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 2015, 36 researchers from 10 departments and 16 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

E-cadherin suppression in epoxomicin-resistant cells may be regulated by expression of zinc finger E-box-binding homeobox 1

The Ish/EXM strain, comprised of endometrial carcinoma Ishikawa cells resistant to epoxomicin, a proteasome-specific inhibitor, was established, and several features were examined to overcome the resistance to treatment.

The 50% growth inhibition concentration for epoxomicin against Ishikawa cells and Ish/EXM cells was 20 and 400 nM, respectively. The Ish/EXM cells have also acquired resistance to the proteasome inhibitors MG132, PSI, and PS-341.

Acquiring resistance to epoxomicin led to the disappearance of both E-cadherin 1 gene (*CDH1*) messenger (m) RNA and E-cadherin protein in Ish/EXM cells and to the induction of epithelial-mesenchymal transition (EMT) in Ish/EXM cells. Because E-cadherin protein expression is regulated by a transcriptional suppression factor, we used the reverse transcriptase–polymerase chain reaction to measure mRNA expression of several factors related to E-cadherin suppression, specifically Snail, Slug, zinc finger E-box-binding

homeobox 1 (ZEB1), ZEB2, E12/E47, and Twist, in Ish/EXM cells. Among these suppressors concerning epoxomicin induction, expression of ZEB1 and ZEB2 was especially enhanced in Ish/EXM cells, and expression of the ZEB1 protein was markedly increased. On the other hand, because E-cadherin was suppressed in Ish/EXM cells, we expected EMT to be induced in these cells. Therefore, we measured the migration of both Ishikawa and Ish/EXM cells. The invasive capacity of Ish/EXM cells increased to 5.7 times that of Ishikawa cells.
To identify the primary transcriptional suppressor for E-cadherin suppression, the factors Snail, Slug, ZEB1, ZEB2, and Twist were knocked down in Ish/EXM cells. Treatment of Ish/EXM cells with ZEB1 small– interfering (si) RNA but not with ZEB2, Snail, Slug, or Twist siRNA restored the expression of both E-cadherin mRNA and E-cadherin protein. Of note, treatment of Ish/EXM cells with ZEB2 siRNA partially restored expression of E-cadherin mRNA.

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. The X-ray–irradiated cells show a longer tail than did the control nonirradiated cells. However, because the observed results were not quantified automatically, the experimental operation needs to be improved.

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 with a liquid scintillation counter. With this method, the chemical separation of 24 hours could be evaluated and compared with 2 weeks with a conventional technique. The detection limit in this procedure from 1 liter 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 concentration of spring waters designated as the 57 best waters by the Tokyo Metropolitan Government Bureau of Environment. The results of this study were presented at the 68th annual meeting of the Japanese Society of Hot Spring Sciences (September 2015, Yamagata, Japan).