

## Principal Research Results

# Enhancement of Tumor Rejection in Mice by Low Dose-rate $\gamma$ Irradiation

### Background

It is known that medicine or alcohol have different biological effects according to the dose. It becomes clear that radiation has different effects between high dose and low dose by the recent worldwide studies. However the studies of the effects of low dose irradiation at high dose-rate were major. Recently the effects of low dose-rate irradiation are receiving attention. It is well known that acute irradiation of high dose increases the risk of carcinogenesis. But we found the suppressive effect of low dose-rate irradiation on the process of tumor induction by animal experiments. This result is very important to consider the effect of radiation of “low dose” as low-dose and low-dose-rate.

### Objectives

To elucidate the mechanism of the suppression effect, we examined the effect of low dose-rate irradiation on the ability of tumor cell rejection \* (Fig.1), one of the suppressive functions of cancer progress. In this study the ability was analyzed by TD50 values (number of cells required for successful transplantation to a half of injected site) in non-irradiated control mice and in irradiated mice.

### Principle Results

We transplanted the tumor cells prepared from as Methylcholanthrene-induced tumor into non-irradiated control mice or irradiated mice with Cs-137 gamma-rays at 0.4, 0.7 or 1.2 mGy/hr for 1-8 weeks before tumor cell injection. Using methods of TD50 assay, we investigated the difference of TD50 values by the irradiation conditions.

1. TD50 values in irradiated mice with total 250 mGy at low dose-rate increased compared to those in control mice (Fig.2). It was reported that TD50 values in acute irradiated mouse with 100mGy at high dose-rate (1Gy/min) increased with an optimum, in the report of spontaneous carcinoma using single irradiation by Dr. Sakamoto (1997). Our result and the others suggest that the region of total dose between 100 and 250mGy has the ability of cancer progress suppression.
2. TD50 values in the irradiated mice with 400mGy-1.2Gy did not increase or decrease compared to the non-irradiated control mice. The mice irradiated with 1.2Gy usually showed enhancement of carcinogen-induced tumor incidence and radiation-induced tumor. This result indicates the ability of tumor cell injection does not decrease by high dose (1.2Gy) irradiation when the dose-rate is low.

### Future Development

To find the enhancement factor of the ability of tumor cell rejection, we will examine using the mice of different hereditary background.

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### Reference

Y.HOSHI et al., “Enhancement of tumor rejection in mice by low dose-rate gamma irradiation”, CRIEPI Report, G03011(March 2004)in Japanese

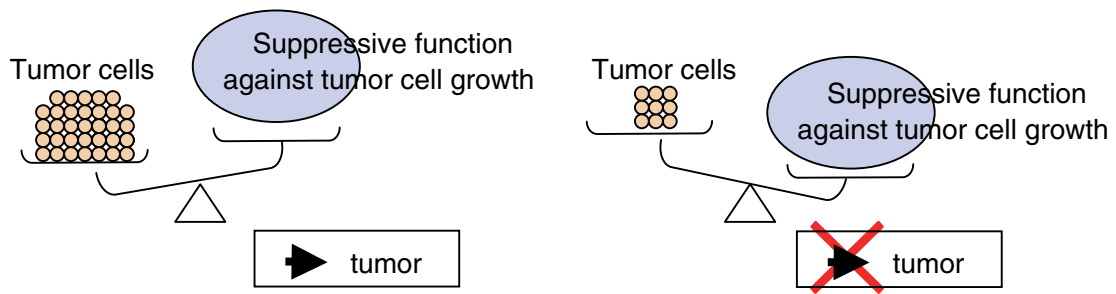
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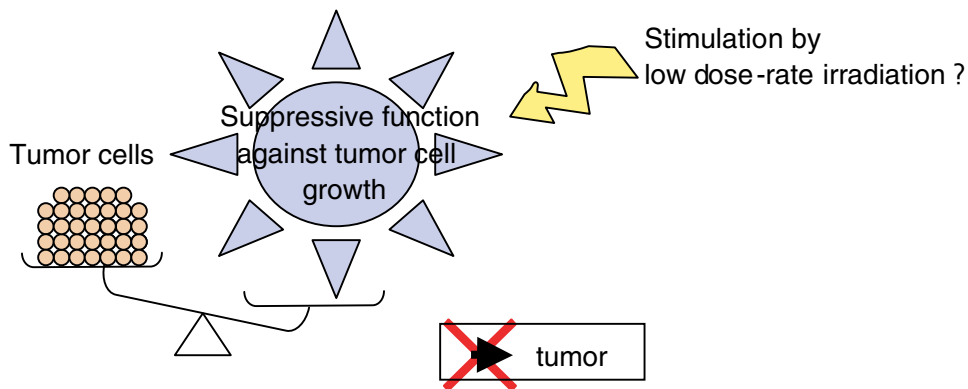
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\* : If the mouse was injected with one tumor cell, the tumor cell can not grow and the tumor take is not successful. This is because living organisms including mice and human beings have the suppressive effect against tumor cells. Injection with the large number of tumor cells which surpass the rejective ability are required to the tumor take.

