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Harnessing innate immune training to improve sepsis management

Sepsis is a leading cause of mortality worldwide. Unfortunately, all sepsis-directed immunotherapies have failed to improve patient's outcome. Since sepsis is a heterogenous syndrome, 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 approaches 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. Contrary to adaptive immune memory, trained immunity is not antigen specific, suggestive of wide-ranging effects. 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). Our project aims to delineate the impact of age on the establishment of trained immunity as well as the persistence and impact on vaccine response of trained immunity. We also decipher molecular and metabolic pathways involved in 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 sever infections and sepsis) or normalize dysregulated host responses in sterile and infectious pathologies.