

Bystander effectors of chondrosarcoma cells irradiated at different LET impair proliferation of chondrocytes

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While the dose-response relationship of radiation-induced bystander effect (RIBE) is controversial at low and high linear energy transfer (LET), mechanisms and effectors of cell-to-cell communication stay unclear and highly dependent of cell type.

In the present study, we investigated the capacity of chondrocytes in responding to bystander factors released by chondrosarcoma cells irradiated at different doses (0.05 to 8 Gy) with X-rays and Carbon ions. Following a medium transfer protocol, cell survival, proliferation and DNA damages were quantified in bystander chondrocytes. The bystander factors secreted by chondrosarcoma cells were characterized.

A significant and major RIBE response was observed in chondrocyte cells (T/C-28a2) receiving conditioned medium from chondrosarcoma cells (SW1353) irradiated with 0.1 Gy of X-rays and 0.05 Gy of C-ions, resulting in cell survivals of 36% and 62%, respectively. Micronuclei induction in bystander cells was observed from the same low doses. The cell survival results obtained by clonogenic assays were confirmed using impedancemetry. The bystander activity was vanished after a heat treatment or a dilution of the conditioned media. The cytokines which are well known as bystander factors, TNF-alpha and IL-6, were increased as a function of doses and LET according to an ELISA multiplex analysis.

Together, the results demonstrate that irradiated chondrosarcoma cells can communicate stress factors to non-irradiated chondrocytes, inducing a wide and specific bystander response related to both doses and LET.