

## §29. Assessment Study on Biological Effects of Radiation in LHD

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The main results of this program were as follows.

(1) Effect of exposure to tritiated water and gamma rays during gestation on androgen receptor mRNA expression in the offspring mice epididymis (Ichimasa, Y.)

The fetus is known to be radiosensitive. Vergouwen et al (1995) reported that the radiosensitivity of the gonocytes was increased with fetal age when pregnant mice were exposed to single doses of X rays. Fetuses are also very sensitive to environmental endocrine disruptors. In the present study, we examined whether low dose radiation exposure at fetal period caused similar antiandrogenic effects such as feminized males and change of androgen receptor (AR) mRNA expression in epididymis etc. in offspring male mice or not. Pregnant mice were orally administered HTO (10.9kBq/g body weight) or exposed to <sup>137</sup>Cs gamma rays (0.3Gy/h) at gestational day 14, and then body weight, ano-genital distance, survival rate, ability of reproduction and organ weight of its offspring were determined, and quantitative AR mRNA expression in caudal epididymis at day 82 of male offspring by using competitive RT-PCR. As for each measurement items and AR mRNA expression in caudal epididymis, no significant effects of HTO or gamma ray exposure were observed.

(2) Uptake of tritium from tritiated water exposure in the medaka and zebra fish and estimation of DNA damage due to tritium (Ichimasa, Y.)

In the present work, the biological effect of tritium on tissue and erythrocyte DNA of fresh water fishes was estimated by the comet assay during long term exposure of tritiated water (HTO). Medaka or zebra fishes were exposed to HTO (146 – 1042Bq/ml) added to an aquarium for 10-26 days and the uptake, retention and release of tritium in fish body were investigated. Total tritium per g fresh weight of medaka equilibrated rapidly, around 40min after the start of exposure, to about 50% of the aquarium water concentration while organically bound tritium reached only 1% of the aquarium water concentration after 10 days exposure. The biological half time of tritium in the fishes transferred to fresh water after 26days exposure was 14 min. The effect of long term exposure to low dose tritium on fresh water fish was examined using medaka fed in HTO (2Bq/ml) containing aquarium for 232 days. No significant effect was observed in the liver cell.

(3) Mutation induction by low dose rate tritium radiation: An analysis using hyper sensitive detection system (Tauchi, H.)

An exposure condition of tritium radiation from nuclear fusion reactor could be a long-term exposure with low dose rate. The biological effects of low dose (rate) radiation are not clear because any suitable detection system has not been established. Regarding to mutation induction by high LET radiation such as neutrons, the reversed dose rate effect has been reported when the dose rate is lower than a certain value. This might be caused by hypersensitivity of G2/M cells for mutation induction by high LET radiation. However, it is not clear whether this phenomenon could be seen in the case of tritium radiation. To examine the low dose rate effect of tritium, we established a hypersensitive mutation detection system using hamster cells carrying a human X-chromosome. We have tested mutation induction by tritiated water at dose rate between 0.15 and 4.4 cGy/h. Our results suggest that mutation frequency seems to be slightly increased at lower dose rate tritium radiation but the increase level was much less than that by neutrons.

(4) Subcellular distribution of organically bound tritium in the rat liver after ingestion of tritiated water and some tritiated organic compounds (Takeda, H.)

Tritiated water and some tritiated organic compounds (leucine, glucose and thymidine) were administered to rats by oral ingestion and the content of organically bound tritium (OBT) in subcellular fractions (cold PCA soluble, ethanol-ether soluble, hot PCA soluble and alkali soluble) of the liver were determined at various time points after ingestion. In the case of tritiated water, the initial OBT content was high in the cold PCA soluble fraction, which contains low molecular weight components, but as the time proceeded the OBT was distributed to other fractions, which contains relatively high molecular weight components. Significant time variation in the OBT content was observed in the hot PCA soluble fraction containing nucleic acids, in which the OBT content, expressed as percentage of OBT content in all fractions, changed from 1 % at 12 hours to 15 % at 50 days. In the cases of tritiated organic compounds, the subcellular distribution of OBT was widely changed owing to their biochemical and metabolic characteristics. Thus, the OBT distribution among subcellular fractions was changed depending on the chemical form at ingestion and on the time after ingestion. The OBT distribution among four subcellular fractions after 22 day' continuous ingestion was also dependent on the chemical form of ingested tritium. Present results should be taken into account for internal dose estimation of tritium in different chemical forms.

(5) Nbs1 and its functional role in the DNA damage response. (Komatsu, K)

(6) Interaction of ligand-receptor system between stromal-cell-derived factor-1 and CXCR4 chemokine receptor 4 in human prostate cancer: a possible predictor of metastasis. (Kamiya, K.)

### Reference

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