



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

Charlotte Lepleux, Aurélie Marie-Brasset, Emilie Brotin, Tetsuo Nakajima, Diana Savu, François Chevalier

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



Lepleux C.<sup>1,2</sup>, Marie-Brasset A.<sup>1,2</sup>, Brotin E.<sup>3</sup>, Nakajima T. <sup>4</sup>, Savu D.<sup>5</sup> and Chevalier F.<sup>1,2</sup>

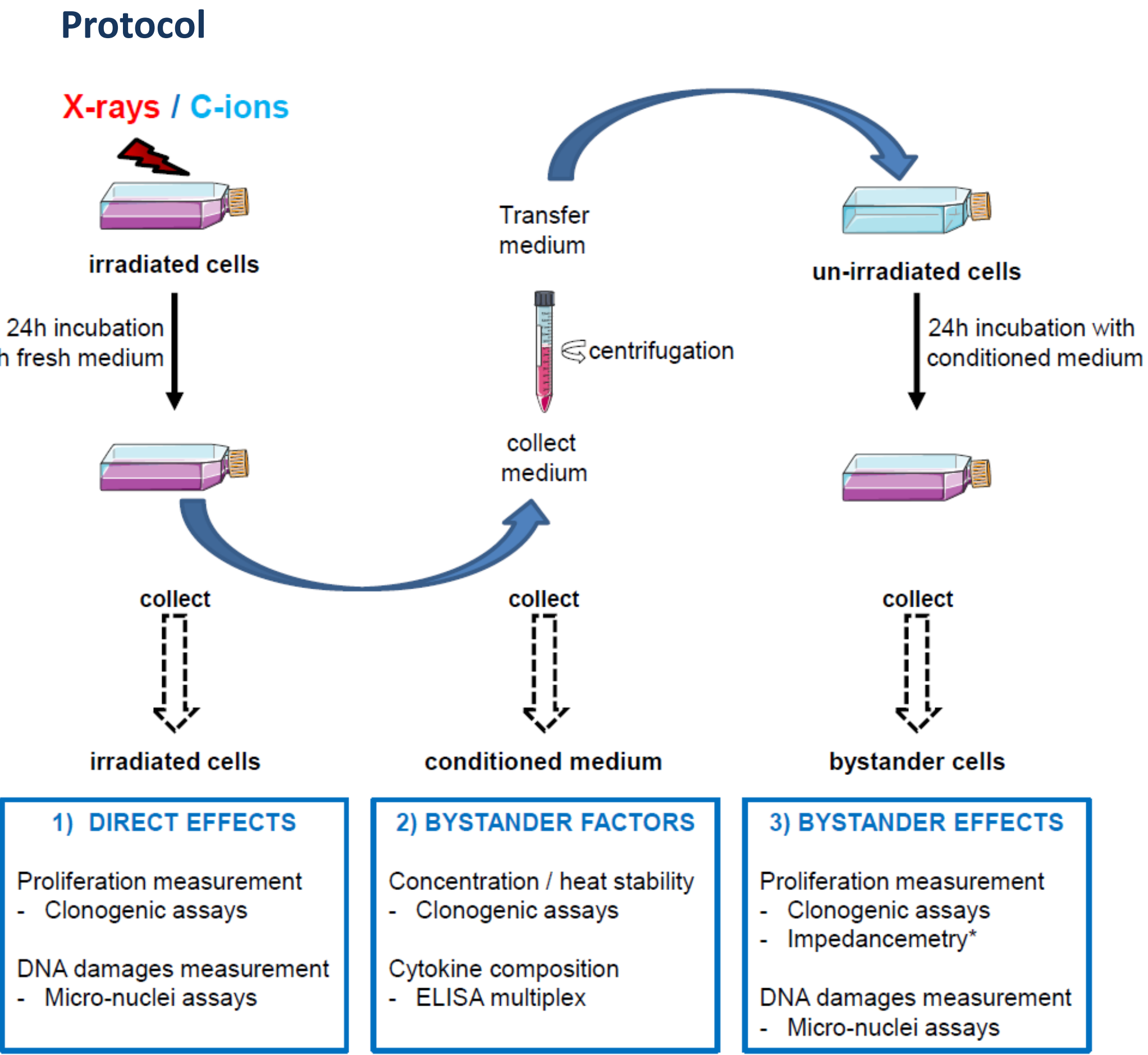
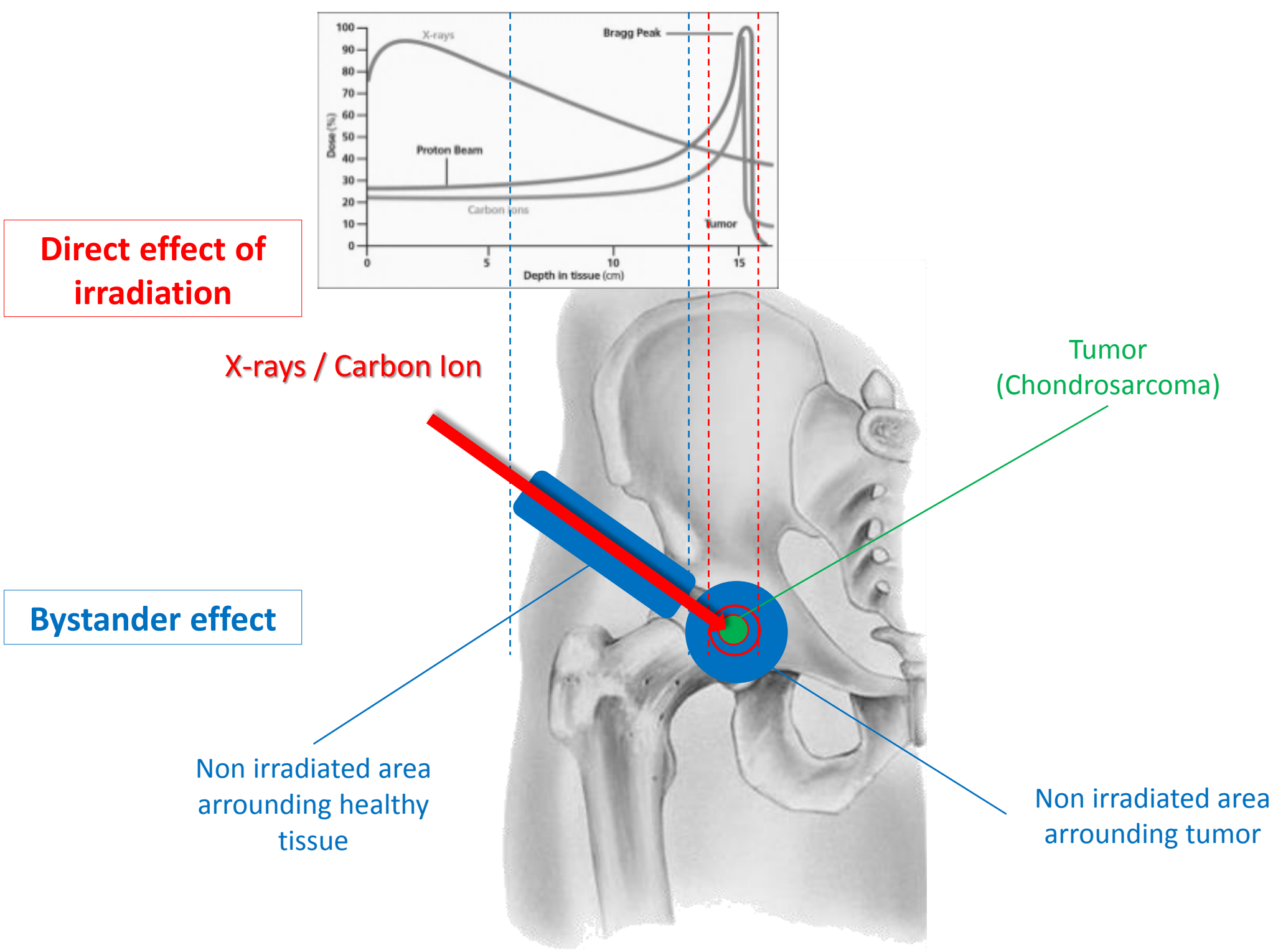
<sup>1</sup> LARIA, iRCM, François JACOB Institute, DRF-CEA, Caen, France ;  
<sup>2</sup> Normandie Univ, ENSICAEN, UNICAEN, CEA, CNRS, CIMAP UMR6252, 14000 Caen, France ;  
<sup>3</sup> ImpedanCELL Platform, Federative Structure 4206 ICORE, Normandie Univ, UNICAEN, Inserm U1086 ANTICIPE « Interdisciplinary Research Unit for Cancer Prevention and Treatment », Biology and Innovative Therapeutics for Ovarian Cancers group (BioTICLA), Comprehensive Cancer Center F. Baclesse, 14000 Caen, France ;  
<sup>4</sup> Dept. of Radiation Effects Research, NIRS, QST, Chiba-shi, Japan;  
<sup>5</sup> Department of Life and Environmental Physics, Horia Hulubei National Institute of Physics and Nuclear Engineering, Reactorului 30, P.O. Box MG-6, Magurele 077125, Romania

