Non-irradiated Bystander Fibroblasts Attenuate Damage to Irradiated Cancer Cells

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Introduction and aim: Radiation-induced bystander effect is described as a different type of responses, displayed by non-irradiated neighbouring cells, induced by signals transmitted from irradiated cells. These responses in bystander cells include genetic damage (SCE, micronuclei, genomic instability), apoptosis induction and other non-necessarily detrimental effects. Bystander effect might bear some implications for coexisting normal cells non-targeted by cancer radiotherapy. However, it is possible, that bystander effect can act in opposite direction, and non-irradiated cells can in some way influence the response of targeted cells. Our experiments in vitro were aimed at evaluating this concept. Materials and methods: Lung Lewis carcinoma cells (LLC), growing in monolayer in 6-well plates, were irradiated with 2 or 4 Gy dose of X-rays (using a 6 MeV accelerator suited for therapeutic purposes). After irradiation, the cells were co-cultured with non-irradiated NIH3T3 mice fibroblasts, the latter growing (in monolayer) in special inserts. Such system allowed separation of the two kinds of cells, with medium freely circulating through the separation membrane (pore size 0.4 μm). Thus, species released by irradiated cells could be transmitted to non-irradiated neighbours and vice versa. Results and discussion: The bystander effects, caused by irradiated cancer cells, which were observed in non-targeted fibroblasts included dose-dependent elevation of micronucleus and apoptosis frequency indicating that irradiated cancer cells can induce damage in normal fibroblast cells. However, irradiated LLC cancer cells co-incubated with fibroblasts presented lower levels of this type of cytogenetic damage and apoptosis in comparison with LLC cells incubated after irradiation without fibroblasts on inserts or without inserts at all. Our current studies attempt to search for agents and signalling responsible for observed bilateral bystander effects.

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