

BAFF selectively enhances the survival and effector function of CD38+ plasmablasts generated from activated human memory B cells

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The generation of Ig-secreting cells (ISC) from memory B cells occurs within secondary lymphoid organs and requires interactions between Ag-specific B cells, T cells, dendritic cells and soluble factors produced within this microenvironment. B-cell activating factor of the TNF family (BAFF, BLyS/TALL/THANK/zTNF4) is a key regulator of B-cell homeostasis. B-cell development is arrested in the absence of BAFF, while elevated serum levels of BAFF occur in some autoimmune patients. BAFF exerts its effect by binding to three receptors – BCMA, TACI and BAFF-R. To elucidate the contribution of the BAFF/BAFF receptor axis to the differentiation of B cells into ISC, we tracked the fate of human memory B cells preactivated with T-cell derived signals (CD40L, IL-2, IL-10) that were subsequently exposed to BAFF or CD40L. BAFF and CD40L significantly increased the overall number of surviving B cells. However, this was achieved via distinct mechanisms – CD40L induced proliferation of non-differentiated B-blasts, while BAFF specifically prevented apoptosis of ISC without enhancing proliferation. The altered responsiveness of activated B cells correlated with changes in expression of BAFF receptors, such that expression of BAFF-R on ISC was reduced while BCMA was induced. Importantly, BAFF increased Ig secretion. These results suggest BAFF may enhance humoral immune responses *in vivo* by promoting survival and effector function of ISC via a BCMA-dependent mechanism.

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