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

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Chondrosarcoma irradiation and bystander response in normal cartilage

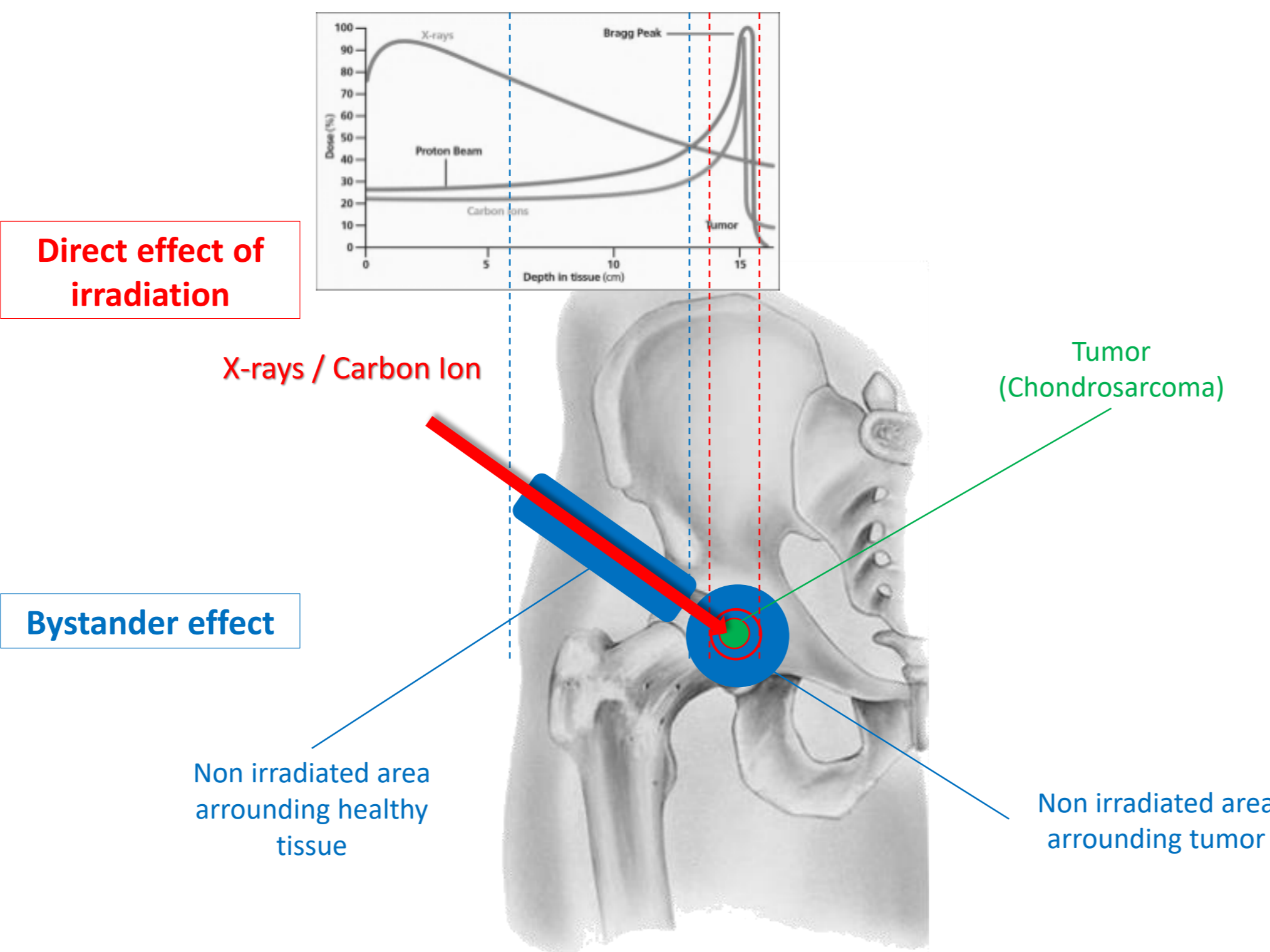
The bystander effect is defined to occur in close proximity to irradiated cells, to induce a biological response in non-irradiated cells, and this effect induces a cellular response typically associated with direct radiation exposure.

