

IN VIVO EFFECT OF MGN-3 ON RAT NK CELL ACTIVITY

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Abstract

We determined In Vivo effect of MGN-3 on rat NK cell activity. Sprague-Dawley rats were fed MGN-3 and NK cell activity were examined at two weeks post treatment. MGN-3 effect was shown to be dose dependent; NK activities were 142%, 130%, and 119% of controls at concentrations of 50, 5 and 0.5 mg/kg/day respectively.

Augmentory effect of MGN-3 was detected as early as four days post treatment (132% of control) at high concentration of 50 mg/kg/day. Augmentation of NK activity by MGN-3 resulted from enhanced lytic effect of NK cells, which was dependent of NK percentages. Inter sex difference toward MGN-3 effect showed that female rats responded better than males toward the immunomodulatory effect of MGN-3. The increase in activities were 162% for females and 135% for males. We conclude that MGN-3 is a potent biological response modifier (BRM) with possible anticancer effects.

Introduction

Natural Killer (NK) cells have received considerable attention because of their potential role in resistance to cancer (Herberman, 1983). The role of NK cells in resisting the development, progression and spread of induced or spontaneous tumors is still unclear. NK cells are considered to be a possible first-line of defense against tumor development. However, early work has demonstrated suppression of NK activity in tumor bearing mice (Ghoneum, et al, 1987, 1989, 1991; Ehrlich, et al, 1983; Gorelik & Herberman, 1981). As a result, many attempts have been made to augment NK activity by the use of biological response modifiers (BRM) as anticancer agents. This work was undertaken in order to investigate the NK augmentory effect of a new BRM known as MGN-3.

Experimental Procedure

Treatment of Rats

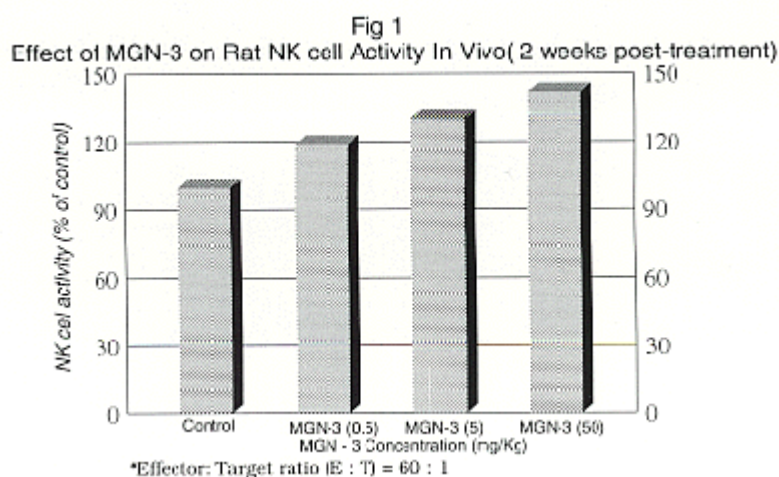
The animals used in this study were two years old Spraque-Dawley rats. Rats were housed five per cage for one week prior to orally feeding with MGN-3. Rats were divided into four groups (5-7 rats in each group) according to the concentration of MGN-3. Group 1, 0.5mg/kg; Group 2, 5 mg/kg; Group 3, 50mg/kg and Group 4 served as control with no MGN-3. MGN-3 was freshly prepared and mixed with rat food everyday. Rats were fed on MGN-3 for two weeks then 5cc were drawn by cardiac puncture and used to examine NK activity and percentage of NK cells. In another set of experiments, male and female rats were examined separately for their response toward immunomodulatory function of MGN-3.

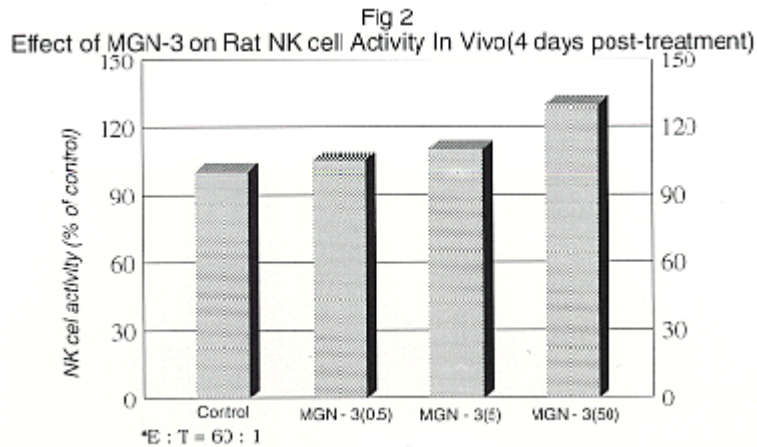
NK cell activity was examined by the standard 51Cr-release assay.

