

Molecular Identification and Cloning of a B Cell Growth Factor : HRF Stimulates B Cell Activation and Proliferation

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As an effort to clone a novel cytokine, we established a murine erythroleukemia cell line, LK cells. The culture supernatants of LK1 cells, showed B cell stimulating activity. Purification and NH₂-terminal sequence analysis revealed that one of candidates was murine IgE-dependent histamine releasing factor (IgE-HRF), which is known to induce histamine from basophils. Recombinant IgE-HRF (rHRF) obtained from *E. coli* or 293-transformed embryonal kidney cells was tested for B cell stimulating activity. Both rHRFs stimulated B cell proliferation in a dose-dependent manner. However, boiling or anti-HRF antibody abolished B cell stimulatory effects of rHRF. rHRF showed strong synergistic effects

with IL-2, IL-4, and IL-5 for B cell activation, having maximal activity in the presence of anti-CD40 antibody. rHRF increased MHC class II expression of B cells. It also increased immunoglobulin (Ig) production from B cells. Polymyxin B (PMB), a neutralizing peptide antibiotic of LPS, treatment did not reduce the activities of rHRF. In addition, FACS analysis using PE-conjugated rHRF showed that HRF bound to B cells. rHRF up-regulated the expression of IL-1 and IL-6 in B cells. *In vivo* administration of rHRF or the cDNA for rHRF increased total and antigen-specific Ig synthesis. Taken together, these results indicate that HRF stimulates B cell activation and function.