



Message from the Chairman

Toshiteru Okubo

FY2011 was a transitional year for the Radiation Effects Research Foundation (RERF) as the organization changed its status to a public interest incorporated foundation from a juridical foundation. RERF became an exceptional incorporated foundation with councilors in April 2011 and made the first step as a new foundation by holding the first meeting of its Board of Councilors. It can be said that RERF literally entered a new era. It was also the year, on February 6, 2012, that RERF Consultant Emeritus Itsuzo Shigematsu, who served as RERF Chairman for all of 16 years, passed away. All employees of the new foundation are determined to take on the aims of Dr. Shigematsu and the others that came before us, utilize the human resources and research achievements accumulated over so many years, enhance our ties with related organizations, and build a firm basis for RERF's next 20 years. To that end, everyone's continued understanding and support are kindly requested.

[I] Major activities

1. Board of Councilors meeting

The first meeting of the Board of Councilors (BOC) was held on June 21–22, 2011 at Hiroshima RERF. BOC is a decision-making body replacing the former Board of Directors (BOD). Of the eight councilors, seven were in attendance at the meeting, and the Board of Councilors deliberated the activities report, settlement of accounts report, activities plan, working budget, procedures for transition to a public interest incorporated foundation, and appointment of directors, among other issues. Also discussed was RERF's response to the Fukushima Dai-ichi nuclear power plant accident.

2. Scientific Advisory Committee meeting

Replacing the Scientific Council, the Scientific Advisory Committee held its 39th meeting on March 5–7, 2012, at Hiroshima RERF, reviewing RERF's research progress and plans. Consisting of 10 external members and three special advisory members selected from the U.S. and Japan, the committee this year focused its review on the Departments of Genetics and Radiobiology/Molecular Epidemiology. The co-chairpersons from the U.S. and Japan will prepare formal recommendations and present them to the second BOC meeting to be held in June 2012.

3. Personnel actions for researchers

- 1) As of July 1, 2011, Dr. Mieko Kodaira, Chief, Biochemical Genetics Laboratory, Genetics Department, was appointed as a fixed-term research scientist upon her mandatory retirement.
- 2) As of July 1, 2011, Dr. Asao Noda, Chief, Cytogenetics Laboratory, was promoted to Assistant Chief of the Genetics Department, and Dr. Yuko Hirai, Senior Scientist, was promoted to Dr. Noda's former post.
- 3) As of August 1, 2011, Dr. Waka Ohishi, Chief, Division of Clinical Laboratories, was promoted to Assistant Chief of the Clinical Studies Department (Acting Chief of the Division of Clinical Laboratories).
- 4) As of August 15, 2011, Dr. Ravindra Khattree, Senior Scientist (fixed-term research scientist), Statistics Department, retired from RERF.
- 5) As of March 31, 2012, Dr. Saeko Fujiwara, Chief, Clinical Studies Department, retired from RERF, and Dr. Ohishi was appointed to serve as Acting Chief of the department.
- 6) As of March 31, 2012, Dr. Akihiko Suyama, Chief, Epidemiology Department, Nagasaki, retired from RERF.

4. Clinical Study of the F₁ Offspring of A-bomb Survivors

The second meeting of the Scientific and Ethics Committee for the Clinical Study of the F₁ Offspring of A-bomb Survivors was held at the Hiroshima Laboratory on January 12, 2012. In the meeting, the committee reported on the following items: the first-year progress of the Longitudinal Clinical Study of the F₁ Offspring of A-bomb Survivors initiated with about 12,000 subjects including the participation rate in the study's health

examinations, and the lack of evidence proving parental radiation exposure-related increases in respective disease risks based on results of additional analyses examining individual multifactorial diseases with use of data from the original disease prevalence study conducted during the period 2000–2006, among other information.

5. Application for research grant

In the five-year project related to the study of age-related decline in immune function accelerated by radiation exposure based on a contract between RERF and the U.S. National Institute of Allergy and Infectious Diseases (NIAID), a full-scale study of flu vaccine effectiveness started in 2011. Blood samples before and after vaccination are being obtained from about 350 A-bomb survivors. This study will provide a window into the degree to which radiation-associated immune changes affect health status. In the next two to three years, measurements of cytokine and immune markers of over 1,600 A-bomb survivors in our clinical study will be completed for establishment of an immunosenescence scoring system, and based on these new studies, substantial numbers of published papers are expected.

