

### Low Dose Radiation Induced Transcriptional Alterations in Directly Irradiated and Bystander Fibroblast Cells

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**Introduction:** Formerly, we studied transcriptional alterations in primary human fibroblast cells after irradiation with 2 Gy (Kis et al. *Int J Radiat Oncol Biol Phys.* 66:1506-14. 2006). We found that about 200 genes responded to radiation and the expression profile depended on individual genetic backgrounds. Thirty consensus radiation response genes answered to radiation in identical manner in all investigated cells. Now, we have investigated low dose radiation induced transcriptional responses in directly hit and bystander cells. **Methods:** F11 primary human fibroblasts were irradiated with different doses (10, 40, 100 and 500 mGy) of <sup>60</sup>Co gamma radiation. To investigate radiation-induced transcriptional alterations in directly irradiated cells, RNA was isolated 2 h after irradiation. To study responses in bystander cells the culture medium was removed from the irradiated cells 2 h after irradiation and transferred to unirradiated recipient cells. RNA was isolated 2 h later and the transcriptional profile analyzed by whole genome microarrays. **Results:** When cells were irradiated with 500 mGy 1119 genes responded to radiation. Ten of the formerly identified consensus radiation response genes changed its transcription (CDKN1A, TP53INP1, CYP26B1, BTG2, BBC3, PPM1D, THSD1, GDF15, NM.024661, BC010544). Irradiation of F11 fibroblasts with 100 and 10 mGy altered the transcription profile of 847 and 1414 genes, respectively. When we compared the transcription profile of cells irradiated with 500 and 100 mGy 377 similar alterations were detected, among them 6 consensus radiation response genes (CDKN1A, TP53INP1, GDF15, BTG2, BBC3, NM.024661) changed its transcription in an identical manner. One hundred and twenty-four genes responded to radiation after all applied doses. In bystander cells 655 and 406 genes responded to 500 and 100 mGy irradiations, respectively on the transcription level. After irradiation with 40 and 10 mGy the number of responding genes were 152 and 619, respectively. When we compared the responses in bystander cells after irradiation with 100 and 40 mGy only 40 genes responded identically. The comparison of the transcriptional profile of 40 and 10 mGy irradiated cells detected 60 similar responses. Altogether fifteen genes responded to all doses of radiation in bystander cells. Finally, we have detected nine genes (DLGAP4, HRASLS5, TMEM167, RPL23, RPL38, PRSS36, and three hypothetical proteins) responding to all doses of radiation both in directly irradiated and bystander cells. **Conclusions:** By the analysis of radiation induced transcriptional alterations one might find potential biomarkers suitable to detect low dose responses.