While hadrontherapy allows a better precision of the radiation towards the tumor, intercellular communication triggered by the irradiated damaged cells could occur, counter-balancing such physical accuracy of accelerated ions by a biological imprecision which may represent an important cause for radiation side-effects. 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.

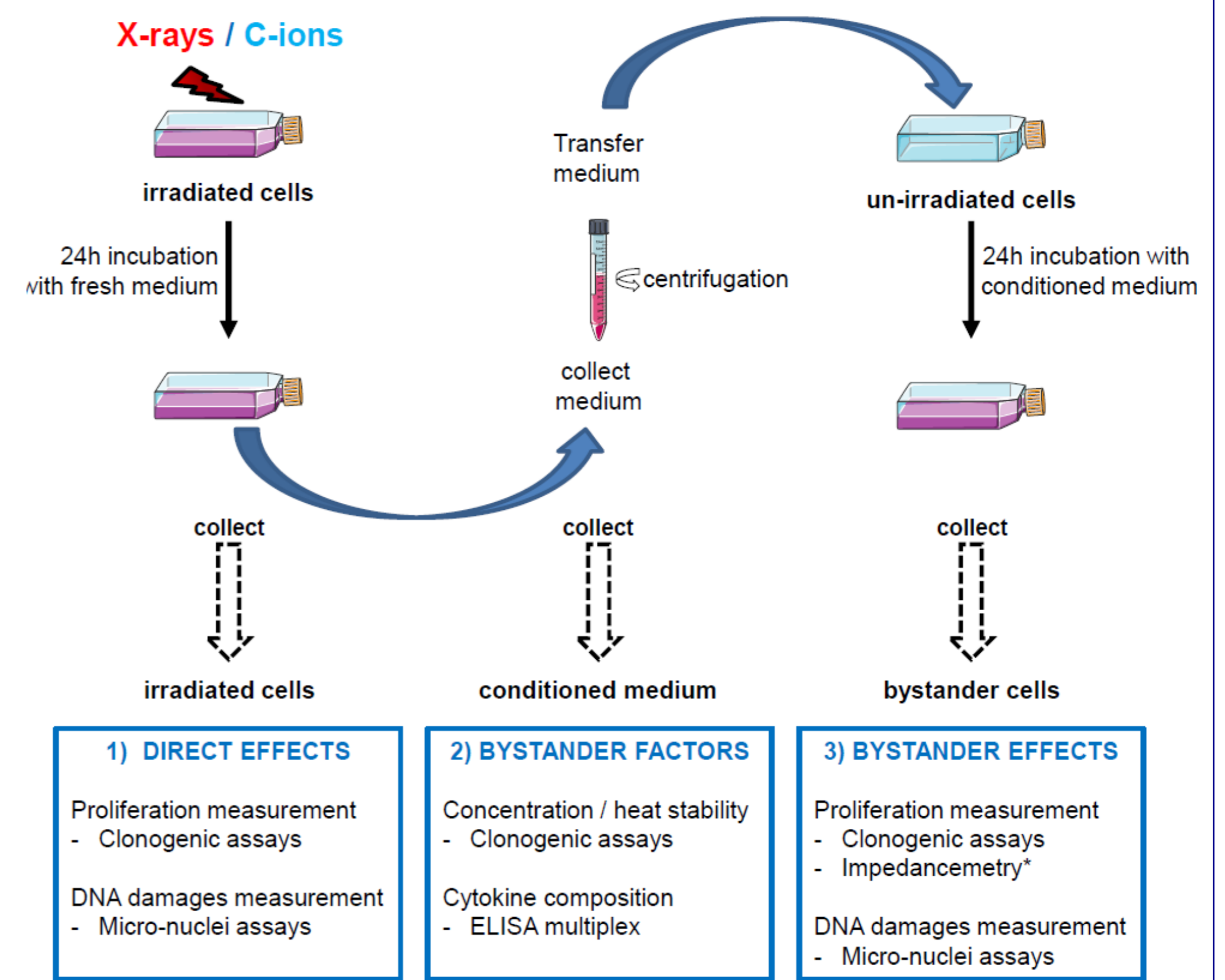
Here, we investigated the capacity of chondrocytes (T/C28-A2 cells) in responding to bystander factors released by chondrosarcoma cells (SW1353 cells) irradiated at different doses (0.05 to 8 Gy) with X-rays and Carbon ions.

