

Paper published in *Radiation Research*⁸

“Fetal Irradiation of Rats Induces Persistent Translocations in Mammary Epithelial Cells Similar to the Level after Adult Irradiation, but Not in Hematolymphoid Cells”

Mimako Nakano, Mayumi Nishimura, Kanya Hamasaki, Shuji Mishima, Mitsuaki Yoshida, Akifumi Nakata, Yoshiya Shimada, Asao Noda, Nori Nakamura, Yoshiaki Kodama

Radiat Res 2014 (February); 181(2):172–6

(doi: 10.1667/RR13446.1)

Study Findings

Examination of rat chromosomes following fetal irradiation showed radiation-induced chromosome aberrations in mammary epithelial cells similar to those found in the mothers, but very few aberrations were observed in lymphocytes. This result demonstrates the presence of tissue specificity with regard to chromosome aberrations following fetal radiation exposure.

Explanation

Previous studies on humans and mice have shown that fetal exposure to radiation fails to induce persistent chromosome aberrations in blood lymphocytes. Such a low level of response to radiation exposure is counterintuitive in view of the generally accepted belief that fetuses are highly sensitive to radiation. In this study, we examined chromosomes of mammary tissues in rats irradiated *in utero* to determine whether or not the same result is observed in other tissues.

1. Objectives

With the aim of determining whether or not the frequencies of chromosome aberration attributable to fetal radiation exposure differ by tissue type, this study examined mammary epithelial cells in rats. In addition, chromosomes of spleen lymphocytes were examined in a subgroup of rats to compare the frequencies of aberration between blood cells and epithelial cells.

2. Methods

Pregnant rats were irradiated at a dose of 2 Gy on day 17.5 of gestation. Mammary tissues were collected from the mothers and their offspring six, nine, and 45 weeks after irradiation. After mammary epithelial cells were cultured, chromosome samples were prepared by a conventional method. To detect translocations, we adopted the fluorescent *in situ* hybridization (FISH) technique to stain chromosomes 2 and 4 green and red, respectively (see Figure), and 800 cells were examined for each rat. The same procedure was followed to examine the chromosomes of cultured spleen lymphocytes.

3. Results

- (1) The mean translocation frequency in mammary epithelial cells of rats irradiated *in utero* with a dose of 2 Gy was 3.7% (n = 23). This figure is similar to the mean frequency of 2.9% observed in the mothers (n = 5).
- (2) The translocation frequency in spleen lymphocytes was 0.0–0.6% among rats irradiated *in utero* (mean frequency: 0.4%, n = 13), which was significantly lower than the mean translocation frequency of 3.5% observed in the mothers (n = 3).
- (3) Translocation frequencies were similar at six, nine, and 45 weeks after irradiation.

As noted above, this study showed that the frequency of chromosome aberrations in the mammary cells of rats irradiated *in utero*, and examined at six to 45 weeks of age, was as high as that in the mothers. In contrast, the translocation frequency in lymphocytes was high in the mothers but considerably lower among rats irradiated *in utero* (about 10% of that of the mothers), supporting the findings in previous studies on mice and humans. These results suggest tissue specificity in the chromosome aberration pattern in fetal exposure. If the translocation frequency is assumed to be an index of the carcinogenic effect of radiation, this study suggests that fetal radiation exposure may induce persistent carcinogenic damage in mammary stem cells and progenitor cells. However, the

results of another report showed that fetal exposure in rats did not increase breast cancer risk. No clear reason has been identified that can explain this discrepancy, highlighting the need for further study.

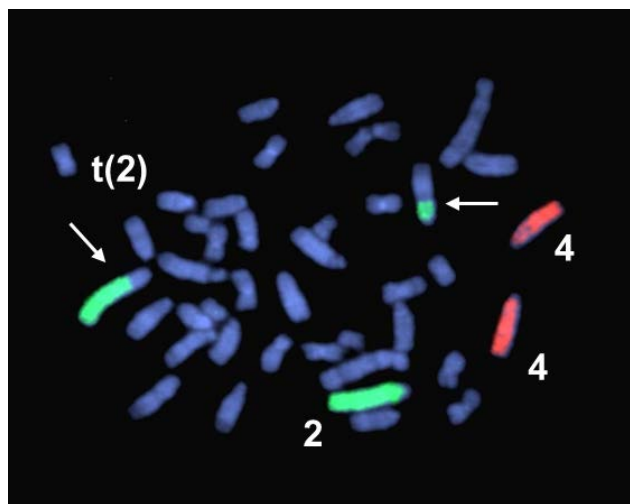


Figure. Detection of translocation (t) by FISH. Chromosomes 2 and 4 are stained green and red, respectively, and the remaining chromosomes are stained blue. Chromosomes stained in two colors (indicated by arrows) are detected as abnormal chromosomes (translocations).

The Radiation Effects Research Foundation has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for more than 60 years. RERF's research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

[§]**Radiation Research**, which is an official monthly journal of the Radiation Research Society, publishes original, peer-reviewed papers and review articles on radiation effects and related issues in the fields of physics, chemistry, biology, and medicine. (Impact factor in 2012: 2.698)