It is now clear that autoreactive B cells contribute to autoimmune disease both as antigen presenting cells functioning to activate autoreactive B cells and as effector cells producing pathogenic autoantibodies, and that the ablation of B cells can ameliorate diseases mediated by either autoreactive cells or autoantibodies.

Autoreactive B cells arise at both moments in B cells maturation when diversification of the B cell repertoire occurs. As B cells develop in the bone marrow, random rearrangements of variable region V, (D) and J segments, junctional insertions and random heavy and light chain combinations yield an extraordinarily large spectrum of antigenic specificities. Autoreactive B cells, estimated to be greater than 70% of the immature repertoire, are eliminated at developmental checkpoints within the bone marrow and spleen by receptor editing, anergy induction, or deletion. When follicular B cells are activated by antigen and T cell help, they can form germinal centers in which clonal populations of B cells undergo immunoglobulin variable region mutation which also generated a large frequency of B cells with autospecificities. Little is known of the mechanisms that eliminate the autoreactivity that arises in the germinal center response.

Multiple molecules involved in intracellular signaling pathways or in cellular interactions help determine the stringency of negative selection of the B cell repertoire. Learning to modulate the expression or function of these molecules represents a strategy for controlling autoreactivity while maintaining immune competence.