

The modulating effect of Oxidative Metabolism and Oxygen Partial Pressure on Propagation of Radiation Bystander Effects

Géraldine Gonon, Sonia M de Toledo, Perumal Venkatachalam, Jean-Paul Jay-Gerin, Edouard I Azzam

▶ **To cite this version:**

Géraldine Gonon, Sonia M de Toledo, Perumal Venkatachalam, Jean-Paul Jay-Gerin, Edouard I Azzam. The modulating effect of Oxidative Metabolism and Oxygen Partial Pressure on Propagation of Radiation Bystander Effects. 5th Asian Congress of Radiation Research, Society for Radiation Research (SRR) with Asian Association of Radiation Research (AARR), Nov 2022, MUMBAI, India. irsn-03937872

HAL Id: irsn-03937872
https://irsn.hal.science/irsn-03937872

Submitted on 13 Jan 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Copyright

The modulating effect of Oxidative Metabolism and Oxygen Partial Pressure on Propagation of Radiation Bystander Effects

G. Gonon[1,2], S. M. de Toledo[2], V. Perumal[3,2], J-P Jay-Gerin[4], E. I. Azzam[2,5]

[1] *Institut de Radioprotection et de Sûreté Nucléaire, PSE-SANTE/SERAMED/LRAcc, Fontenay-aux-Roses, France*

[2] *Department of Radiology, Rutgers New Jersey Medical School, Newark, NJ, USA*

[3] *Department of Human Genetics, Sri Ramachandra Institute of Higher Education and Research (Deemed to be University), Chennai, India*

[4] *Département de médecine nucléaire et de radiobiologie, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Sherbrooke, Québec, Canada*

[5] *Radiobiology and Health Branch, Isotopes, Radiobiology & Environment Directorate (IRED), Canadian Nuclear Laboratories (CNL), Chalk River, Ontario, Canada*

Introduction:

Redox modulated pathways play important roles in out-of-field effects of ionizing radiation. We investigated how the redox environment impacts the propagation of stressful effects from irradiated to bystander cells.

Materials and Methods:

- Normal human fibroblasts that have incorporated [^{3}H]-thymidine were intimately co-cultured with bystander cells during 24 h in a strategy that allowed isolation of bystander cells with high purity. The antioxidant glutathione peroxidase (GPX) was maintained either at wild-type conditions or overexpressed in the bystanders.
- Confluent cell cultures pre-treated with t-butyl-hydroperoxide (t-BOOH), an oxidizing agent, or maintained in low oxygen pressure environment approaching *in vivo* conditions were exposed alongside respective controls to low fluences of 3.7 MeV α particles.

Results:

- Following 24 h of coculture with [^{3}H]-thymidine-labelled cells, levels of stress-responsive $p21^{Waf1}$, p-Hdm2, and connexin43 proteins were increased in bystander cells expressing wild-type GPX relative to respective controls. These levels were significantly attenuated when GPX was ectopically overexpressed in the bystanders, demonstrating by direct approach the involvement of oxidative metabolism.
- By exposing confluent cell cultures to 3.7 MeV α particles wherein only ~2 % of cells are traversed through the nucleus by a particle track, increases in chromosomal damage 3 h post-exposure were greater than expected ($p<0.001$) and further enhanced in presence of t-BOOH ($p<0.05$). While maintaining and irradiating cell cultures at low oxygen pressure (3.3 or 6.7 mmHg) still supported the participation of bystander cells in responses assessed by chromosomal damage and stress-responsive protein levels ($p<0.001$), the effects were attenuated compared to ambient pO_2 (141 mm Hg) ($p<0.05$).

Conclusions:

Together, the results show that bystander effects are attenuated at below ambient pO_2 and when metabolic oxidative stress is reduced but increased when the basal redox environment tilts towards oxidizing conditions. They are consistent with bystander effects being independent of radiation dose rate.