**C. Harmonization of energy and environment**

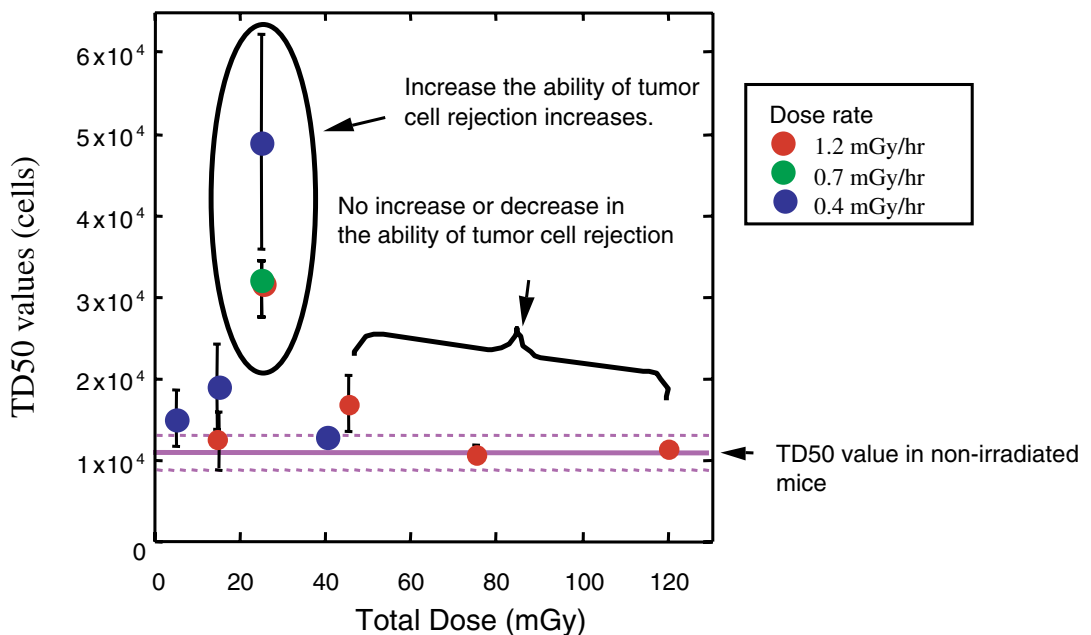


If the number of tumor cells is large enough as shown on the left, tumor cells are able to continue to grow to form a tumor. However, if the number of tumor cells is small as shown on the right, the tumor cells fail to form a tumor.



If the suppressive function against tumor cell growth is enhanced, the tumor take failed when injected with the large number of tumor cells. In other words, the large value of TD50 suggests that the suppressive function against tumor cell growth is high.

**Fig.1** Ability of tumor cell rejection



**Fig.2** TD50 values in irradiated mice