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 2016, 35 researchers from 11 departments and 8 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 ^{3}H.

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.

Proteasome inhibitors are drugs with highly anticipated efficacy as clinical anticancer drugs. One such inhibitor, PS-341, is already being used to treat multiple myeloma. However, little data is available on the clinical use of proteasome inhibitors as anticancer drugs. If a proteasome inhibitor has systemic side effects or if cancer cells have become resistant and reappear after inadequate or incomplete cancer therapy, this type of agent must be administered with extreme care. To evaluate the generation of inhibitor-resistant cells and their specific properties, a strategy for second-line chemotherapy must be developed.

Research Activities

Expression of ZEB1 by repression of microRNA-200 (miR200) in proteasome inhibitor-resistant cells may be suppressed E-cadherin

Endometrial carcinoma Ishikawa which acquired resistance for Epoxomicine (EXM), a proteasome inhibitor caused epithelial-mesenchymal transition (EMT) with the onset of E-cadherin disappearance. I made clear that transcription repressor ZEB1 regulated expression of E-cadherin.

We examined expression of E-cadherin in the microRNA (miR) expression recently because regulation of various kinds of genetic expression by miR was reported. We measured expression of miR in Ishikawa and EXM-resistant Ishikawa (Ish/EXM) as follows: miR9, miR10a, miR10b, miR21, miR23a, miR23b, miR34a, miR141, miR150, miR192, miR200a, miR200b, miR200c, miR205, miR206, miR215, miR217, miR221, miR298, miR374b, miR382, miR429, miR508-3p, miR539. As a result, miR10a and miR10b expressed in Ish/EXM, and miR141, miR200a, miR200b and miR200c suppressed in Ish/

EXM. Because homogeny of the base sequence was high, miR141, miR200a, miR200b and miR200c were called miR200 family, and the regulation of EMT by miR200 family was reported, we examined expression of transcription inhibitor ZEB1.
The miR200 family was highly expressed in Ishikawa where E-cadherin expressed here, and expression of ZEB1 disappeared, and expression of miR200 family disappeared in Ish/EXM where expression of E-cadherin disappeared, and ZEB1 expressed. In addition, because the expression of miR200 family which disappeared was not restored even if I knocked down ZEB1 of Ish/EXM, miR200 family was located in the upstream of ZEB1. Therefore, we regulated expression of miR200 family in Ishikawa and Ish/EXM by transfection of anti-miRNA and pre-miRNA. When we transfected anti-miR200 and knocked down miR200 of Ishikawa which expressed of miR200, ZEB1 appeared, and expression of E-cadherin was repressed with expression of ZEB1. When we transfected pre-miR200 into Ish/EXM which disappeared of miR200 and produced miR200, ZEB1 disappeared, and expression of E-cadherin was restored. These turned out similar at a gene level and protein level, and it was suggested that miR200 family was located in the upstream of ZEB1.

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 Mikawajima 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 50 to 300 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 50WX8, 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 200 mL of seawater was 0.1 Bq/L. This method might be able to be used to survey contaminated seawater.

Study of radon
Radon, which is a gaseous radioactive element, dissolves in groundwater and hot springs and then reaches the surface of the ground. The radon contamination in groundwater reflects the underground structure. We measured the radon concentrations of 57 springs that has been designated by the Tokyo Metropolitan Government Bureau of Environment and discussed the geological features of Tokyo.

Publications

Yokoyama T, Misawa K, Okano O, Minowa H, Fukuoka T. Photostimulated luminescence applicable to pre-screening of potassium-rich phases in chondritic breccias. *J Radioanal Nucl Chem.* 2016; **310:** 81-9.