AUGMENTATION OF PROLIFERATIVE RESPONSES OF MOUSE SPLENOCYTES BY LOW-DOSE X-RAY IRRADIATION

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ABSTRACT

To elucidate the hormetic effect on the immune system, we studied the mitogen-induced proliferation of mouse splenocytes after low-dose X-irradiation. Major results obtained were as follows; Proliferative response of mouse splenocytes induced by Con A or PHA was augmented by a single whole-body irradiation with 2.5 or 5 cGy, and its optimal concentration of Con A rose to 4 μg/ml from 2 μg/ml in the sham-irradiated control group. Furthermore, irradiation with 5 cGy prevented mouse splenocytes from declining of mitogen responses by subsequent 4 Gy irradiation.

INTRODUCTION

Radiation hormesis is a new concept for radiation biology. The concept is that low-dose irradiation stimulates bio-functions[1]. A phenomenon in which low-dose irradiation stimulates mitogen-induced proliferation of human T-cells in in vitro experiments has been reported[2]. In general, however, it was well known that immune cells are easily injured by X-ray irradiation, since they are highly sensitive to X-ray. To verify the hormetic effect of low-dose whole-body X-ray irradiation, in vivo, in cells of immune system, we studied effects on the proliferative responses of mouse splenocytes induced by various mitogens. The results obtained are reported in this paper.

METHODS

Male BALB/c mice of 7 weeks old were given a single whole-body X-ray irradiation of 2.5 or 5 cGy at an irradiation dose rate of 1 cGy/min. HITACHI X-ray irradiator MBR-1505R was used. Another expriment was made, where the dose was divided over 5 days, 1 cGy/day. Spleen was taken out 4 hours after the single irradiation or 4 hours after the final irradiation in the divided irradiation case. Cell suspensions were prepared.

Splenocytes were cultured on RPMI-1640 medium containing 5% fetal bovine serum under an environment of 37°C and 5% CO_2, in the presence of 1-16 μg/ml of Concanavalin A (Con A) or 25 μg/ml of Phytohemagglutinin (PHA) or Lipopolysaccharide (LPS), for 44 hours. Next, ^{3}H-thymidine was added to the culture, and cultivation was continued for 4 hours. Radioactivity taken into the cells was measured by a liquid scintillation counting system.

Some animals were irradiated with 4 Gy 21 days after the low-dose whole-body irradiation of 5 cGy. Spleen was taken out 4 hours or 24 hours after the last irradiation. Response of splenocytes to mitogen was examined in the same manner.

The controls of these experiments were mice for which the low-dose irradiation operation was substituted with a sham operation.

CONCLUSIONS

To conclude, our major results are as follows;

(1) As shown in Fig. 1, proliferative response of mouse splenocytes induced by Con A or PHA was augmented by a single whole-body irradiation with 2.5 or 5 cGy, whereas the proliferation induced by LPS was augmented only by irradiation with 2.5 cGy. And, the fractionated whole-body irradiation

exhibited less effect on PHA-induced proliferation than a single irradiation.

(2) Although the data is not shown in the paper, low-dose whole-body irradiation with 5 cGy prevented mouse splenocytes from declining of mitogen-induced proliferation by subsequent high-dose irradiation with 4 Gy.

(3) As shown in Fig. 2, Con A-induced proliferation of mouse splenocytes was augmented by an irradiation with 2.5 cGy over the range of 1-16 μg/ml of Con A. Its optimal concentration of Con A rose to 4 μg/ml from 2 μg/ml in the sham-irradiated control group.

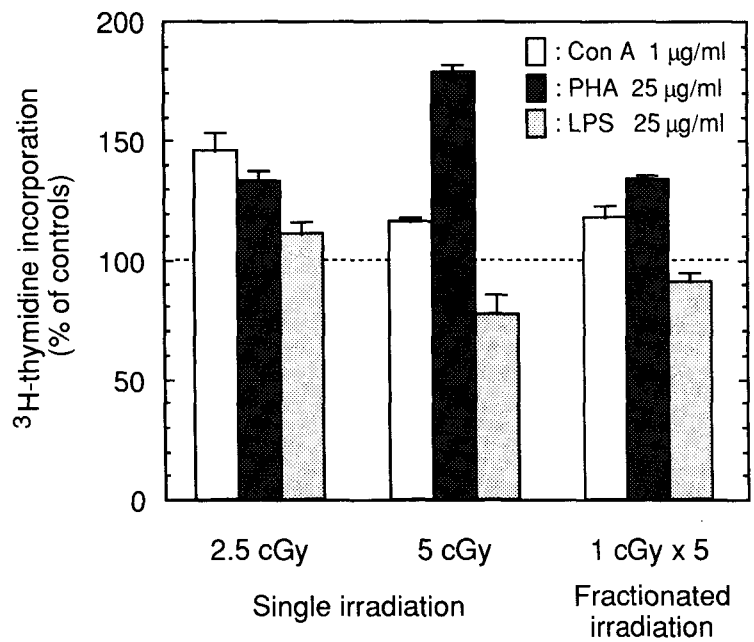

Fig. 1. Effect of a single whole-body X-ray irradiation and fractionated irradiation on mitogen-induced proliferation of mouse splenocytes. The number of mice per experimental point is 13.

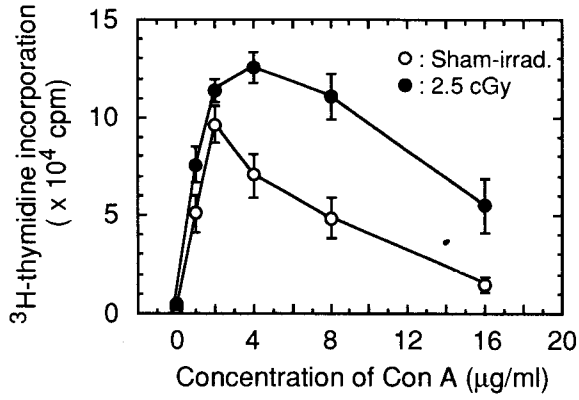

Fig. 2. Effect of a single whole-body X-ray irradiation (2.5 cGy) on Con A-induced proliferation of mouse splenocytes, as a function of concentration of Con A. The number of mice per experimental point is 12.

The augmentation of the response to mitogen in mouse splenocytes this time was also observed in F344/NSlc rats in the past[3]. We considered significant augmentation of mitogen-induced proliferation of mouse splenocytes by low-dose whole-body X-ray irradiation is one of hormetic effects. And, our finding suggests some functional alteration in splenocytes from low-dose irradiated mice.

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