6. Update of information processing system

In FY2011, RERF established an internal committee to resolve the numerous issues related to the organization's information processing systems, and the committee deliberated on approaches for understanding/resolving the issues based on recommendations submitted by an outside expert organization in the form of report on system analysis/evaluation. Based on these efforts, a report was prepared in terms of proposals related to streamlining of departmental system use, measures for improvement of work request forms, and enhanced security, and others.

7. Standing committee on radiation dosimetry

As for reassessment of individual dose estimates for the Life Span Study (LSS) participants at Hiroshima and Nagasaki RERF, we started reconfirmation work of exposure location using aerial photographs regarding about 20,000 survivors for whom neighborhood drawings describing shielding history were available.

With respect to the LSS participants, cross-checking work between hardcopy questionnaire dose-related information (location, shielding, etc.) and electronic data was completed. In conjunction, information pertinent to "black rain" exposure was newly entered into the database, with such information very limited in the original records.

8. Workshops and meetings

The international workshop "Radiation Effects on Mutation in Somatic and Germline Stem Cells" was held at RERF's Hiroshima Laboratory on January 18–19, 2012. The workshop, aiming at obtaining information on the quickly advancing field of stem cell research and the debate about effects of radiation on stem cells, was attended by four stem cell researchers from abroad and five from Japan invited to attend the event.

9. Response to the Fukushima Dai-ichi nuclear power plant accident

On April 25, 2011, six faculty members of Fukushima Medical University, including Dr. Seichi Takenoshita, Vice Chairman of the university, visited RERF's Hiroshima Laboratory. RERF representatives briefed the visitors at the Auditorium on the forward-looking studies of health effects of radiation that have been conducted by ABCC-RERF, followed by active discussion between the group and RERF representatives. The next day, April 26, the faculty members visited the Nagasaki Laboratory and were briefed by Dr. Masazumi Akahoshi, Chief of the Department of Clinical Studies, on the studies conducted in Nagasaki. On August 12, 2011, RERF and Fukushima Medical University signed an agreement for strengthening collaboration in the fields of education, research, and public health at the university. Specifically, the agreement aims at further development of both organizations and establishment of a pioneering educational/research center concerning health effects of radiation through promotion of educational and academic research activities in the field of radiation effects research, closer interactions between university faculty members and RERF researchers, and improvement of the health and welfare of residents of Hiroshima, Nagasaki, and Fukushima prefectures.

[II] Government-mandated personnel reduction plan

The ongoing personnel reduction plan mandated by the Japanese national government requests that RERF reduce its employee number by 24 persons over a five-year period starting in FY2010. RERF has adopted a management policy of maintaining its present strength of research staff, and as a result, the number of general staff fell by 53.4 persons from 240, a decrease of about 22%, over the past 11 years. Vacancies in multiple research staff positions have become a normal state of affairs, and RERF has finally managed to fill the posts vacated by those who resigned. RERF intends to maintain the current 48 budgeted personnel slots for its research staff.

[III] Senior Review Panel on Future Planning for RERF

The Panel had recommended that the U.S. and Japanese governments and RERF discuss and reach a conclusion over a two-year period about RERF's future after conclusion of its core studies. At the BOD meeting in June 2010, at the completion of the two-year time limit, the U.S. and Japanese governments reported to the BOD that any such conclusion would take more time, a situation that was accepted by the BOD. Discussion on RERF's future was thus continued this fiscal year.

[IV] Liaison with local communities and related organizations

1. Local Liaison Councils

The first BOC meeting in June 2011 appointed two of the local advisors tasked with conveying opinions from the local community directly to the BOC and BOD. The 20th meeting of the Nagasaki Local Liaison Council was held at the Nagasaki Laboratory on July 14, 2011. Following that meeting, the 17th meeting of the Hiroshima Local Liaison Council was held at Hiroshima RERF on July 27. At both meetings, RERF reported on its present status, recent study results, clinical study of second-generation A-bomb survivors, status of the collaborative study with NIAID, and its PR activities. RERF's report on its response to the Fukushima Dai-ichi nuclear power plant crisis led to active discussion concerning RERF's support for long-term epidemiological studies in Fukushima and strengthening of collaborative arrangements with other related institutes. In addition, members made vigorous demands in particular for relocation of the Hiroshima facilities, just as the group did at last year's meeting.

2. Council of Radiation Effect Research Organizations

The Council of Radiation Effect Research Organizations, which was established to promote mutual understanding and partnership among radiation research organizations, held its sixth meeting in Tokyo in April 2011.

In addition, under the sponsorship of the council, the training seminar "Epidemiological Training Workshop for Biologists" for study about epidemiological approaches from a multidisciplinary perspective regarding radiation risk was held at Hiroshima RERF on September 26–27, 2011. The seminar was attended by radiobiologists and geneticists (56 non-RERF researchers and 26 RERF researchers), contributing to understanding among biologists of epidemiological research and communication between biologists, epidemiologists, and statisticians.

