CHARACTERIZATION OF AN ANTI-MOUSE CLASS I MHC MONOCLONAL ANTIBODY WHICH INHIBITS THE PROLIFERATION OF MOUSE LGL LINES

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A monoclonal antibody (AH-2) which inhibited the proliferation of IL-2-dependent cell lines has been developed. AH-2 was raised in rats immunized with IL-2-dependent large granular lymphocytes (LGL) followed by screening by the capacity to inhibit the growth of LGL with IL-2. Various evidence indicated that AH-2 recognized an epitope of H-2D^d class I MHC antigen distinct from that recognized by allo-anti H-2D^d monoclonal antibody: (1) AH–2 immunoprecipitated 46KD and 14KD molecules that were non-covalently associated with the cell surface. (2) The precipitation of the molecules was specifically abolished by preclearance with allo-anti H–2D^d antibody, although the binding of AH–2 to the cell surface was not affected by allo-anti H–2D^d antibody as judged by flowcytometry, and (3) AH–2 reacted to whole lymphocytes from H–2^d mice without reacting to those from other H–2 haplotypes at all.

AH–2 significantly inhibited the IL–2–dependent proliferation of LGL lines from H–2^d BALB/c mice in a dose dependent fashion but not the CTLL line from H–2^b B6 mice, eliminating the possibility that the inhibitory effect was due to nonspecific toxicity. AH–2 also inhibited the proliferation of a B cell line (DW34/5) induced by both IL–5 and IL–7. In contrast, the proliferation of myeloid cell lines (FDC–P2 and IC–2) by IL–3 and GM–CSF was not affected at all by AH–2 despite the positive binding to these cells. Using primary BALB/c spleen cells, AH–2 inhibited the IL–2–induced proliferation of fresh spleen cells without affecting their IL–3–induced proliferation.

Binding of labeled IL–2 to the IL–2–dependent LGL was not affected by AH–2, indicating that the inhibitory effect was not due to interference with the process of IL–2 binding to IL–2 receptors (R) on cells. Furthermore AH–2 failed to immunoprecipitate IL–2R from the cells treated with labeled IL–2 and a chemical cross-link. These results thus strongly suggested that the growth-inhibitory effect of AH–2 antibody was exerted through interference with the signal transduction process by the cytokines in the cells rather than through the inhibition of the ligand binding on the cell surface receptors.