

Small quantities of self-antigen positively select and activate low avidity self-reactive B cells.

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We studied the development of hen egg lysozyme (HEL)-specific B cells in presence of varying amounts of HEL neo self-antigen. We found that both the quantity of antigen and the avidity of the B cell determine the fate of the self-reactive B cells. High doses of antigen delete or functionally impair “high and low avidity” B cells. Low quantities of antigen, allow “high avidity” B cells to escape negative selection and positively select “low avidity” self-reactive B cells that express few HEL-specific BCRs. A fraction of these B cells is activated and secretes self-reactive IgMs, which form immune complexes in the serum with circulating self-antigen. These results suggest that natural serum antibodies may be the result of the selection and activation of low avidity self-reactive B cells by self-antigen.

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