# Factors Coordinating Follicular Helper T Cell Biology and Humoral Immunity

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The formation of germinal centers (GC), the differentiation of GC B cells, and the generation of antibody-producing plasma cells require help from follicular helper T cells ($T_{FH}$), a specialized subset of CD4 T cells. The transcriptional repressors Bcl6 and Blimp1 are well-known for their unique roles in $T_{FH}$ and B cell differentiation. To identify novel factors regulated by Bcl6 or Blimp1 transcription factors (TFs) in $T_{FH}$ differentiation, we employed integrated analytical approaches using ChIP-seq, RNA-seq, and ATAC-seq data from multiple knockout mice, including Bcl6/Blimp1 double-deficient mice. Id2, a direct target of Bcl6, enhanced $T_H1$ differentiation and inhibited E2A to suppress $T_{FH}$ differentiation. Bcl6 induced CXCR5 expression in $T_{FH}$ cells by repressing the Id2-E2A pathway. Furthermore, we identified that Runx3 and Klf2 function as Bcl6-targeted repressors that regulate crucial $T_{FH}$ genes. Multiple experiments involving enforced expression of these TFs via a retrovirus and Crispr/Cas9-mediated gene knockdown of *Runx3* or *Klf2* confirmed that Runx3 and Klf2 regulate differentiation of $T_{FH}$, GC B, and plasma cells, and the optimal production of antigen-specific antibodies. Additionally, we tested multiple vaccine adjuvants that affect GC B cell generation and antigen-specific antibody production. Among them, a STING ligand enhanced the humoral immune response. In summary, the regulation of Bcl6-targeted TFs and the use of adjuvants that influence the optimal differentiation of Tfh cells and GC B cells have the potential to enhance humoral immunity.