



A system biology approach to provide a mechanistic understanding of radiation induced premature senescence in endothelial cells

Task 7.3 "Feasibility study towards a systems biology approach of radiation response of the endothelium" is one of nine tasks in WP 7 for risk evaluation of radiation-induced non-cancer effects. Task 7.3 started 2010 with seven partners (SU, STUK, IRSN, HMGU, UNIPV, ISS, SCK-CEN) and ended after 36 months in 2012.

The non-cancerous diseases in focus of Task 7.3 are those of the vascular system. Diseases of the vascular system are the number one cause of non-cancer mortality and endothelial dysfunction is their hallmark. The risks of developing circulatory diseases are strongly linked with age thus endothelial dysfunction may correlate with the onset of senescence of the endothelial cell layer. The hypothesis was that low dose rate chronic exposure will induce premature senescence of the endothelial cells leading to a more rapid progression of the disease.

The strategy of the system biology approach was to provide the modelers with experimental data on changes of biomarkers of senescence, oxidative stress, the proteome, the genome, cytokines, inflammatory responses and genomic instability in chronically irradiated human umbilical vein endothelial cells (HUVEC).

In brief, cells in culture were chronically exposed to ^{137}Cs γ -radiation at dose rates < 5 mGy/h from passage one until they entered senescence. The stress induced by 2.4 and 4.1 mGy/h resulted in significant reduction in proliferation rate and induced premature senescence at an accumulated dose of 4 Gy. The main conclusions, supported by the biomarkers of senescence, oxidative stress, cytokines and the omic studies, are that radiation induced premature senescence involve biological pathways regulating oxidative stress,

cytoskeletal organization, inflammation, cell-cell communication and adhesion (1–4). The modelling and system biology approach is ongoing and the aim is to finish in 2014.

The project has provided new facts about cellular responses to low dose rate chronic exposures that can provide the modellers with data for a detailed mechanistic understanding of radiation induced premature senescence in cultured endothelial cells. The close collaborations and the interaction with all partners both scientifically and socially have been very stimulating and new collaborative projects between the partners have been initiated.

I gratefully acknowledge the contributions of all partners and the DoReMi support.

Mats Harms-Ringdahl
DoReMi Task 7.3 leader

References

1. Yentrapalli, R. *et al.* Quantitative proteomic analysis reveals induction of premature senescence in human umbilical vein endothelial cells exposed to chronic low-dose rate gamma radiation. *Proteomics*. 2013. 13, 1096–1107.
2. Yentrapalli, R. *et al.* The PI3K/Akt/mTOR pathway is implicated in the premature senescence of primary human endothelial cells exposed to chronic radiation. *PLoS One*. 2013; 8(8): e70024
3. Yentrapalli, R. Doctoral thesis Stockholm University 2013, Novel radiation targets in the endothelium and heart muscle, ISBN978-91-7447-718-4
4. Rombouts, C. *et al.* Transcriptomic profiling suggests a role for IGFBP5 in premature senescence of endothelial cells after chronic low dose rate irradiation. Manuscript submitted 2013.



OPERRA call for research proposals

The OPERRA – Open Project for Radiation Research Area has recently opened a call for research proposals. More information available [here](#).

EU-Rays • European Radiation Research Association for Young Scientists

EU-Rays is a recently born European association established to help and support young scientists working in the field of radiation research, focusing mainly (but not only) on low dose risk. After 2 month from its birth, the association counts more than 70 members. More information about EU-Rays is available [here](#).



DoReMi Training courses

Two training courses will be organised in early 2013:

- 17–28 February: “Radiation-induced effects with particular emphasis on genetics, development, teratology, cognition as well as space-related health issues” by SCK-CEN in Mol, Belgium. More information about this course is available [here](#).
- 31 March – 11 April: “CELOD: cellular effects of low doses and low dose-rates with focus on DNA damage and stress response” by SU in Stockholm, Sweden. More information about this course is available [here](#).

For the courses scheduled in 2014, please visit [here](#).

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The DoReMi consortium wishes you all

Merry Christmas & Happy New Year 2014



DoReMi and related events

Future events

- **The 2nd International Symposium on Ethics of Environmental Health** will be organised in Budweis (České Budějovice), Czech Republic, on 15–19 June 2014. More information available [here](#).

Past events

- **DoReMi Workshop “Low dose radiation effects on the immune system: current knowledge and future research needs”** was organised on 5–7 November 2013 in Budapest, Hungary. More information available [here](#).

Highlights and interesting documents available

A new peer-reviewed publication is available in the DoReMi Scientific Information Centre:

- [“The complex interactions between radiation induced non-targeted effects and cancer”](#) by Campa A et al, published in *Cancer Letters*.