The Role of DNA double-strand break repair in cellular response to low dose radiation exposure.

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It has been assumed that molecular pathways that involved in the biological response for low dose of radiation should be similar to those for high dose radiation in general. The low dose-rate effect and DNA double-strand break repair are inextricably linked in mammalian cells. It has been reported that mammalian mutant cells deficient in nonhomologous end join (NHEJ) pathway have little or no cellular recovery when expose to low-dose-rate radiation. Recently, it has also been reported that cells deficient in NHEJ express elevated bystander effect induced by low dose of high LET radiation. These experiments strongly suggested that cellular ability in DSB repair would affect its sensitivity to low dose radiation. However, IR induced gene expression analysis in mammalian cells indicated that DNA repair factors are not the most frequent genes that are immediately activated upon low or high dose radiation. This observation is in consistent with the recent understanding that protein post-translational modifications rather than activation of DNA repair proteins plays an essential and immediate role in DNA damage sensing, signaling and repair upon IR exposure. Our laboratory has been focused on the molecular and cellular responses to DNA DSBs induced by IR in mammalian cells. Especially, we are interested in DNA-dependent protein kinase (DNA-PK). DNA-PK complex consisting Ku70 and Ku80 heterodimer and DNA-PK catalytic subunit (DNA-PKcs), is the key component of the non-homologous end-joining (NHEJ) pathway of DNA double strand breaks (DSBs) repair. In this report, I'll discuss the mechanism by which DNA-PK is activated and the biological significant of DNA-PK phosphorylation induced by IR.