

The Ku dependent non-homologous end-joining pathway contributes to low dose radiation-stimulated cell survival

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ABSTRACT

Low dose radiation (≤ 0.1 Gy)-induced adaptive responses could protect cells from high challenge dose radiation-induced killing. The protective role is believed to promote the repair of DNA double strand breaks (DSBs) that are a severe threat to cell survival. However, it remains unclear which repair pathway, homologous recombination repair (HRR) or non-homologous end-joining (NHEJ), is promoted by low dose radiation. To address this question, we examined the effects of low dose (0.1 Gy) on high challenge dose (2-4 Gy) induced killing in NHEJ or HRR deficient cell lines. We showed that 0.1 Gy reduced the high dose radiation-induced killing for wild type, or HRR deficient cells, but enhanced such killing for NHEJ deficient cells. These results suggest that low dose radiation-induced adaptive response on protecting cells from high challenge dose-induced killing depends on NHEJ. We also showed that low dose radiation could not arouse any protective role in the cells exposed to high challenge dose radiation with high-linear energy transfer (LET), which further supports this prediction because it is known that high-LET radiation inhibits the Ku-dependent NHEJ. In addition, we showed that low dose radiation activated the DNA-PK catalytic subunit (DNA-PKcs) and the inhibitor of DNA-PKcs destroyed low dose radiation-induced protective role in reducing cell killing following high challenge dose. These results indicate that low dose radiation promotes NHEJ through stimulating DNA-PKcs activity and, therefore, protects the cells from high challenge dose radiation-induced killing. This information is useful for improving radiation protection or radiotherapy. This work is supported by grants: DOE (DE-FG02-09ER64755), NASA (NNX09AF24G) to YW and NASA (NNX07AP84G) to BC.