

Mutation Induction by heavy-ion irradiation of *gpt Δ* transgenic mice

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Abstract

Using the new transgenic mice produced by mating *gpt Δ* with p53 knockout, mutation induction by heavy-ion irradiation and the effect of p53 background on such induction were studied. After the whole body irradiation with 10 Gy of 135 MeV/u carbon-ion beam, the genomic DNA was isolated from the different organs and the lambda DNA was rescued as a phage. Mutations in the transgene on the lambda DNA were determined by the *spi(-)* selection (deletion assay). The *spi(-)* mutation was induced by the above irradiation, but enhancement of the mutant frequency by the knockout of p53 gene was found not in the phages recovered from liver but in those from kidney. We are now making an effort to determine the nature of *spi(-)* mutation to confirm such p53 effect.

KEYWORDS: Transgenic mice, heavy-ion, *spi(-)* mutation.

1. Introduction

Studies on biological effects of accelerated heavy-ions could contribute to estimate biological influences of space environments, because this type of radiation can be considered as an important component among the cosmic rays. We analyzed the heavy-ion induced mutations in the transgene of the transgenic mice as well as its involvement of p53 function.

2. Materials and Methods

The outline of experimental procedures are schematically illustrated in Figure 1 [1]. After the whole body irradiation with 135 MeV/u carbon-ion beam, X-rays and γ -rays, the genomic DNA was isolated from the different organs and the lambda DNA was rescued as a phage. Mutations in the transgene on the lambda DNA were determined by both *gpt* assay (6-TG^R colonies) and deletion assay (*spi(-)* plaques).

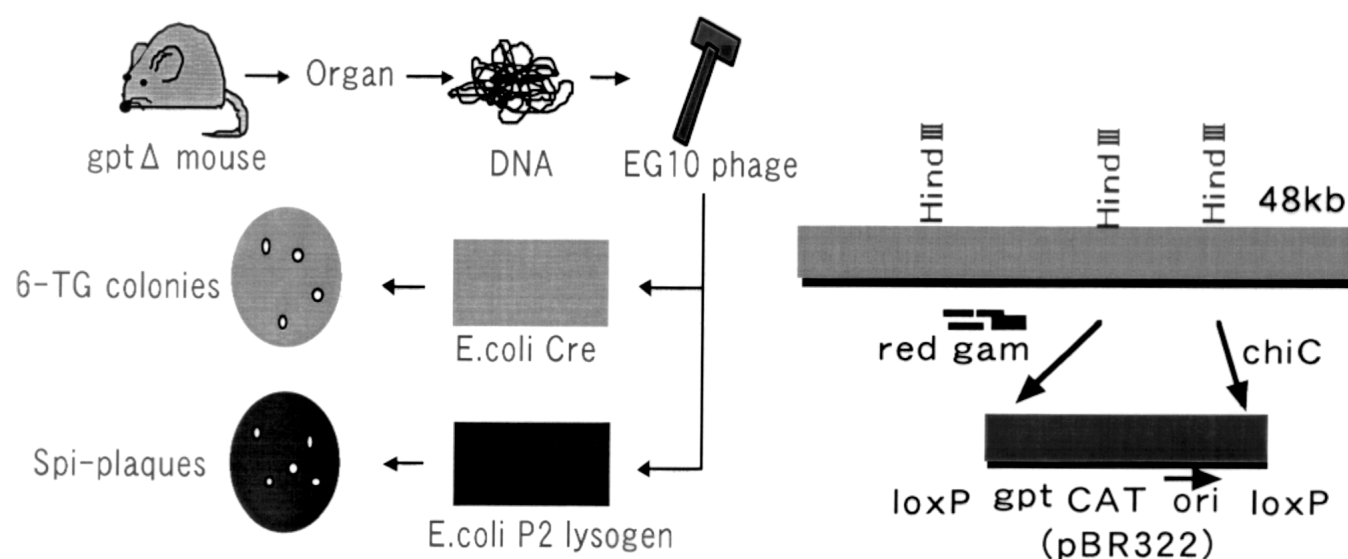


Fig. 1 – A schematic illustration for *gpt Δ* mouse mutagenicity test.

3. Results and Discussion

In this transgenic mouse system, spi(-) mutation was enhanced in liver, spleen and kidney recovered after whole-body exposure to 5 or 10 Gy carbon-ion beam (Fig. 2). The spi(-) mutation frequency for liver recovered from the C-ion exposure seemed to

be a little higher than that from X-ray or γ -ray case. Although data is not shown here, the following preliminary results are obtained: enhancement of spi(-) mutation by the lack of p53 gene was not observed in liver, but such effect might exist in kidney. A sequence analysis for these mutants is now under the study.

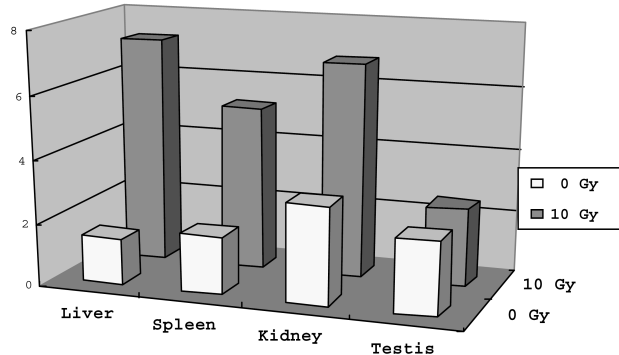


Fig. 2 – Spi(-) mutant frequency of the carbon ion-irradiated gpt delta mice.

REFERENCES

- [1] Nohmi T, Katoh M, Suzuki M, Matsui K, Yamada M, Watanabe M, Suzuki N, Horiya O, Ueda T, Shibuya H, Ikeda H, Sofuni T. Spi- selection: an efficient method to detect gamma-ray-induced deletions in transgenic mice. *Env Mol Mutagen* 1999; 34; 9-15.