§28. Assessment Study on Biological Effects of Radiation in LHD

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The main results of this program were as follows.

(1) Analysis of mutation induction by low dose rate tritium radiation using a hyper- sensitive system.

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An exposure condition of tritium radiation from nuclear fusion reactor could be a long-term exposure at low dose rate. The biological effects of low dose (rate) radiation are not clear because none of suitable detection system has 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. On the other hand, 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 radiation, we established a hypersensitive mutation detection system using hamster cells carrying a human X-chromosome. In this system, any mutation or deletion in the human X chromosome will not affect cell viability when cells are cultured in normal medium. This system appears to be able to detect a wide spectrum of mutations, even mutations affecting the expression of important genes in the neighborhood of the Hprt gene. We have tested mutation induction by tritiated water at dose rate between 0.13 and 4.4 cGy/h. Although mutation frequency seems to be slightly increased at lower dose rate tritium radiation, it was not statistically significant. Our results suggest that the reversed dose rate effect may not be seen for mutation induction by tritium radiation.

(2) Tritiated Water Behavior in Vinclozolin Administered Pregnant Mouse

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The fetus is known to be radiosensitive. The increased radiosensitivity of the gonocites with fetal age was reported 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 the effects of multiple contamination of tritiated water and vinclozolin, an endocrine disruptors with antiandrogen activity, orally administered to pregnant mouse on the fetus. Pregnant mice were orally administered HTO and vinclozolin at the middle gestation, and tritium concentrations of urine of pregnant mouse, blood and tissues of fetus and placenta and fetal membrane were determined with time until 20 days after the administration. The accumulation doses and biological half lives of HTO in mother mouse and fetus were calculated. Antiandrogenic effects of vinclozolin were also examined.

1) Transfer of tritium from the pregnant mice administered HTO to their fetus and offspring.

Pregnant mice ware administered HTO(20MBq) by oral ingestion at gestatinal day 14, and tritium contents in urine, tissues fetus and offspring were determined at various time points after ingestion. Offspring were born at gestational day 19. The accumulation dose for 15 days after ingestion of HTO was 108mGy for the parent mice and 122mGy for their offspring, respectively. No significant difference in the dose was observed ($p<0.05$).

2) Combined effects of HTO, gamma ray and Vinclozolin one of environmental hormone disruptors). Five groups of pregnant mice were exposed to Vinclozolin, HTO, Vinclozolin + HTO, gamma ray, gamma ray + Vinclozolin, respectively gestational day 14. Vinclozolin and HTO ware administered orally. Fetus survival rate and testis weight of male fetus were determined at gestational day 19. No significant combined effects ware observed.

(3)Function analysis of fuman Rad62 in SMC5-6 complex member.

Kenshi Komatsu, Saori Itoh, Hiroko Fujimoto, Junya Kobayashi, Kiyoshi Minagawa

The structural maintenance of chromosome (SMC), family proteins that plays a central role in chromosome dynamics and stability, is categorized to three groups in eukaryotes: SMC1-3 as a core protein of the cohesions which regulates the chromosome synapsis, SMC2-4 as a core protein of condensins which plays a role in chromosome condensation during miosis and SMC5-6 complex possibly involved in DNA repair and chromosome segregation. Yeast SMC5 or SMC6 mutants showed increased sensitivity to DNA damage-inducing agents such as methyl methanesulfonate (MMS) and hydroxyurea (HU), suggesting the potential involvement in homologous recombination repair and stabilization of replication fork. Moreover, high sensitivity to MMS and ionizing radiation is reported in the mutants of yeast Rad62, non-SMC proteins formed complex with SMC5-6.

To clarify the function of SMC5-6/non-SMC protein complex in higher eukariotes, we identify human Rad62 gene and analysis the role in a response to radiation damage. Two orthologs of Rad62, Rad62A and Rad62B, were identified when human cDNA was screened. The modification of Rad62A protein was observed after exposure to radiation (IR). We are presently preparing Rad62A knock-down cells to examine the sensitivity to DNA damage agents, such as UV and radiation.

(4) Radioadaptation response for protection against radiation-induced apoptosis in mouse spleen.

Toshiyuki Norimura, Ryuji Okazaki, Akira Ootsuyama

The effects of priming dose on the frequency of apoptosis and the expression of p53 in C57BL/6N mouse spleen were investigated. Mice received a whole body irradiation with 0.02Gy and 2Gy (an omission of a middle part.)

It was suggested that p53 stimulates repair system and then protects from apoptosis in the adaptive response.