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マウスを用いた宇宙空間模擬環境による生体影響評価

Biological effects of simulated space environments in mice

柿沼志津子 [1], 鈴木健之 [1], 鶴岡千鶴 [1], 森岡孝満 [1], 柳原啓見 [1], 神戸崚輔 [2], 髙橋昭久 [2],
Shizuko Kakinuma[1], Kenshi Suzuki[1], Chizuru Tsuruoka[1], Takamitsu Morioka[1], Hiromi Yanagihara[1], Ryosuke Kanbe[2], and Akihisa Takahashi[2]

1 量研・放射線医学総合研究所，National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST),
2 群馬大学重粒子線医学研究センター，Gunma University Heavy Ion Medical Center,

1. Introduction

The present manned space missions have been ongoing to stay for 6 months to 1 year at the International Space Station (ISS) at the Earth's low earth orbit. As a next step, expeditions to the Moon and Mars is planned. Specially, the mission to Mars requires nearly three years in space. For safe long-term stays in space, it is urgent that we evaluate any detrimental effects on human physiological, behavioral, and psychological health to ensure astronaut health and performance under outer space-specific conditions. It is expected that astronauts will be affected by the combined biological effects of weightlessness and harsh radiation during their long stay in space, but the effects have not yet been fully clarified.

The tail suspension by lifting the hind limbs of a mice has been widely used as an experimental system to simulate a microgravity state and a behavioral suppression state in outer space. Using this system, Takahashi et al has reported that tail suspension promoted the growth of transplanted tumor and lymphoid organ atrophy [1].

We aimed to analyze the effects of tail suspension on spontaneously-developed or radiation-induced tumor development in a model animal C3B6F1 *Apc*$^{Min/+}$ mice that induces intestinal tumors spontaneously.

2. Methods

2.1 Mice

Male C57BL/6J *Apc*$^{Min/+}$ and female C3H/HeNCrl mice were intercrossed to obtain male F1 hybrid C3B6F1 *Apc*$^{Min/+}$ mice. The *Apc* genotype was determined by PCR using DNA from mouse ear punch. The F1 mice were housed in environmentally controlled clean conventional room, under the condition of a 12-hours dark-light cycle, temperature of 23 ± 2℃, and 50 ± 10% humidity.

2.2 Irradiation and tail suspension

The male C3B6F1 *Apc*$^{Min/+}$ mice were randomly divided into 4 experimental groups: Non-irradiated with/without tail suspension; 2 Gy-irradiated with/without tail suspension. All mice were whole body irradiated with 0 Gy or 2 Gy of X-rays at 2 weeks of age which was most susceptible age to radiation [2]. X-ray irradiation was carried out using a PANTAK X-ray generator. Mice were suspended the tail from 7 to 10 weeks of age, as same condition of Takahashi's report [1].

Mice in all groups were sacrificed at 10, 15, or 17 weeks of age under isoflurane anesthesia for grossly and histological examination on small intestinal tumors, and measured the weight of body, thymus and spleen.. All mice were handled according to the principles and procedures outlined in our institution's animal welfare committee of Health Guide for the Care and Use of Animals.

The small intestines were collected carefully, washed with cold physiological saline, opened longitudinally and the

mucosal layer spread out over filter paper to expose any tumors protruding into the lumen. They were then fixed with 10% neutral-buffered formalin for 24 hours. The number and size of tumors were measured under the stereomicroscope.

3. Results and Conclusion

At 10 weeks of age, just after tail suspension, the weight of body, thymus and spleen were reduced after tail suspension compared with un-suspension group. These data confirmed the previous report, suggesting this tail suspension experiment works similarly. Number of tumors after irradiation was tend to higher than without irradiation. However, number of tumors did not show difference regardless tail suspension. The results at 15 and 17 weeks of age has been analyzing, and that will be clarified the effect of tail suspension on the spontaneous or radiation induced tumor development. The goal is to understand the complex biological effects that are expected in outer space, and to connect them to risk assessments and countermeasures for future long-term stays in space.

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