Project Research — **Establishment of Optimal Risk Management**

# Elucidation of the Mechanisms of Low-dose Radiation Effects

**Background and Objective**

The current system for radiation protection has been established according to the linear non-threshold (LNT) model, which mainly employs epidemiological data on human populations exposed to high-dose/high-dose-rate radiation and which uses a linear extrapolation down to the low-dose/low-dose-rate to estimate the possible risks. Recently, there is emerging evidence indicating that the risks associated with exposure to low-dose-rate radiation that is below that of 10 times higher than natural background level are lower than those estimated by the LNT model. An accurate estimation of the health risk of low-dose radiation should lead to the establishment of reasonable protection criteria supported by scientific evidence, along with the relief of public anxiety regarding radiation exposure.

This project is undertaken to illustrate that there is no increase in radiation risks at a low-dose-rate, and it aims to decipher underlying mechanisms, through human epidemiological studies in high background radiation areas (HBRAs) and experimental studies in animals and cultured cells. Thus, the scientific basis to achieve reasonableness in radiation protection criteria will be strengthened.

**Main results**

## 1 Epidemiological Research Study of Residents in HBRAs in China

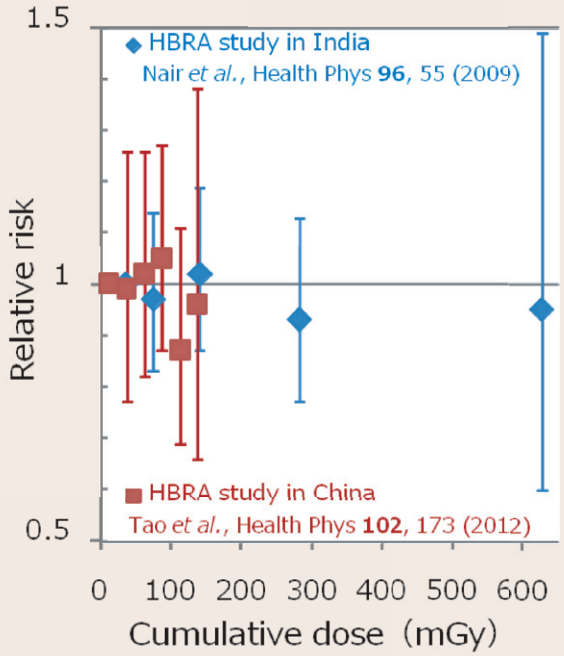
The results from an epidemiological study of HBRA residents in Yangjiang, Guangdong Province, China were published. The group of subjects included about 32,000 persons aged 30–74 years, and the follow-up period was extended to 20 years, compared with the previous report. Mean cumulative radiation doses from natural radiation in the HBR and control-area*1 residents were 84.8 mGy and 21.6 mGy*2, respectively. No significant increases of excess relative risk were observed for cancer mortality (Fig. 1), leukemia, or non-cancer mortality (Table 1). These results indicate the possibility that the risks associated with prolonged low-dose-rate exposure would be lower than those estimated by the LNT model, as with the results of an HBRA study in India (Fig. 1).

## 2 Suppression of Spontaneous Mutation by Radiation-induced Bystander Response

Radiation-induced bystander response is defined as a response of cells that are not directly targeted by radiation but that are in the vicinity of cells that have been directly exposed. Due to its nature, it has been often suggested that the number of cells in which biological effects are induced is higher than that of the irradiated cells under low-dose and/or low-dose-rate irradiation conditions where both irradiated and unirradiated cells coexisted in the same tissue. The aim of this study is, using the X-ray microbeam irradiation method, to clarify the relationship between radiation-induced bystander responses and mutagenesis, one of the requisites of carcinogenesis. Five cells within $1 \times 10^5$ cells on a dish were irradiated with a series of doses from an X-ray microbeam, and the dose response of the surviving fraction (Fig. 2A) and mutation frequency (Fig. 2B) in the bystander population was determined. Both the surviving fraction and the mutation frequency decreased at doses around 1 Gy. The similarity of these behaviors suggests that the enhancement of bystander cell killing participates in a mechanism that eliminates the cells having mutagenic DNA regions, selectively. In other words, biological effects at low-dose regions cannot be enhanced by bystander response.

