INTRODUCTION
Survival and self perpetuation are the central forces of life. Immune system developed in face of need for self perpetuation and defense from pathogens and tumors. In the same vain, microbes and tumor cells must devise ways to counteract the immune system to ensure their survival. It is crucial that we understand the tactics used by microbes and tumors to foil the attempts of the immune system and escape destruction, because only then will we be able to devise strategies to come to the aid of the immune system in fighting infections and cancer.

Natural killer (NK) cells constitute an important component of the immune surveillance anti-tumor mechanisms of the immune system. Utility of NK cells may be two fold. NK cells may recognize and kill tumor cells as and when the latter originate by oncogenic transformation of normal cells, much before cytotoxic tumor specific T-cells can be recruited against them. Secondly, those tumor cells which try to escape T-cell immune surveillance by down regulating the expression of their MHC class I antigens, may become susceptible to NK cells since a class of NK cells can specifically lyse target cells lacking MHC I expression. There is not much information available in the literature about any mechanisms that tumor cells might utilize to block the activity of NK cells, and the present study was designed to explore this important question.

We report in this thesis, our findings which point out the existence of several mechanisms that might be utilized by tumor cells to inhibit NK cell system. In summary, these include (a) secretion by tumor cells of some suppressor factor(s) which blocks the activation of NK cells by interleukin-2 (IL-2) and also exerts an anti proliferative effect which is non specific and extends to T and B cell proliferation also, and (b) tumor cell induced
upregulation of the expression of isotypes of Ly 49 molecule, a member of killer inhibitory receptor (KIR) family, on NK cells. Enhanced expression of KIRs may render NK cells more susceptible to inhibition by tumor cell expressed class I MHC molecules, loaded with tumor derived peptides.

We also found that paraformaldehyde fixed tumor cells can boost NK activation in response to IL-2 and the boosting effect appears to have a degree of tumor specificity. This suggests that specific antigen induced activation, which is characteristic of adaptive immune system, may also be associated with NK cells, albeit to a lesser extent. This is an interesting finding specially since NK cells are in general not considered to be a part of the adaptive immune system comprising T and B lymphocytes. Finally, tumor cell expressed MHC I antigens play a crucial role in determining their susceptibility to lysis by NK cells. We have demonstrated that the masking of MHC class I antigens by antibodies, at a time when NK cells are being activated by IL-2, results in a poor activation of NK cells. Significance of these results is not yet clear but they point to an important role of MHC I antigens in regulation of NK cell activation process. KIRs are NK cell receptors for MHC I molecules. Our demonstration of regulation of KIR expression by tumor cells, as well as the role of MHC I molecules in NK activation may have an important bearing on the understanding of interactions between NK and tumor cells.