

Effects of Low Dose Radiation on the Main Immune Parameters in Healthy Mice

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Objectives: We investigated the effect of low dose ionizing radiation on the quantitative and qualitative changes of major immune parameters in healthy mice. **Methods:** To study radiation effects on various lymphocyte subsets, mice were irradiated with different acute doses (0.01, 0.05, 0.1, 0.5, 1, 2 and 4 Gy) of Co60- γ rays. Animals were killed at different time points after irradiation, and splenocytes were isolated. Quantitative and functional changes were determined in the Thelper (CD3+CD4+), Tcytotoxic (CD3+CD8+), Treg (CD4+CD25+), NK (NK1.1+) and DC (MHCII+CD11c+) cells. The ratio of various lymphocyte subsets was determined by flow cytometry. The apoptotic rate of the cells was determined by TUNEL assay 4 hours after the in vivo irradiation of the animals. The proliferative response of lymphocytes to non-specific stimuli (Concanavalin A) was determined. The T-cell activation potential of irradiated DCs was studied in mixed lymphocyte culture. Cytokine expression of irradiated lymphocytes was investigated by real-time RT-PCR. **Results:** Flow cytometry data show that low dose irradiation affects the main compartments of T-cell immunity, but ample differences exist in the radiosensitivity of various cellular compartments, with the CD3+CD8+ compartment being the most radiosensitive and the CD4+CD25+ compartment being the most radioresistant. Certain lymphocyte subsets presented hypersensitivity to radiation at low doses (10, 50 and 100 mGy). The proliferation rate of ConA stimulated lymphocytes was either not affected or slightly depressed after irradiation with low doses. Higher doses led to a marked decrease in lymphocyte proliferation. Spontaneous apoptosis rate was around 3% and doses up to 0.1 Gy did not change apoptosis frequency. A steep increase in the apoptotic rate was detected after irradiation with doses of 0.5 Gy or above. The capacity of splenic DCs to activate allogeneic T cells was investigated three days after the irradiation of the animals. Preliminary data showed, that an increased T cell activation could be detected, if DCs were irradiated with low doses. The ratio of IFN- γ expression in the ConA stimulated versus unstimulated lymphocytes showed a dose-dependent decrease. **Conclusion:** The experiments suggest that even low doses of ionizing radiation might have substantial impact on various compartments of the immune system. Different lymphocyte subpopulations react in very different ways to irradiation, which clearly point to a heterogeneous radiation response of the immune cells mostly involved in the anti-tumor immune response.