Tunable dynamics of B cell selection in gut-draining germinal centers

C. Nowosad[1,2,3], L. Mesin[2], T.B.R. Castro[2,3], C. Wichmann[2,3], T. Araki[2], A. Schiepers[2], A. A. K. Lockhart[3], A. M. Bilate[3], D. Mucida[3] and G. D. Victora[2].

[1]New York University Grossman School of Medicine, Department of Pathology, 550 First Avenue, New York, NY, USA
[2]Rockefeller University, Laboratory of Lymphocyte Dynamics, 1230 York Avenue, New York, NY, USA
[3]Rockefeller University, Laboratory of Mucosal Immunology, 1230 York Avenue, New York, NY, USA
carla.nowosad@nyulangone.org

Abstract

B lymphocytes are central to maintaining balanced enteric responses through production of immunoglobulins (Igs). A large fraction of Igs are produced in germinal center (GC) responses, which form upon immunization or infection in the majority of secondary lymphoid organs, but are constitutively present in gut-associated lymphoid tissue. However, gut-associated GC responses were poorly understood in terms of their ontogeny and antigenic drivers. Using a multicolor fate-mapping approach to visualize GC clonal expansions with a confetti fluorescent allele, we observed single-color GCs in the steady state intestine, suggestive of a strong selection event. By coupling fate-mapping gnotobiotics and Ig sequencing, we showed affinity-driven selection occurring in response to members of the microbiome. We observed that GCs persist even in the absence of microbiota, although their isotype distribution and clonal composition are altered. We identified several prominent public Ig clonotypes in intestinal GCs, whose presence were tuned by microbial diversity.