Introduction

Cytotoxic lymphocytes constitute an important defence mechanism against transformed cells, virus infected cells, parasites and some invading microbes. Two classes of lymphocytes participate in cytotoxic reactions. Cytotoxic T cells mediate an antigen specific adaptive cytotoxicity which is restricted by class I Major Histocompatability Complex (MHC) antigens. Natural killer cells form the other class which unlike the T cells, mediate cytotoxicity without any prior sensitization and are not restricted by class I MHC antigens.

NK cells activity can be augmented by a number of cytokines such as interferons, interleukins etc. Interleukin-2 (IL-2) is a T cell derived lymphokine which is produced primarily by activated T-helper cells in response to antigens or mitogens. Co- culture of mouse spleen cells and human peripheral blood lymphocytes with IL-2 leads to generation of lymphokine activated killer (LAK) cells. The precursor population for these cells are primarily the NK cells. These cells are characterized by their ability to lyse a broader spectrum of tumor targets which include both NK sensitive and NK resistant tumors. Like NK cells, LAK cells are also not restricted by class I MHC antigens.

In spite of the MHC I non restriction, target cell levels of class I MHC antigens regulate their sensitivity to NK/LAK cells. Several reports suggest an inverse relation between the levels of the class I MHC antigens on the target cells and their sensitivity to lysis by NK/LAK cells, though exceptions to this rule are known. Mechanism by which class I MHC antigens on target cells regulate their susceptibility to NK/LAK lysis remains unclear. Two possibilities which have been proposed in this regard are, (a) class I MHC antigens may send an inhibitory signal to the effector cells thereby resulting in poor target lysis, and (b) class I MHC antigens may interfere in the effector-target interaction, leading to a depressed target lysis. Experimental evidence to support either of these proposals has not yet come.

The present study was aimed at understanding the influence of target cell class I MHC antigens on their susceptibility to lysis by LAK cells. Panels of five murine and five human tumor cell lines were studied in detail for this purpose. The direct effect of class I MHC antigens on tumor cell susceptibility was studied by (a) correlating the basal expression of class I MHC antigens on different tumor cells with their basal susceptibility to LAK lysis, (b) studying the effects of target cell class I MHC antigen modulations on LAK susceptibility and (c) correlating the influence of changes in class I MHC antigens and the ability of tumor cells to competitively inhibit the lysis of other tumor targets cells.

Our studies show that the hypothesis of inverse relation between class I MHC levels on tumor cells and their susceptibility to LAK lysis can not be generalized. The results of the cold target competition experiments suggest the existence of distinct subpopulations of LAK cells (mouse system) as well as multiple target structures (human system). In addition, IFN-g modulation of performance of tumor cells in competition assays, support the proposition that class I MHC antigens may interfere with the recognition of target structures by LAK cells.