SUMMARY

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NK cells have a prominent role in immunity against malignancy. In the present study, efficacy of NK cells to mount cytotoxic response against fibrosarcoma cells *in vitro* has been studied and adoptive transfer experiments have been carried out to test their effectiveness in curbing malignant growth *in situ* .

To begin with , the number of NK^N and NK^T cells obtained from spleen of swiss albino mice were determined. Tumour bearing mice contained four times more NK cells than normal mice. The increase in the number of NK cells seem to have some correlation with the development of tumour.

Kinetics of blastogenesis and DNA synthesis of NK^N cells after treatment with 50µl of gIL-2 and different doses like 200U, 100U, 50 U, and 10U of rIL-2 were studied *in vivo*. Maximum number of blasts were observed at 24hrs after treatment with 50µl of gIL-2 and 100U of rIL-2. The blasts also incorporated maximum amount of ^{3}HTdR. 50µl of gIL-2 was found to have equivalent activation capacity as 100U of rIL-2.

Difference in cytotoxicity of NK^N cells and NK^T cells before and after IL-2 activation was tested in a ^{51}Cr release assay. Even without activation, NK^N cells exhibited minimal cytotoxic response. This minimal cytotoxic value of NK^N cells however increased four times at 24 hrs of IL-2 activation. NK^T cells as such were found to be twice as cytotoxic than NK^N cells. This increased marginally by IL-2 treatment

for 24hrs. NK^T cells being in continuous exposure to tumour cells are likely to be sensitized and do not get boosted further with IL-2 treatment. At 48hrs of IL-2 activation, the cytotoxic values of both NK^N cells and NK^T cells came down to minimal values.

Besides being spontaneously cytotoxic, NK cells also bear Fc receptors which suggests their participation in ADCC type of reaction against tumour target cells. NK^N cells showed very high index of ADCC, and IL-2 could do little to increase this index. However, NK^T cells showed lower index in ADCC which increased marginally after IL-2 treatment. This lowered ADCC response of NK^T cells indicated the possibility of some suppressor phenomenon operative in tumour bearing hosts. However, as NK^T cells perform well in spontaneous cytotoxicity and some increment with IL-2 treatment, depression of ADCC index may be accounted for by loss of Fc receptors of these cells. Demonstration of anti TAA antibody in serum of tumour bearing mice indicated their possible role in ADCC type of reaction *in vivo* rather than only acting as blocking factors.

^{3}HTdR- labelled IL-2 activated syngeneic NK^N cells were found to home preferentially at the tumour site. Highest radioactive count was obtained from the centre of the tumour at 12 hours of adoptive transfer with second highest count at the periphery of tumour at the same hours. Reasonable incorporation of radioactivity was observed in other tissues studied, with least incorporation at the skin site. Besides, the highest count in tumour, significant level of count from liver, spleen and mesenteric lymph nodes and skin reflect the preference of these cells for organs that harbour them. Relatively high count from kidney may be the released radioactivity that has found its way to the kidney in the process of excretion.

Study of homing of NK cells at the tumour site suggested the possibility of using NK cells for therapeutic purpose.

Firstly, low dose IL-2 intravenous infusions could activate the resident NK cells in tumour bearing hosts and effectively curbed the growth of tumours. Secondly, adoptive transfer of NK^N cells and NK^T cells from syngeneic mice was a lot more effective in curbing tumour growth especially when used after activation with IL-2. Increasing the number of IL-2 activated NK^N cells to two folds, followed by weekly IL-2 injections showed very effective restriction of tumour growth and also increased the survivality of the tumour bearing animals.

After surgical removal of tumour load, adoptive transfer of IL-2 activated NK^N cells followed by weekly IL-2 injections successfully inhibited tumour recurrence in 92.3% cases, thereby suggesting the use of this protocol for better therapeutic purpose.