

## **Control mechanisms of normal and malignant B cell development**

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Canonical and alternative NF $\kappa$ B signaling plays a vital role in B cell maintenance and a variety of B cell lymphomas, and NF $\kappa$ B activity is induced by activation of two surface receptors that are crucial for the survival of mature B cells, the BCR and the BAFF-R. Using loss- and gain-of-function mutants of various components of these signaling pathways we show that canonical NF $\kappa$ B signaling is dispensable for B cell development up to the stage at which the cells become dependent on BAFF:BAFF-R interaction, and that constitutive activation of both the canonical and the alternative NF $\kappa$ B pathways can rescue B cells from BAFF-R deficiency. Mature B cells with constitutive NF $\kappa$ B activation have a prolonged lifespan, but are not driven into proliferation. However, these cells proliferate more extensively and survive better upon mitogenic activation, and are prone to lymphomagenesis

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