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.

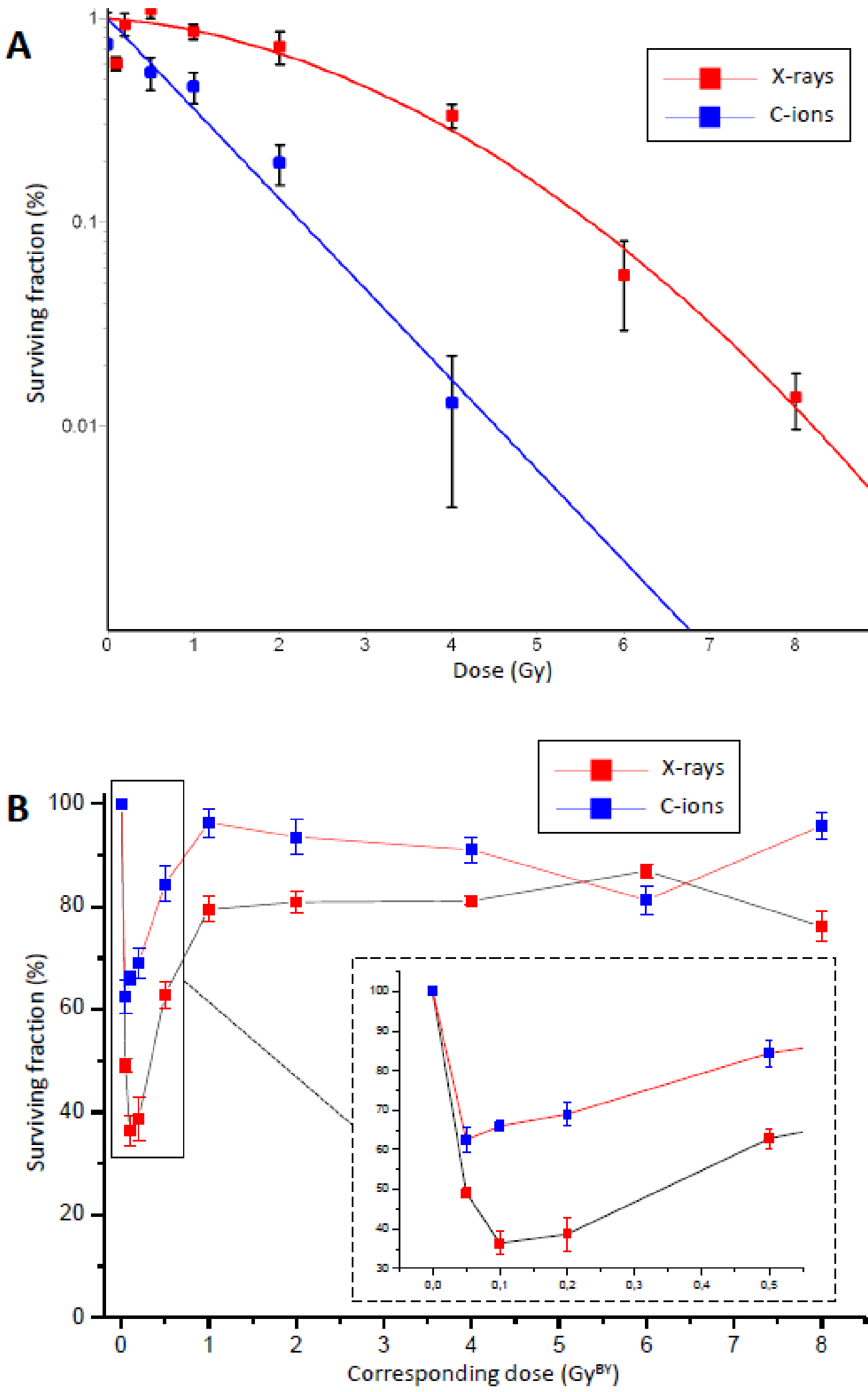
from Lepleux et al. 2019, Journal of Cell Communication and Signaling

