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B Cell Immunotherapy – Strategies to Improve the Current Clinical Candidates

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Monoclonal antibodies directed to cell surface molecules have emerged as a major strategy in the therapeutic armamentarium for the treatment of autoimmune diseases. Treatment with antibodies directed against B cell specific antigens has been efficacious in a variety of B cell derived cancers. Emerging clinical data suggests their potential use for a variety of autoimmune indications that have a B cell pathogenic component[1]. Using a mouse model that recapitulates human CD20 expression we and others demonstrated that B cell circulatory dynamics and microenvironment factors play critical roles in defining B cell sensitivity to anti-CD20 mediated in vivo B cell depletion[2-4]. As an example, blockade of BAFF/BLyS was demonstrated to synergize with anti-CD20 in removing various B cell subsets. These findings provide a basis to combine existing therapies and for developing new strategies to address the B cell pathogenic component of human autoimmune diseases. As new generations of B cell targeted therapeutics we are developing strategies to enhance known B cell killing mechanisms as well as ways to combine several mechanisms into one molecule. Examples for such strategies will be discussed with special focus on the BAFF/BLyS pathway where depleting and blocking antibodies against the BR3/BAFF-R are shown to be efficacious in B cell dependent autoimmune scenarios in mouse models[5].

Reference List

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