## **Elucidation of the Mechanisms of Low Dose Radiation Effects**

# Background and Objective

The current system for radiological protection has been established according to the linear non-threshold (LNT) model, which mainly employs epidemiological data on high-dose-exposed human populations and uses a linear extrapolation down to low dose to estimate the possible risks. This model has been a foundation for asserting that radiation is harmful even at tiny doses. However, advances in research on the low dose radiation effects are revealing evidence that risks associated with exposure to low-dose and low-dose-rate radiation are lower than those estimated by the LNT model (Fig. 1). The accurate estimation of health risks of low dose radiation should lead to the establishment of the reasonable protection criteria supported by scientific evidence, and the relief of public anxiety toward radiation exposure.

This project is undertaken to illustrate the radiation risks at low dose and low dose rate, and decipher its underlying mechanisms, through human epidemiological studies and experimental studies in animals and cultured cells. Thus, the scientific basis for the optimization of radiological protection standards will be strengthened.

## Main results

## 1. Epidemiological research study of residents in high background radiation areas (HBRA)

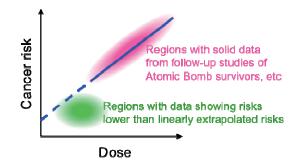
No increases of excess relative risk were observed at total doses less than about 0.6 Gy in the epidemiological study in Kerala, India (Fig. 2)<sup>1)</sup>. We expanded the cohort to show that the effects of long-term low-doserate exposures like HBRA would be statistically significantly lower than those of short-term acute exposures such as A-bomb survivors. In order to achieve international recognition of these results, we proposed these results to the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) as a theme of the next technical report.

### 2. Cellular response to targeted irradiation of cellular compartments

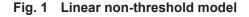
Role of cellular compartments (nucleus and cytoplasm) in cellular response to ionizing radiation was assessed using X-ray microbeams, which enabled us targeted single cell irradiation and moreover the targeted part of cell nucleus irradiation. We found that the cell surviving fraction in whole-cell irradiated (including cytoplasm) cells was higher than that in the only-cell-nucleus irradiated cells, although the irradiated dose in cell nucleus was same. This phenomenon was obvious in the low dose region under 1 Gy. The results obtained suggest that low doses of radiation-induced biological effect cannot be extrapolated easily from the results of high doses radiation (Fig. 3)<sup>2</sup>). In addition, a radiation-induced bystander response<sup>\*1</sup> was also partly suppressed in case of the whole-cell irradiation of the targeted cells in comparison with only-cell-nucleus irradiation.

**References:** 1) Health Physics, 96, 55 (2009), 2) Radiation Research, 174, 37-45 (2010)

<sup>\*1:</sup> The radiation induced bystander response is defined as a response in cells which have not been directly targeted by radiation, but which are in the neighborhood of cells which have been directly exposed.

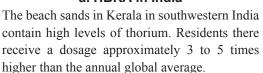


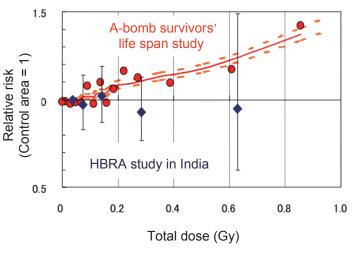
In 1993, UNSCEAR defined a dose of  $\leq 0.2$  Gy as a low dose, and a dose rate of  $\leq 0.0001$  Gy/min as a low dose rate.





### a. HBRA in India

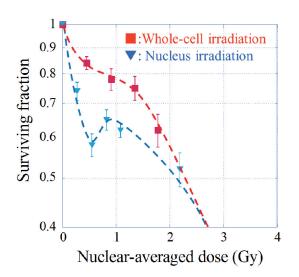




### b. Risk of the incidence of solid cancer

No increases of risk were observed in HBRA compared with surrounding control areas where the life style is same and radiation levels are low (blue diamonds). The trend is apparently different from that of A-bomb survivors showing almost proportional increase with dose (red circles).

### Fig. 2 Result of epidemiological study of HBRA residents in India



Cell surviving fraction in the whole-cell irradiated (including cytoplasm) cells was higher than that in the only-cell-nucleus irradiated cells, although irradiated dose in cell nucleus was same, suggesting that cellular radiation sensitivity is different by irradiated part of the cells.

Fig. 3 Difference of cellular response to targeted irradiated part of the cells