Cartilage irradiation and Bystander effect

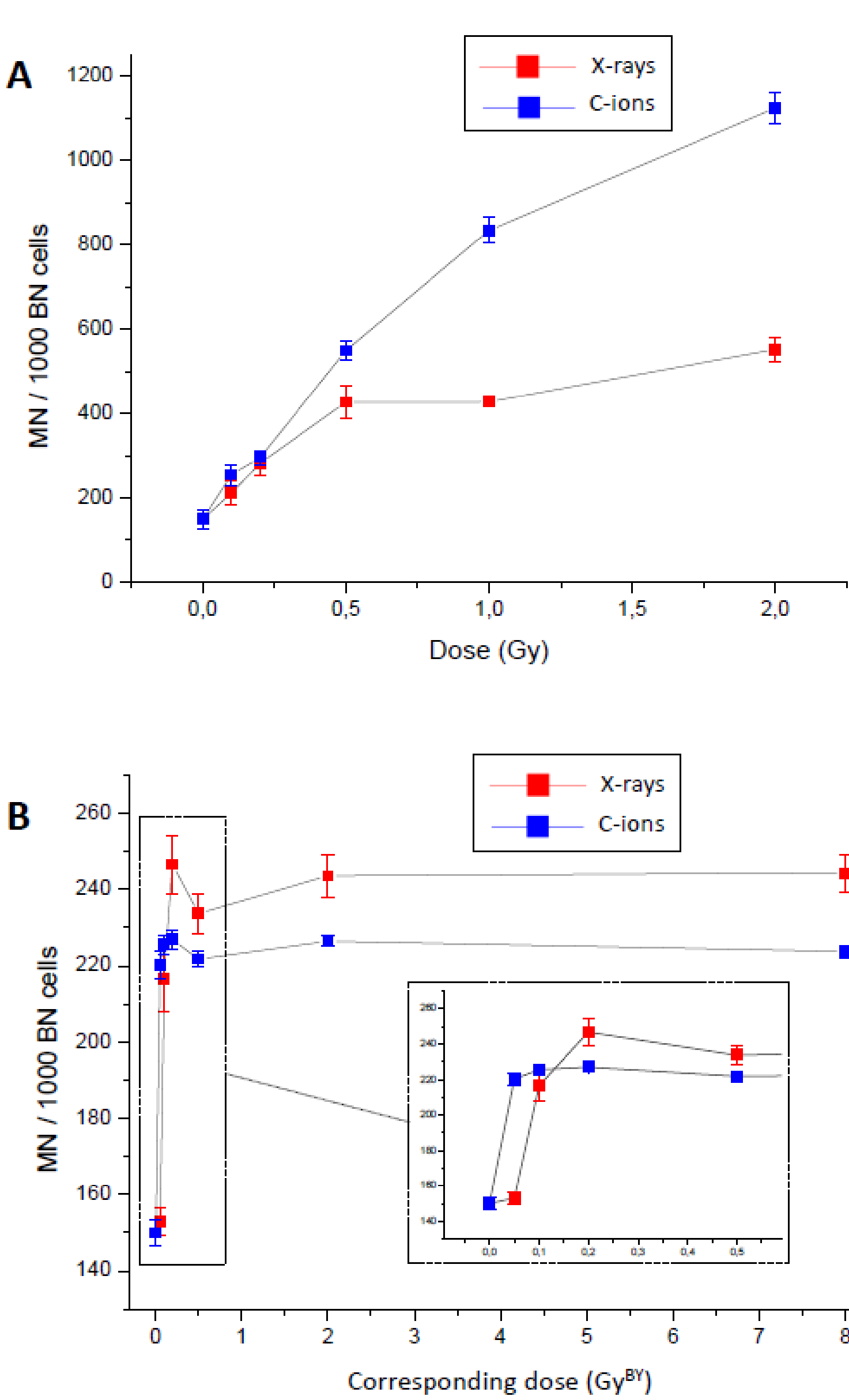


