Dendritic cells pre-condition naive T cells to promote their proliferation and effector differentiation potential

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In secondary lymphoid organs, dendritic cells (DCs) form an extensive cellular network to present their antigenic content to naive T cells. Upon cognate recognition, naive T cells become activated and initiate a proliferation and differentiation program. Naive T cells display a large range of sensitivities towards cognate stimulation independently of their TCR specificity. In vitro studies have suggested that the steady-state interactions between DCs and T cells have a physiological function by promoting basal tonic T cell receptor signaling and pre-conditioning T cells for enhanced proliferation in response to an antigenic challenge. Here we investigated whether in vivo interactions between DCs and naïve T cells in the absence of specific antigen influence the proliferation and differentiation capacity of naive T cells upon subsequent cognate activation. Our results show that different naive T cells of the same specificity respond to their cognate antigen with various proliferation kinetics and effector differentiation outcomes. The variability in T cell responses were largely independent of TCR specificity. Rather, pre-conditioning of naive T cells by DCs prior to antigen-specific activation has a fundamental effect on the exit kinetics from quiescence as well as on effector differentiation. DC loss during sepsis de-sensitised naive CD4 T cells resulting in loss of tonic TCR signalling, decreased proliferation and impaired differentiation in response to subsequent antigenic challenge, which may contribute to the observed impairment in Th1 differentiation observed in sepsis survivors. These results demonstrate that pre-conditioning of naive T cells by DCs prior to cognate recognition is a key process shaping the magnitude and quality of the T cell response.

Keywords : Dendritic cells, T cells, self-recognition, sepsis
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