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Bleomycin - induced bystander effects and stress response

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Purpose: In the present study, we propose to evaluate the ability of bleomycin to induce bystander effects and the stress response mechanisms that might be involved in this process.

Materials and Methods: L929 fibroblasts were treated with different concentrations (less than 60 µg/ml) of a DNA damaging agent, bleomycin. These cells were assessed for DNA damage, cell death and induction of stress response pathways (heat shock cytoplasmic stress, ISR and ER stress, mitochondrial stress). The media preconditioned was used to analyse induction of bystander damage. The assays to estimate the bystander effect are: DNA damage (micronuclei), clonogenic survival, induction of stress response by qPCR for specific markers of organellar stress.

Results: We observed an increased DNA damage in L929 fibroblast treated with bleomycin. This increase is proportional with the concentration used. The level of micronuclei is also increased in bystander cells but does not depend on bleomycin concentration. Preliminary data show a consistent transcriptional down-regulation of all the stress response factors tested (i.e. Hsp70 Cyt, Hsc70cyt, BiP, CHOP, Hsp60mit) in the bystander cells and their down-regulation in the direct treatment with the exception of Hsp70cyt. This indicates that bleomycin might induce an arrest of transcription both in direct treatment and in bystander cells.

Conclusion and prospective: Bleomycin induced bystander response reflected in increased DNA damage. Unexpectedly, stress response pathways markers are inhibited at transcriptional level. The stress response mechanisms involved in this process will be further investigated together with the role of reactive oxygen species and nitric oxide.

Primary author: Dr SAVU, Iulia Diana (Horia Hulubei National institute of Physics and Nuclear Engineering –IFIN-HH)

Co-authors: Mr MUSTACIOSU, Cosmin (Horia Hulubei National institute of Physics and Nuclear Engineering – IFIN-HH); Dr PETCU, Ileana (Horia Hulubei National institute of Physics and Nuclear Engineering –IFIN-HH); Ms TEMELIE, Mihaela (Horia Hulubei National institute of Physics and Nuclear Engineering –IFIN-HH); Dr MOISOL, Nicoleta (MRC Toxicology Unit, Leicester, UK)

Presenter: Dr SAVU, Iulia Diana (Horia Hulubei National institute of Physics and Nuclear Engineering – IFIN-HH)

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