

Research Center for Medical Sciences Radioisotope Research Facilities

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General Summary

The Radioisotope Research Facilities were established to support medical and biological research using radioisotopes. The Facilities also accept the research using non-radioactive isotopes. We have supported researchers by suggesting methods and practical techniques for experiments. Lectures and training courses are held for researchers and for medical students and graduate students. In 2017, 42 researchers from 14 departments and 12 students of 2 curriculums used the laboratory of this facility. Major nuclides used for experiments were ^{32}P , ^{51}Cr , ^{125}I , ^{14}C , and ^3H , ^{134}Cs , ^{137}Cs .

The Fukushima Dai-ichi Nuclear Power Plant was damaged by the Tohoku-Pacific Ocean Earthquake on March 11, 2011. Large amounts of fallout were released into the environment by the accident. We focus on the study of the behavior and distribution of the radioactive materials in the environment. Education related to radiation is also an interest.

Research Activities

E-cadherin suppression in epoxomicin-resistant cells may be regulated by expression of ZEB1

Our previous study has demonstrated that proteasome inhibitor, epoxomicin (EXM)-resistant endometrial carcinoma Ishikawa cells (Ishikawa/EXM) were suppressed E-cadherin via expression of transcriptional repressor gene ZEB1. Down-regulation of E-cadherin plays an important role in epithelial-mesenchymal transition (EMT). The expression of ZEB1 was concerned with suppression of dual specificity protein phosphatase 6 (DUSP6) via ERK1/2 signal transduction. As we found DUSP6/MKP3 disappearing in Ishikawa/EXM, we studied here participation of DUSP6/MKP3 in E-cadherin expression on Ishikawa/EXM. Suppression of DUSP6 and expression of Fos-related antigen 1 (Fra1) was observed in Ishikawa/EXM compared in Ishikawa cells. It was reported that activated ERK2 was expressed ZEB1/2 following phosphorylation of Fra1. Both knock-down of DUSP6 by treatment of Ishikawa with siRNA for DUSP6 and inhibition of DUSP6 activity by treatment of Ishikawa with (E)-2-Benzylidene-3-(cyclohexylamino)-2,3-dihydro-1H-inden-1-one (BCI), an inhibitor of DUSP6 activity, induced expression of Fra1 by activation of ERK2, and induced repression of E-cadherin following expression of ZEB1. Moreover, over-expression of Fra1 in Ishikawa transfected with Fra1/pcDNA3.1 caused ZEB1-induced suppression of E-cadherin. On the other hand, expression of DUSP6 by transfection of Ishikawa/EXM with DUSP6/pcDNA3.1 induced expression of E-cadherin following suppression of Fra1 and ZEB1. These results suggest that disappearance of DUSP6 in Ishikawa/EXM caused up-regulation of ZEB1 via expression of Fra1 and

induced EMT.

Analysis of resistance mechanisms in radiation-resistant organisms

Tardigrades, which are called water bears, can tolerate extreme environments, including ionizing radiation and dryness. The sludge water bear *Isohypsibius* were isolated from the activated sludge in Morigasaki Water Reclamation Center, and the terrestrial water bear *Milnesium tardigradum* were isolated from moss collected at Minato Ward in Tokyo. To clarify the radiation-resistant mechanism, tardigrades were irradiated with X-ray at 250 Gy, and DNA damage was analyzed with the comet assay method.

Measuring and tracing of radioactive fallout in the environment

The distribution and behavior of radioactive fallout released into the environment by the accident of the Fukushima Daiichi Nuclear Power Plant in March 2011 have been investigated. Because contaminated water had been leaked into the ocean by accident, we recently examined a safe, simple and rapid method of analyzing radioactive strontium in seawater. Radioactive strontium was separated by a column of cation exchange resin (Dowex 50W \times 8, Dow Chemical Company, Midland, MI, USA) and was measured using newly developed plastic scintillator bottle with liquid scintillation system (LSC-LB7, Hitachi Ltd.). With this method, the chemical separation of 10 hours (total 2 days) could be evaluated and compared with 2 weeks with a conventional technique. The detection limit in this procedure from 1 L of seawater was 0.02 Bq/L. This method might be able to be used to survey contaminated seawater.

Anti-tumor effect of thoron

Thoron, which is a gaseous radioactive element and radioisotope of radon, dissolves in groundwater and hot springs and then reaches the surface of the ground. We studied the anti-tumor effect of thoron in hot springs on tumor-bearing mouse.

Publications

Ohkawa K, Asakura T, Tsukada Y, Matsuura T. Antibody to human α -fetoprotein inhibits cell growth of human hepatocellular carcinoma cells by

resuscitating the PTEN molecule: *in vitro* experiments. *Int J Oncol.* 2017; **50**: 2180-90.