Clonogenic assays

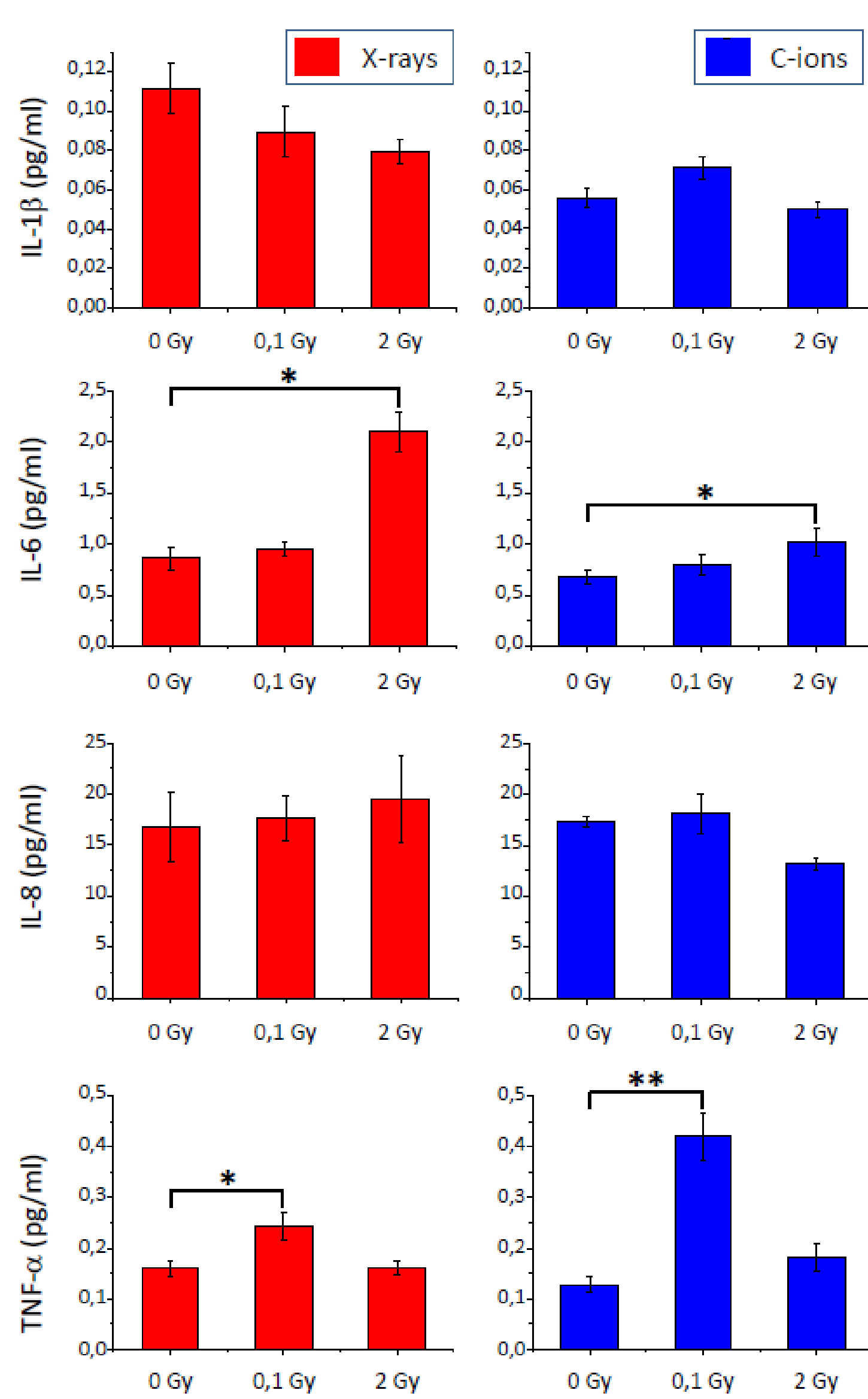
(A: direct effects ; B : Bystander)



