Title: A New Paradigm for B-Cell Activation and Tolerance

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Short Abstract:

A key step in the activation and inactivation of a B cell is the clustering of B cell receptors to form patches that move a large fraction of the receptors into a limited region (a cap). According to classical lore, this clustering is the trigger that activates the cell. This idea was supported by experiments showing that only high-valence antigen can activate a cell. These experiments were explained by the “immunon” theory that argues that a minimum amount of cross-linking is necessary to activate a cell. This theory did not take into account receptor endocytosis. We will propose a simple, new mechanism for the activation of B cell, leading to division and antibody production. The theory is based on the equilibrium between the binding of antigen on the surface of the B cell and its presentation on MHC molecules. We will show that this mechanism explains both the valence cutoff and the low and high zone tolerance. It also defines a framework to explain new results, such as the role that multiple receptors play in immune tolerance.