Low dose radiobiological studies have shown effects, observable in cells that are in the vicinity of irradiated cells, which are due to the release by irradiated cells of several cellular mediators among which Reactive Oxygen and Nitrogen Species (ROS, NRS), and cytokines are likely to play a key role. Despite the large number in the literature of studies on bystander effects induced by ionizing radiation the results are still conflicting, and further studies are therefore needed on the possible underlying mechanisms. The dependence on radiation quality deserve particular attention because bystander mechanisms are probably more important with high-LET irradiations, where many cells are not hit (bystander). Moreover, due to the different patterns of energy deposition, the cellular response to low LET and high LET radiation can be different. Understanding whether these cells can contribute to the adverse effects of low radiation doses in a radiation quality-dependent fashion might have important implications in risk estimates for both cancer induction and non-cancer diseases. In this context, we addressed to the study
of the bystander induced cell killing after incubation with “conditioned medium” from primary human fibroblasts irradiated with 0.1 and 0.5 Gy of α-particles or γ-rays. Medium transfer was performed after 1h incubation from irradiation. The results have confirmed a reduction in clonogenic survival after incubation with medium from α-irradiated cells, independently of the dose; similar results were obtained after γ-irradiation, although in this case a slight dose dependence could be envisaged. Interleukin-6 (IL-6) and Interleukin-8 (IL-8) levels were measured in the conditioned medium collected up to 20 hours after irradiation with α-particles and γ-rays in the dose-range of 0.1-1.0 Gy, in parallel with evaluation of their receptor expression in irradiated and bystander cells. Concerning IL-6, we observed the strongest modulation of its release at 20 hours post exposure, whereas IL-8 release was significantly increased at shorter times, i.e. 5-7 hours after irradiation. The expression of their receptors was modulated in both irradiated and bystander cells, although it is not apparently correlated with the relative interleukin release. In order to investigate possible correlation between NRS and cytokines as early and late mediators in the signalling chain leading to bystander induced cell killing, experiments were performed using c-PTIO, a well known scavengers of RNS. In these experiments conditioned medium taken after 1h or 5h from α-particle irradiated cells was used. The results obtained after 5h in the absence of c-PTIO didn’t show any further decrease in clonogenic survival of bystander cells. The presence of the scavenger seems to reduce, the bystander induced cell killing indicating that RNS are involved in the transduction of the bystander signal. Experiments, performed with both c-PTIO and DMSO, a scavenger of hydroxyl radicals, showed that RNS and ROS play a role in some cytokine pathways (interleukins release and their receptor expression) activated by irradiation.

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