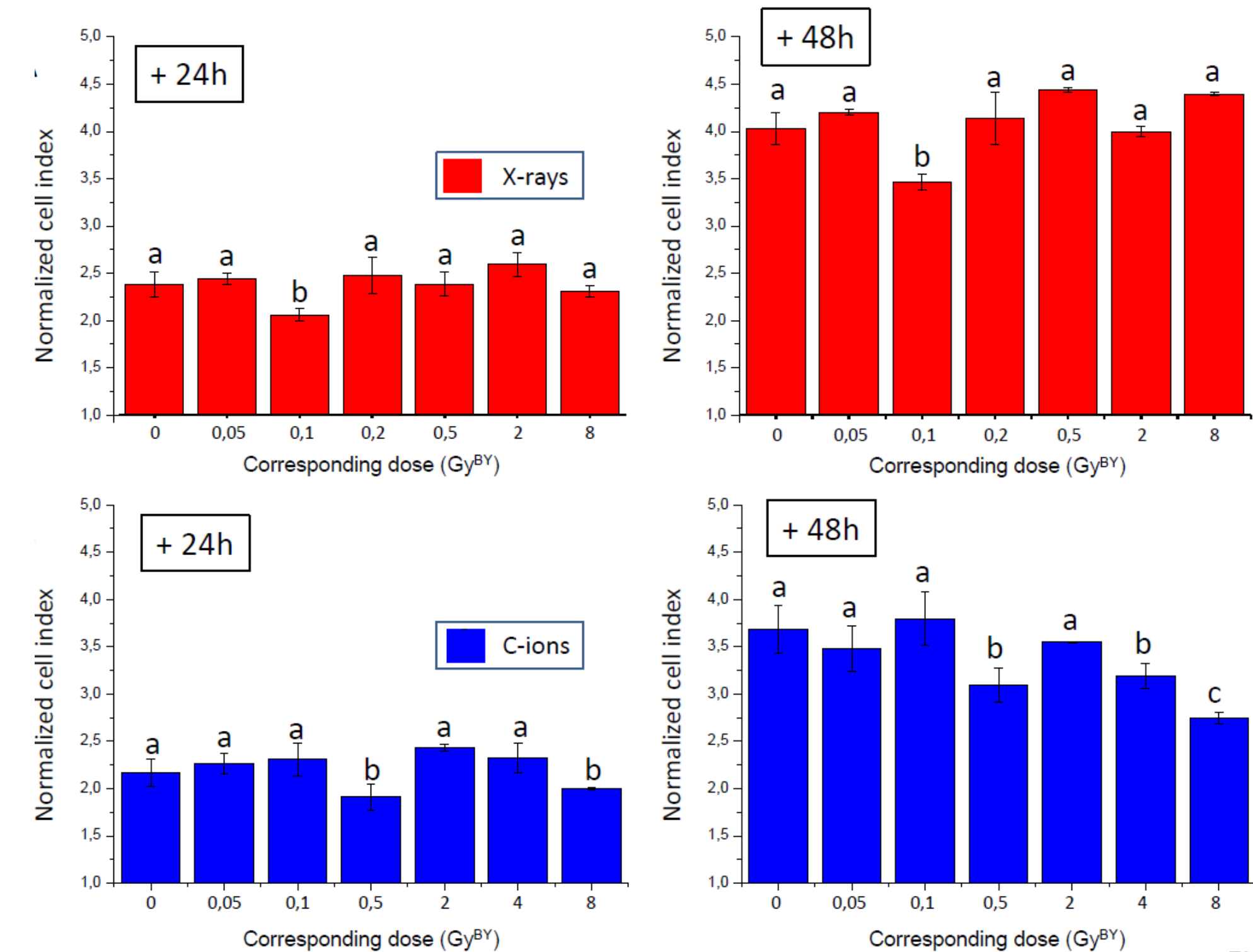
Micro-nuclei assays



ELISA multiplex (in the conditioned medium)