Results

Augmentation of NK cell activity by MGN-3

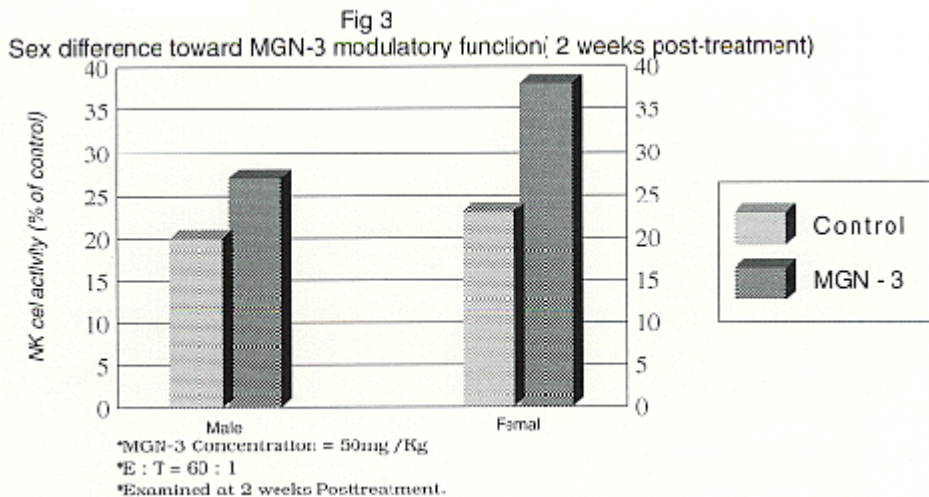
Figure 1 summarizes the data showing the augumentory effect of MGN-3 on NK cell activity. Rats fed MGN-3 (0.5 mg/kg) showed increased NK cell activity (119% of control). NK cell activity was further increased (130%) in rats given 5 mg/kg MGN-3, while the peak response was observed in rats fed 50 mg/kg where their NK cells showed 142% of control. (Figure 1). Augumentory effect of MGN-3 was detected as early as four days (132% of control) but only at high concentration of 50 mg/kg. (Figure 2).





Inter sex difference

Male and female rats were examined separately for their response toward the immunomodulatory function of MGN-3. Results in Figure 3 showed differential response between female and male rats toward augmentory effect of MGN-3. Female rats had 162% increase in their NK cell activity post treatment with MGN-3, while male rats had 135% increase.



Effect of MGN-3 on NK cell subset

NK cell subset examined by flow cytometry showed no change in their percentages post treatment with MGN-3 in comparison to control group .

Discussion

In the present investigation, we demonstrated that MGN-3 is a prominent BRM, as manifested by enhancing NK cell activity. The augmentory effect was detected as early as four days post treatment . In addition, different concentrations of MGN-3 caused enhancement of NK activities that was significantly increased at 50mg/kg. It is interesting to note that, MGN-3 enhances NK activity without increasing the percentage of NK cells, thus it appears that MGN-3 may augment NK cells and other cell population that may have anticancer activity such as Cytotoxic T Lymphocytes (CTL) .

The mechanism by which MGN-3 enhances NK activity is not fully understood. Recent study (Ghoneum et al, 1996) show that MGN-3 significantly increases interferon (IFN) production of human Peripheral Blood Lymphocytes (PBL) . IFN has proven to be a potent NK modulator. Further studies are needed to find out the source of PBL that produce IFN, whether T cells or NK cells. Some biological agents can induce IFN production from NK cells, and it is the production of IFN which produces self-activation of NK activity. Among the IFN stimulators studied, bacteria appear to have specificity for IFN production in the NK population alone (Djeu 1983) .

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