In this study, 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.

Reference: Lepleux et al. *Journal of Cell Communication and Signaling* 2019 Mar 22. doi: 10.1007/s12079-019-00515-9



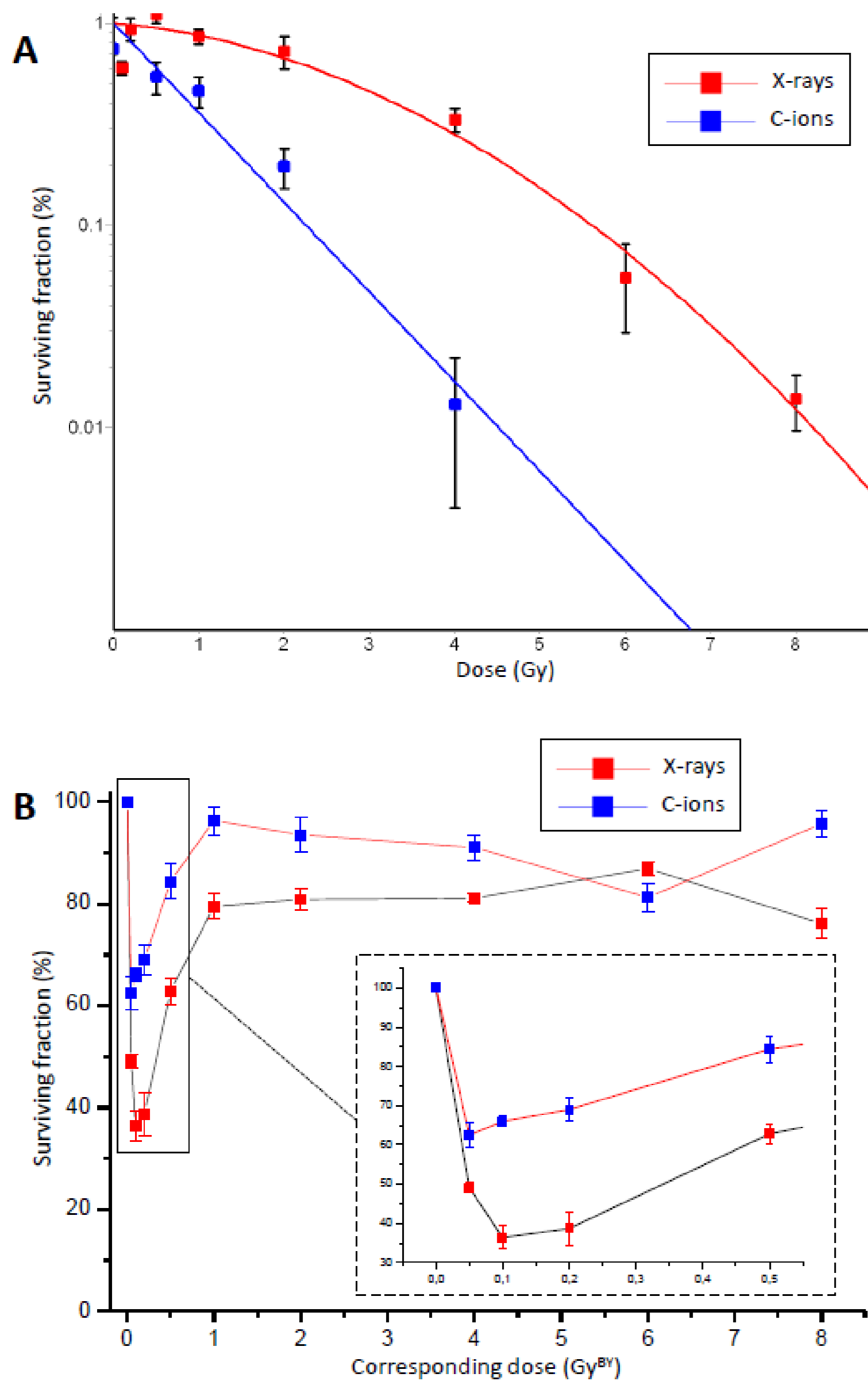
Protocol



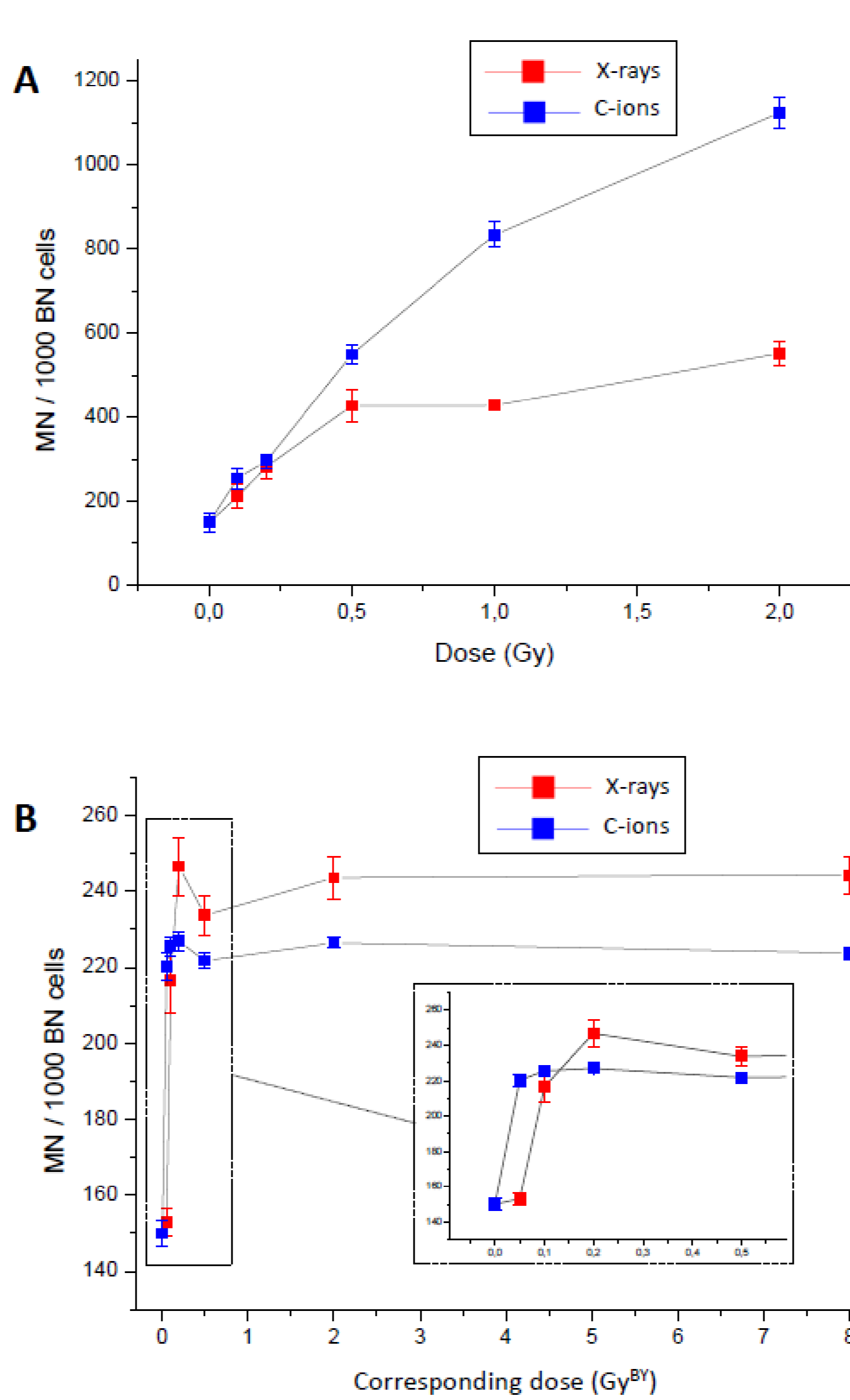
1) DIRECT EFFECTS	2) BYSTANDER FACTORS	3) BYSTANDER EFFECTS
Proliferation measurement - Clonogenic assays DNA damages measurement - Micro-nuclei assays	Concentration / heat stability - Clonogenic assays Cytokine composition - ELISA multiplex	Proliferation measurement - Clonogenic assays - Impedancemetry* DNA damages measurement - Micro-nuclei assays

