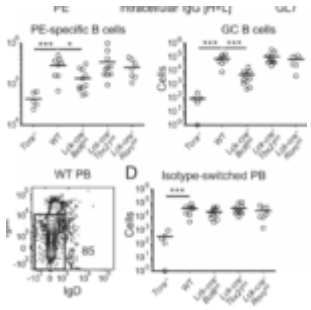
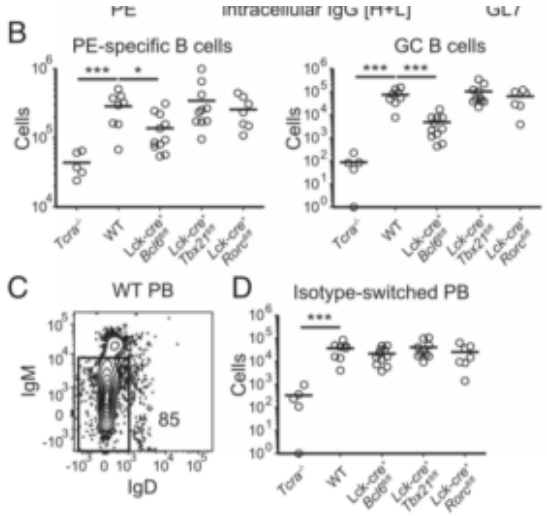
Plasmablast formation: which T helper phenotype is important?



Antigen specific B cells receive T cell help to activate proliferation and undergo isotype switching. Some activated B cells differentiate into antibody secreting plasmablasts, while others migrate to the germinal centre. In the germinal these B cells receive further signals from follicular helper (Tfh) T cells resulting in production of higher affinity isotype-switched antibodies. Early plasmapblasts require CD4 T cell help, however it is uncertain with Tfh cells or other T helper subsets such as Th1 and TH17 cells play an important role in plasmablast formation and isotype switching.



Early T cell–dependent PBs form in the absence of single dif- ferentiated CD4+

T cell subsets. (A) Identification of PE+ cells among CD90.22CD11c2F4/802Gr-12 cells (left panel) from PE-enriched spleen and lymph node samples from WT mice immunized with 2W-PE in CFA 11 d earlier. The middle and right panels show gates used to identify PE-specific PBs (B220lowIgG [H+L]high) or GC B cells (B220highCD382GL7+). (B) Numbers of PE-specific total (left panel) and GC B cells (right panel). (C) Gating and (D) numbers of IgM2IgD2 PBs. Data are expressed as the mean value and repre- sentative of two independent experiments (n = 2–6 mice/group). The p values were obtained from a one-way ANOVA and Dunnett posttest that compares all groups with the WT control group. *p , 0.05, ***p , 0.001.

Researchers from the University of Minnesota used an in vivo murine model of vaccination to assess the role of Tfh, Th1 or Th17 cells in plasmablast formation and antibody class switching. They utilized mice that lacked functional exons for the transcription factors *Bcl6, Tbx21, Rorc* and *Tcra*, which results in the absence of Tfh, Th1, Th17 ad T cells, respectively. All knock out mice resulted in the expected

phenotype, however, RORγt-deficiency also led to a small but significant reduction in Tfh cells in addition to very low levels Th17 cells compared to wild type.

As expected mice that lacked Tfh cells developed lower levels of antigen specific B cells as well as germinal center B cells. Further confirming the importance of Tfh cells in B cell development at the germinal centre. In spite of this, levels of vaccine-specific plasmablasts were unaffected by the absence of Tfh cells, as well as Th1 and Th17 cells. Illustrating that neither T helper subset is uniquely required for plasmablast formation. Finally, researchers showed that cognate interaction between B cells and T cells, as well as CD40L (T cells)-CD40 (B cells) signaling play an important role in plasmablast class switching. This was illustrated by lower levels of plasmablasts and class-switched plasmablasts in the absence of MHC II molecules and CD40L expression.

In summary, researchers showed that B cell-T cell interactions and CD40 signalling and not T helper lineage plays a role in formation and isotype switching of plasmablasts.

Article: Kotov & Jenkins, 2018. Cutting Edge: T Cell–Dependent Plasmablasts Form in the Absence of Single Differentiated CD4+ T Cell Subsets. Journal of Immunology

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