial infections, and intergenerational transmission of trained immunity conferring heterologous resistance to infections (Ciarlo et al. *J Infect Dis.* 2020; Théroude et al. *Front Immunol.* 2021, Katzmarski et al. *Nat Immunol.* 2021). Using multiple omics approaches, our project aims to delineate the impact of age on the establishment of trained immunity, the persistence and impact on vaccine response of trained immunity, as well as the interplay between metabolism, microbiota and trained immunity. On the long-term, therapies directed at trained immunity might offer new treatment options to improve vaccine efficacy, especially in elderly who are particularly susceptible to severe infections and sepsis, or normalize dysregulated host responses in sterile and infectious pathologies.