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**Pivotal role for the BAFF/BLyS - BAFFR axis in B-cell responses
- analysis by an anti-human BAFFR mAb, 8A7.**

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The tumor necrosis factor (TNF) superfamily ligand BAFF (B-cell activating factor from the TNF family), also known as BLyS (B lymphocyte stimulator), is a potent B-cell survival factor and co-stimulatory molecule. Our recent study suggested that BAFF/BLyS may play an important role in interactions of follicular dendritic cells with B cells through the B-cell co-receptor complex and a possibly sequential link between the T-cell-independent and -dependent B-cell responses in germinal centers (Blood 103: 2257, 2004). BAFF/BLyS binds to three separate receptors on B cells; BAFFR (BR3), TACI and BCMA. To further examine the role of interactions between BAFF/BLyS and BAFFR in B-cell responses, we have generated an agonistic anti-human BAFFR mAb, 8A7. 8A7 mAb significantly up-regulated CD54 expression, NF- κ B p52 expression, B-cell proliferation, IgG production, Pax5 expression, and CD19 phosphorylation in B cells if BCR was ligated. Importantly, their magnitudes by 8A7 mAb significantly exceeded those by BAFF/BLyS alone and weakened if BAFF/BLyS was added later. These results clearly indicate that the BAFF/BLyS and BAFFR axis plays a critically positive role in B-cell responses and BAFF/BLyS stimulation includes a negative-signal that inhibits BAFFR-mediated activation.