Mutations induced by tritiated water in mouse spleen

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Mutation is an alteration of genetic information and plays important roles in the induction of cancer, life shortening and fetal malformation after exposure to radiation. Although quantity as well as quality of radiation-induced mutations have been studied in several biological systems, the study of mutations in complicated organisms including humans has been limited because of a lack of technology to detect small number of genetic alterations. This was overcome through an application of genetic engineering. Bacterial genes whose mutations could be detected easily, were integrated into mouse genome, where they behave like mouse genes. These mice were examined to study radiation-induced mutations and found to have low sensitivity to detect mutations in many cases. Thus, there are few studies on mutation induction with sub-lethal dose of radiation, and no data is available yet for tritium-induced mutations.

We first examined two lines of transgenic mouse, gpt delta and Muta, for sensitivity of radiation-induced mutations in spleen. The gpt delta mouse could detect mutations induced by 2 to 8 Gy of gamma-rays with 2-times higher sensitivity than Muta mouse. The reason seems to be that radiation induces predominantly deletion type mutation which is rather rare in natural background and gpt delta mouse can detect exclusively this deletion type mutation, whereas Muta mouse detect all types of mutation including the deletion. Next, we applied the gpt delta mouse to study mutation induction by tritiated water. A half ml of saline containing 0, 266 or 532 MBq of tritated water was administered to the mice intraperitoneally and mutations in spleen were examined 7 days later. The estimated absorbed doses were 3 Gy and 6 Gy, respectively. With 3 Gy, the mutant frequency was elevated approximately 2-fold above control level, and it remained at a similar level with 6 Gy. These indicate that gpt delta mouse could be a good model animal to study genotoxicity of tritium.