Clonogenic assays

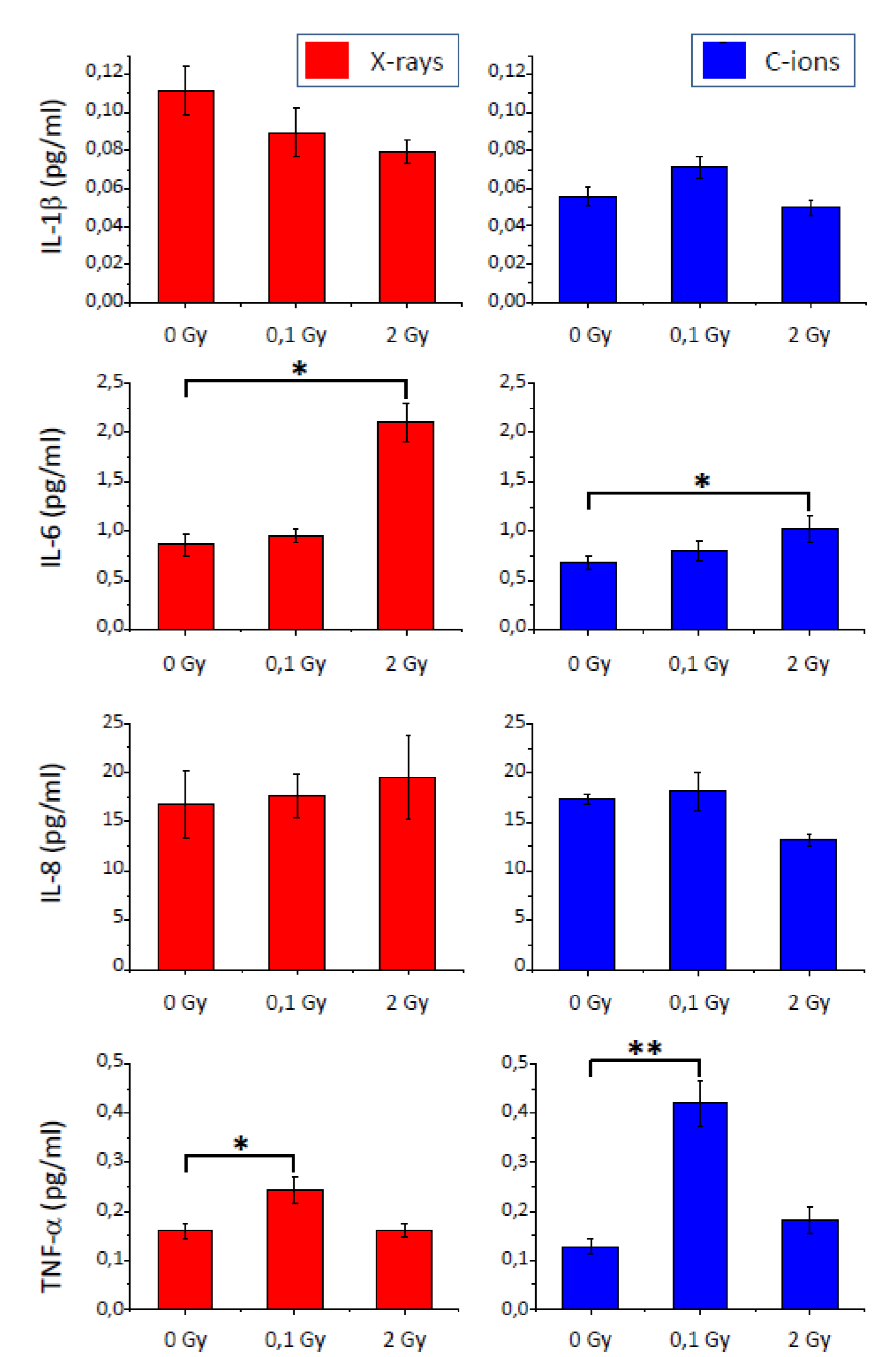
A: direct effects - B : Bystander



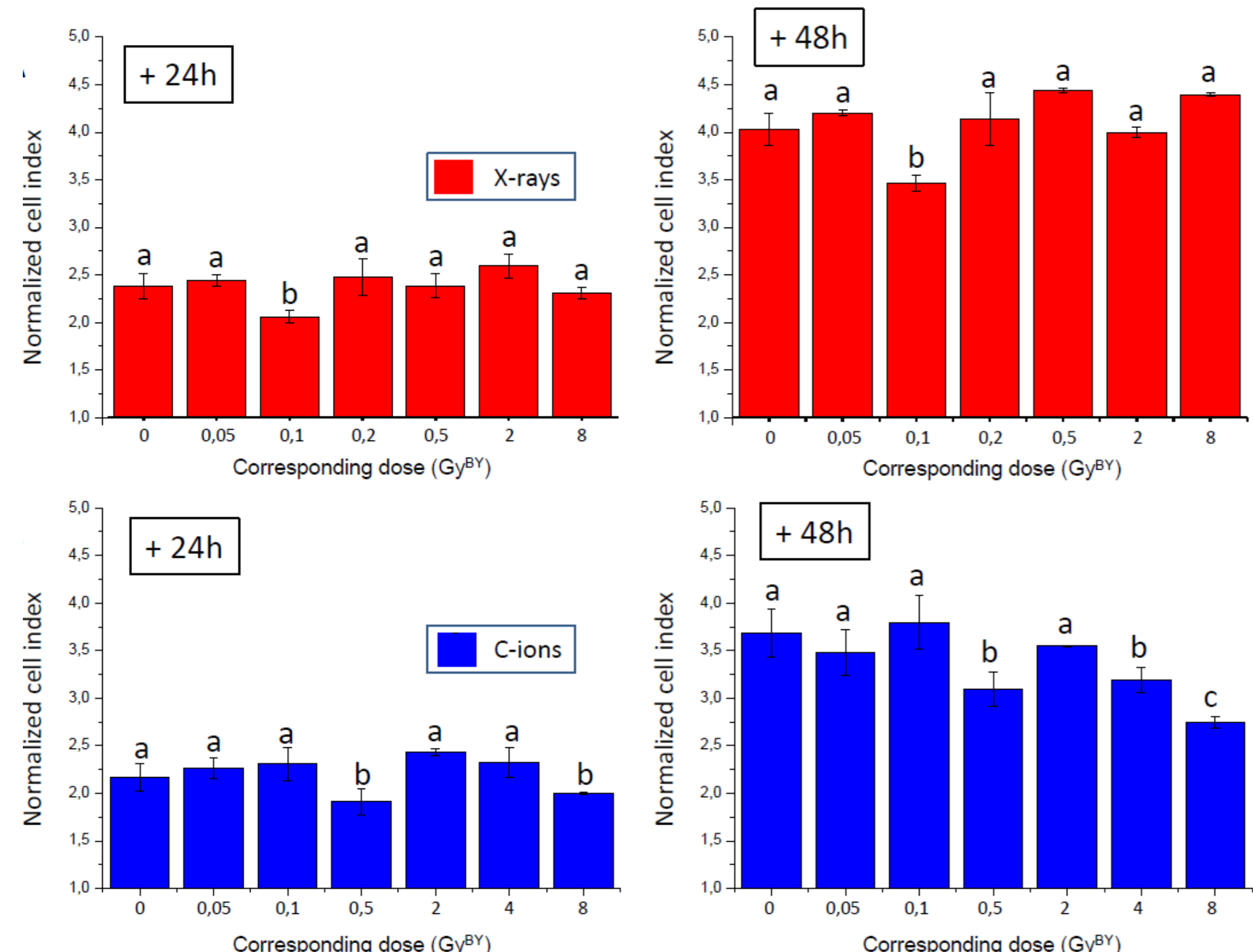
Micro-nuclei assays



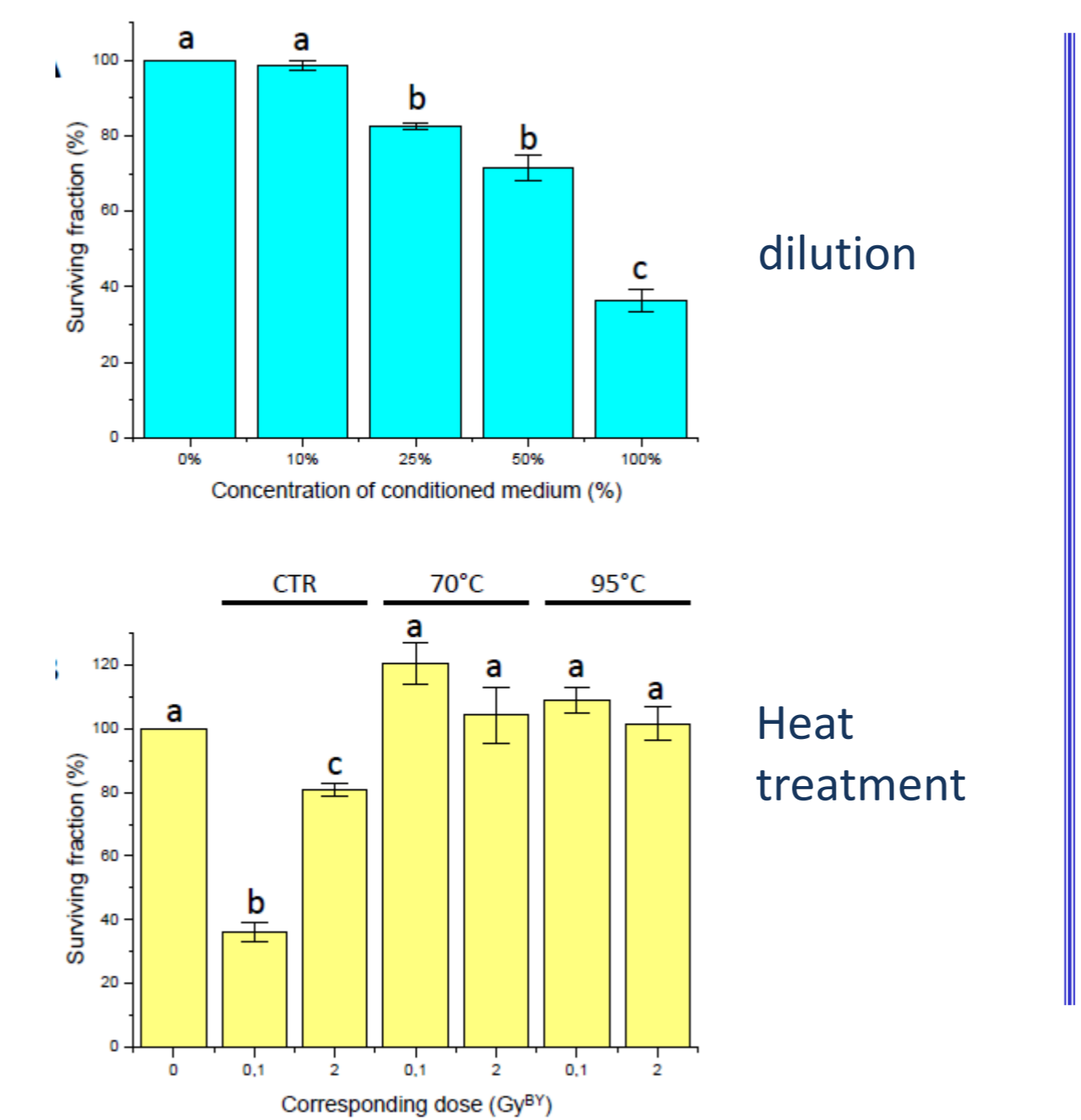
ELISA multiplex (in the conditioned medium)



Impedancemetry of Bystander cells (Xcelligence assays)



Clonogenic assay (treatment of the conditioned medium)



Conclusions

- SW1353 and T/C-28A2 cells communicated after an irradiation particularly at low dose (0,05 and 0,1 Gy)
- This signal induces a proliferation delay in T/C-28a2 bystander cells
- This signal induces an increase of micronuclei in T/C-28a2 bystander cells
- This effect is observed but lower with C-ions as compared with X-rays
- This effect can be diluted and it is heat-sensitive
- SW1353 cells produced bystander factors in the conditioned medium
- Some of these bystander effectors are proposed : IL-6 and TNF-alpha