Dynamic Regulation of T follicular helper cell selection during the germinal center reaction

Julia Merkenschlager[1], Maximilian Uhlig[1], Michel C. Nussenzweig[1, 2]
[1]Laboratory of Molecular Immunology, The Rockefeller University, New York, NY, USA.
[2]Howard Hughes Medical Institute, The Rockefeller University, New York, NY, USA.
e-mail: jmerkensch@rockefeller edu

Abstract

B cells in germinal centers (GC) undergo somatic hypermutation of their antibody coding genes followed by selection of high-affinity clones by T follicular helper (T_{FH}) cells. While GC B cells are subject to extensive division, T_{FH} cells are thought to be quiescent to preserve stringent B cell selection. In contrast to this widely held belief we provide evidence that T_{FH} cells do proliferate in response to antigen throughout the lifetime of the GC reaction. Longitudinal analysis of ongoing T_{FH} cell repertoires allowed us to identify expanding as well as contracting clones, revealing the dynamic nature of the repertoire. Whether a cell expanded or contracted was reflected on the level of gene expression: clones that expanded showed increased expression of genes related to TCR-signaling and mitosis. This means that the amount of proliferation is tightly linked to a T cells ability to recognize antigen, resulting in an enrichment of high-affinity T_{FH} cells as the GC reaction progresses. In summary, interactions between T- and B lymphocytes in GCs are much more symbiotic than previously envisioned, where GC B cells select for T_{FH} cells too.