*1 The area near the HBRA in which the terrestrial radiation levels are low and the lifestyle is similar to the HBRA.
*2 Unit of absorbed dose; 1 mGy = 1 mSv in this case, as the doses in this study consist of those from external exposure with terrestrial gamma rays.

Other reports: Tao et al., Health Phys., 2012 and Maeda et al., J.Radiat.Res., 2012




| | Deaths | ERR/Gy | 95% CI |
|---|---|---|---|
| All cancer excl leukemia | 941 | -1.01 | -2.53, 0.95 |
| Leukemia | 15 | 10.68 | <0, infinity |
| Non-cancer diseases | 4,525 | 0.10 | -0.64, 0.94 |
| Circulatory diseases | 2,344 | 0.14 | -0.84, 1.29 |

ERR: Excess Relative Risk, the value of relative risk minus one; relative risk is the ratio of mortality in the subject group versus the control group. ERR/Gy corresponds to the values of the slopes in Fig. 1, indicating an increase of relative risk per unit dose.

When both the lower limits (left figures) and upper limits (right figures) of the 95-percent confidence intervals (95% CIs) are positive or negative, it can be concluded that significant effects due to radiation exposure were detected. No significant effects on the mortalities of diseases in the table were shown.

**Table 1, Fig. 1: Results of an epidemiological study of HBRA residents in China**

No increase of risk with the dose was observed in comparison with the control area. This result is the same as the Indian study, and it is different from the atomic bomb survivor study, which shows the increase of cancer risks in proportion with dose. The cumulative dose of each Chinese data point in Fig. 1 was calculated as a center value of the mGy dose categories of 0–24, 25–49, 50–74, 75–99, 100–124, and 125 and up.

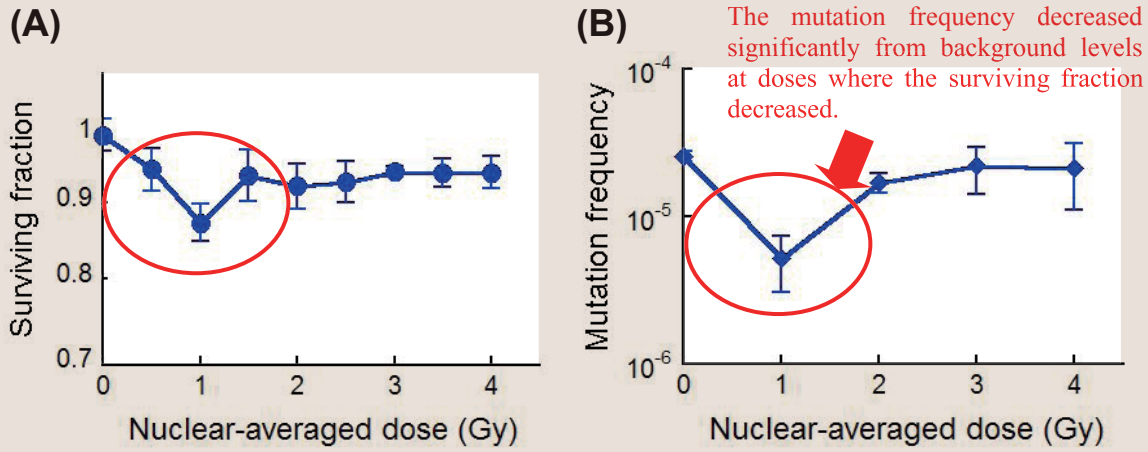



**Fig. 2: Suppression of spontaneous mutation by X-ray-induced bystander response**

(A) Effect of bystander response on the surviving fraction of Chinese hamster V79 cells as a function of the nuclear-averaged dose in the irradiated cells; the surviving fraction decreased as a result of bystander response at doses around 1 Gy, but at higher doses, the surviving fraction recovered. (B) Mutation frequency measured in the same cell populations used in Fig. 2A; the mutation frequency decreased significantly from background (0 Gy) levels at doses where the surviving fraction decreased. At higher doses, the mutation frequency did not become higher than background levels.