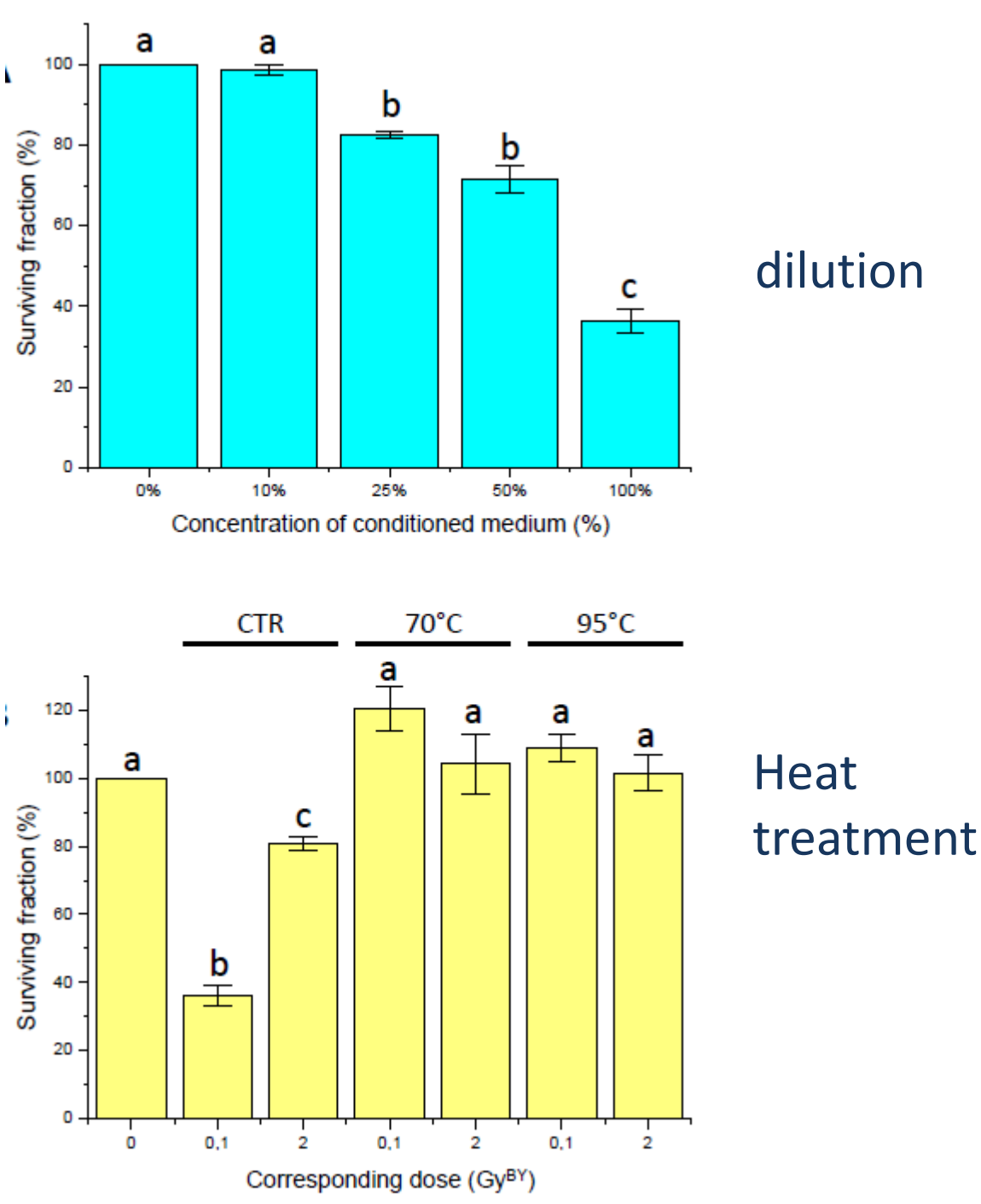


Impedancemetry (Xcelligence proliferation assay)



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