Human B Cell Subsets in Health and Disease: Phenotypic, Functional, and Genetic Analyses

Nicholas Chiorazzi


In mice and men, B cells in secondary lymphoid follicles can be divided into three general categories: mantle zone cells, germinal center cells, and marginal zone cells. These B cells, located in distinct areas in and around follicles, display unique phenotypic and functional characteristics. Using a combination of separation techniques, these three subsets have been isolated from human tonsillar tissues.

Phenotypic evaluation of these subsets indicates that resting mantle zone B cells display IgM, IgD, CD39, and CDw75™, and lack CD38 and CD10. In contrast, marginal zone B cells exhibit the following phenotype: IgM+ or IgG+, IgD-, CD39-, CD38-, CD10-, CDw75Int. Finally, germinal center cells are IgG+, IgD-, CD39-, CD38+, CD10+, CDw75Bri.

Immunohistochemical analyses of cryopreserved tissues indicate that cells with these three distinct phenotypes can be identified in and around the characteristic areas of a tonsillar secondary lymphoid follicle. Cells with characteristics of marginal zone B cells are located within and below the tonsillar crypts.

Functional analyses of these three tonsillar B cell subsets demonstrate that virtually all of the immune responsiveness to T cell-independent polyclonal B cell activators resides in the CD5+ mantle zone population, whereas only the CD5− marginal zone B cells respond to the thymus independent type 2 antigen TNP-Ficoll. Germinal center B cells responded only to thymus-dependent stimuli.

Molecular analyses concentrated on determining the IgV gene use in B cell subsets from normal individuals and from patients with various disease states. In normal individuals, CD5+ mantle zone B cells use Ig Vh genes of restricted repertoire that undergo limited degrees of somatic mutation, whereas germinal center cells and marginal zone B cells exhibit a less restricted V gene use that can display more extensive degrees of mutation. These data were confirmed in certain lymphoid malignancies (e.g., chronic lymphocytic leukemia and Burkitt’s lymphoma) and in autoimmune conditions (rheumatoid arthritis). Collectively, these data suggest that distinct B cell subsets may be stimulated by different types of antigens in various malignant and autoimmune conditions.

Department of Medicine, Cornell University Medical College