Dose Rate Dependence of Radiation Induced IgG Membrane Receptor Alteration [1]

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Mouse lymph node lymphocytes are irradiated at different dose rates and the B-cell receptors to anti IgG are tested. The expression of receptors is inhibited by irradiation. It is shown that the effectiveness of irradiation increases with decreasing dose rate suggesting that membrane damage may be important for situations of chronic irradiation or implant radiotherapy.

The effect of radiation on the immunological system is expressed by the alteration of its functions. These alterations may be caused by cell death or by modifications in the behaviour of one or more cell populations. For example, the biological consequence of membrane alterations in the lymphoid system will alter important events in regulation of effector mechanisms of the immune response such as antigenic recognition, cell cooperation, migration pattern, adhesiveness and mobility. Irradiation effect on lymphocytes with alterations in the membrane are known to take place, producing inhibition of cap formation [2], expression of Fc receptors [3], temporal changes in Con A receptors [4], and transient loss of stainability of irradiated B cells labelled with anti-immunoglobulin sera [5]. The present work studies the importance of dose rate in the radio-induced changes at the membrane level using this last model.

Mouse lymphocytes were obtained from cervical and axillary lymph nodes of 2 month old RK mice. The nodes were teased in Hank Balanced Salt Solution (HBSS). After Passing through gauze and washing, the cells were adjusted at 5 x 10^7 cell/ml and irradiated with an X-ray source (Phillips type PW 1140/00), operated at 80 KV, with 3 mm of pyrex glass as filter, and at dose rates of 0.9; 4.5 and 27.6 rad/min. The process was carried out in the cold. Then irradiated and sham irradiated cell suspension were incubated for 10 minutes at 37 °C in a water bath. After incubation, the cells were spun down, and the pellet resuspended in 0.1 ml of rabbit antimouse IgG serum (Miles Yeda Rehovot Israel). The labelling procedure was carried out at 4 °C for 20 minutes with the antisera diluted 1:400. Subsequently, the cells were washed 3 times and the pellet resuspended in 0.1 ml of goat antirabbit IgG conjugated with fluorescein isothiocianate (second antibody) after incubation (4 °C, 20 min) and washing (3 times). The percentage of fluorescent cells were determined with a fluorescence microscope under standard conditions. The results were expressed as a percentage of IgG+ cells in the irradiated suspension over the control non-irradiated value.

We have previously reported that when IgG positive cells are irradiated and incubated at 37 °C, a radioinduced modulation of IgG receptor molecules takes place [5]. There is first a disappearance phase dependent on temperature, metabolic energy and cytoskeletal structure followed by a reappearance phase with only temperature requirements [6]. In the series of experiments reported here the effect of dose rate on the radiation effect was tested. As can be seen in Fig. 1 the effectiveness of irradiation increases with a decreasing dose rate. This last characteristic of the phenomenon may be explained.

![Fig. 1. Dose rate dependence of radiation induced loss of s-IgG expression. Cells were irradiated at a dose rate 0.9 (---), 4.5 (-----) and 27.6 (----) rad/min. and incubated for 10 min at 37 °C. Each point represents the mean of 3 to 7 independent experiments ± standard deviation. Sham irradiated controls are represented in the 0 dose point and showed 19.7 ± 1.5% labelled cells.](image-url)
assuming that the primary target is the membrane, and the effect is enhanced by oxidative chain reactions that take place in the lipid components, as has been postulated to be the case for irradiated artificial phospholipid membranes [7] and lipid micelles [8]. The cell being a more complex structure it is not surprising that the expression of the damage, in our case the transient loss of IgG receptors, highly depends on cytoplasmic structures, as was postulated earlier using another experimental model [9].

A similar dose rate effect has been reported recently for hemolysis and K⁺ release in erythrocytes [10]. These findings taken together, open the possibility that small alterations of the immune function, often nondetectable, appear after therapeutical or accidental exposures to low doses of irradiation given at a low dose rate. This may result in a loss of surveillance mechanism against tumor growth, or in a flaring-up of an autoimmune disorder “a posteriori”.