# A snapshot of germinal center plasma cell differentiation during a viral infection

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## Abstract

Affinity maturing germinal center (GC) B cells can differentiate into memory B cells capable of recall, or plasma cells (PCs) that secrete antibody. The PC fate is generally considered to be instructed by strong selection cues and only adopted by the highest affinity GC B cells. These principles have been demonstrated in clonally-restricted experimental systems where B cells affinity mature towards single epitope antigens, but their implications in physiological immunization and infection settings are not clear. Viral antigens display multiple epitopes, each recognized by large numbers of responding B cell clones; whether PC differentiation is restricted to just high affinity GC lineages, or to the best members within lineages, has not been investigated. We have followed the evolution of a native polyclonal anti-viral antibody response, using a temporally controlled genetic fate-mapping approach to isolate newly differentiated antigen-specific PCs, alongside B cells from the GCs that generated them. Through single-cell antibody sequencing and FAB characterization, we assessed the roles of antibody clonality and BCR affinity in the PC differentiation process. This approach also enabled us to characterize the dynamics of PC formation, unveiling both shared principles and striking differences between infection and vaccination challenges. Our results help define the criteria by which GC B cells are selected to enter into PC compartments, and shed light on the impact of immunological context on response magnitude.