Vaccine-elicited CD4 T cells prevent the deletion of antiviral B cells in chronic infection

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Abstract

Chronic viral infections subvert protective B-cell immunity. An early type I interferon- (IFN-I-) driven bias to short-lived plasmablast differentiation leads to clonal deletion, so-called “decimation”, of antiviral memory B-cells. Therefore, prophylactic countermeasures against decimation remain an unmet need.

We show that vaccination-induced CD4 T cells prevented the decimation of naïve and memory B-cells in chronically LCMV-infected mice. Although these B-cell responses were largely T-independent when IFN-I was blocked, pre-existing T help assured their sustainability under conditions of IFN-I-driven inflammation by instructing a germinal center B-cell transcriptional program. Prevention of decimation depended on T cell-intrinsic Bcl6 and Tfh progeny formation. Antigen presentation by B-cells, interactions with antigen-specific T helper cells and costimulation by CD40 and ICOS were also required. Importantly, B-cell-mediated virus control averted Th1-driven immunopathology in LCMV-challenged animals with pre-existing CD4 T cell immunity.

Our findings show that vaccination-induced Tfh cells represent a cornerstone of effective B-cell immunity to chronic virus challenge, pointing the way towards more effective B-cell-based vaccination against persistent viral diseases.