

# ANALYSIS OF CELLULAR RESPONSE BY EXPOSURE TO ACUTE OR CHRONIC RADIATION IN HUMAN LYMPHOBLASTOID TK-6 CELLS

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To clarify the biological effects of low-dose rate radiation on human health for long-term stay in space, we analyzed the induction of apoptosis and apoptosis-related gene expression after irradiation with different dose-rate in human lymphoblastoid TK-6 cells harboring wild-type *p53* gene.

We irradiated TK-6 cells by X-ray at 1.5 Gy (1 Gy/min) and then sampled at 25 hr after culturing. We also irradiated by gamma-ray at 1.5 Gy (1 mGy/min) and then sampled immediately or 25 hr after irradiation. For DNA ladder analysis, we extracted DNA from these samples and electrophoresed with 2% agarose gel. In addition, we extracted mRNA from these samples for DNA-array analysis. mRNA from non-irradiated cells was used as a control. After labeling the cDNA against mRNA with [ $\alpha$ - $^{33}\text{P}$ ]-dCTP and hybridizing onto DNA array (Human Apoptosis Expression Array, R&D Systems), we scanned the profiles of the spots by a phosphorimager (BAS5000, FUJI FILM) and calculated using a NIH Image program. The data of each DNA-array were normalized with eight kinds of house keeping genes. We analyzed the expression level of apoptosis-related genes such as *p53*-related, *Bcl-2* family, *Caspase* family and *Fas*-related genes.

DNA ladders were obviously detected in the cells exposed to a high dose-rate radiation. We detected the induction of the gene expression of apoptosis-promotive genes. In contrast, almost no apoptosis was observed in the cells exposed to the chronic radiation at a low dose-rate. In addition, we detected the induction of the gene expression of apoptosis-suppressive genes as compared with apoptosis promotive-genes immediately after chronic irradiation. These results lead the importance of biological meaning of exposure to radiation at low dose-rate from an aspect of carcinogenesis. Finally, the effects of chronic irradiation become a highly important issue in space radiation biology for human health.