Clonal replacement sustains long-lived germinal centers primed by respiratory viruses

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Abstract

Germinal centers (GCs) form in secondary lymphoid organs in response to infection and immunization and are the source of affinity-matured B cells. The duration of the GC reaction spans a wide range, and long-lasting GCs (LLGCs) are potentially a key source of highly mutated B cells. We show that, rather than consisting of continuously evolving B cell clones, LLGCs elicited by influenza or SARS-CoV-2 infection in mice are sustained by progressive replacement of founder clones by invader B cells derived from the naïve repertoire and not detectably specific for viral antigens. Rare founder clones able to resist replacement for 6 months are enriched in heavily mutated B cells and include B cells with very high affinity for antigen. Our findings reveal underappreciated aspects of the biology

of LLGCs generated by respiratory virus infection and identify clonal replacement as a constraint on the development of highly mutated antibodies within these structures.