

Improved cellular survival of bystander cells via NF- κ B associated recovery after X-irradiation

[Sebastian Diegeler](#), [Christa Baumstark-Khan](#), [Christine Hellweg](#)

German Aerospace Center Cologne (DLR), Department of Radiation Biology, Cellular Biodiagnostics Workgroup

Contact: Sebastian.Diegeler@dlr.de

Abstract

Radiation-induced bystander effects (RIBE) are an acknowledged issue of radiation therapy. Radiation of tumor tissue has been shown to affect non-irradiated neighboring cells in a paracrine and endocrine manner. Transduction of bystander signaling though remains to be investigated in detail. A part of the transduction is the receptor-initiated activation of signaling pathways by secreted factors of the irradiated cell during irradiation damage response. This work focusses on the activation of the transcription factor Nuclear Factor kappaB (NF-kappaB) in bystander cells after irradiation. NF-kappaB is a well-known contributor to inflammatory processes like cyto- / chemokine production as well as to stress reactions such as the DNA damage response and cell cycle regulation. Using a mouse embryonic fibroblasts (MEF) in vitro model with a genetic knock-out of an NF-kappaB regulator (NEMO, NF-kappaB essential modulator), clonogenic survival and cell cycle distribution was determined in directly irradiated cells and in cells incubated with conditioned medium from X-irradiated cells (bystander treatment). Directly irradiated NEMO ko cells, plated for clonogenic survival immediately after X-irradiation, display the same dose-effect curve as the wildtype (wt) (a/b NEMO ko = 13.92 ± 2.4 vs. a/b wt = 12.37 ± 2.6). But when allowed to recover for 24 h, the wt cells show a broader shoulder in the curve (a/b = 3.5 ± 2.9), indicating a role of NF-kappaB in the repair of radiation induced DNA damages. Looking into the survival of bystander cells, the survival curves show a statistically different slope, with NEMO ko cells surviving better than wt cells (S16 Gy: NEMO ko = 1.66 vs wt = 0.83). The different behavior may correlate with NF-kappaB dependent DNA repair in bystander cells for NEMO ko and wt cells. Cell cycle analysis revealed a 6 hour delayed arrest in G2/M phase in directly irradiated NEMO ko cells compared to wt cells. This indicates that NF-kappaB regulated DNA repair pathways are important for recovery of radiation induced damages. Bystander NEMO ko show an even further delayed arrest at 48 h, while wt bystander cells show no G2/M arrest at all. This supports the assumption that damages have to overcome a certain threshold to be recognized as repair-worthy. As NF-kappaB has been reported to be involved in homologous recombination; cells with impairment in NF-kappaB pathways, such as NEMO ko, register damages caused by bystander treatment differently from wt cells. This leads to G2/M arrest extending time for repair in NEMO ko bystander cells.

Poster

4th German-French DNA Repair Meeting

21.-23. September 2017, Cologne, Germany

<http://dna-repair-2017.dgdr.de/>

Venue: Max Planck Institute for the Biology of Ageing, Joseph-Stelzmann-Strasse 9b, 50931 Cologne, Germany