3. International collaboration

In response to recommendations from the Scientific Council and the Senior Review Panel, we have filed an application with the International Atomic Energy Agency (IAEA) for designation as an IAEA collaborating center. At the same time, we are now preparing to apply for registration with the IAEA Response Assistance Network (RANET), an organization that promptly responds to requests for assistance in the case of nuclear accident or radiation emergency.

In FY2011, RERF received 149 trainees from abroad on its own or through collaboration with the Hiroshima International Council for Health Care of the Radiation-exposed (HICARE), Nagasaki Association for Hibakusha's Medical Care (NASHIM), and Japan International Cooperation Agency (JICA), among others, and also received a total of 229 trainees from Japanese educational/research organizations (including those visiting RERF to attend research scientists' lectures). In addition, nine RERF officers and staff members attended meetings for the purpose of international collaboration.

4. Major visitors

- 1) On the afternoon of August 5, 2011, Dr. Rethy Chhem, Director, Division of Human Health, Department of Nuclear Sciences and Applications, IAEA, visited the RERF Hiroshima Laboratory. Dr. Chhem was visiting Hiroshima to exchange opinions on research collaboration with HICARE.
- 2) On February 24, 2012, two officials from Ukraine visited RERF. One was Dr. Dimitry Anatolijovich Bazyka, Director-General and Head of the Department of Clinical Immunology in the Research Centre for Radiation Medicine of the National Academy of Medical Sciences of Ukraine. The other was Dr. Valery Alexandrovich Kashparov, Director of the Ukraine Institute of Agricultural Radiology of the National University of Life and Environmental Sciences of Ukraine. The two visitors were briefed on RERF by RERF officials and others, and Dr. Bazyka then described the composition and research activities underway at the Research Centre for Radiation Medicine in Kiev, Ukraine. This was followed by an exchange of opinions regarding the findings from the center and RERF.
- 3) On January 13, 2012, Japan's Ambassador to Iceland Masayuki Takashima paid a visit to RERF's Hiroshima Laboratory. Ambassador Takashima spent two days in Hiroshima with the aim of studying issues involving peace in the city, touring the Hiroshima Peace Memorial Museum and other peace-related facilities as well as RERF. At the laboratory, RERF Chairman Toshiteru Okubo and RERF Vice Chairman Roy E. Shore provided Ambassador Takashima with a brief overview of RERF and an outline of the foundation's research efforts. The Ambassador was then led on a tour of the facilities by RERF's directors, who explained the organization's biosample storage facilities and permanent exhibitions.
- 4) Dr. Daud Mohamad, Deputy Director General of IAEA, visited RERF's Hiroshima Laboratory on November 22, 2011, accompanied by Dr. Eduardo Rosenblatt, Head of the Applied Radiation Biology and Radiotherapy Section, Division of Human Health, Department of Nuclear Sciences and Applications, IAEA. The two officers visited Hiroshima as keynote speakers for the 2011 HICARE International Symposium "The Effects of Radiation on the Human Body—Toward Establishing an International Network for Medical Care for the Radiation-exposed," held on November 23 by HICARE in cooperation with the IAEA. At RERF, they were briefed on recent research results by Chairman Okubo and Vice Chairman Shore, and then were guided by the directors, Chief Scientist Kazunori Kodama, and other senior staff on a tour of the facilities, including the biosample storage area and the Departments of

- Genetics and Epidemiology.
- 5) Ambassador Mari Amano, Delegation of Japan to the Conference on Disarmament, visited the Hiroshima Laboratory on September 16, 2011. After being briefed on RERF's current status and research activities by Chairman Okubo and other officers, Mr. Amano toured the facilities. Mr. Amano, who was appointed to the position of Japan's ambassador to the Conference on Disarmament on September 1, 2011, came to Hiroshima for the purpose of making a courtesy visit to the mayor of Hiroshima. He visited RERF to gain a general understanding of RERF's research studies.
 - 6) Dr. Jan Wondergem, Applied Radiation Biology and Radiotherapy Section of IAEA, visited the Hiroshima Laboratory on the afternoon of September 15, 2011. Dr. Wondergem is an expert in the field of biodosimetry based on chromosomal aberrations and plays a core role in research collaboration between the IAEA and HICARE. After touring the facilities, including the biological specimen storage facilities, Dr. Wondergem had a substantive discussion regarding collaborative research programs with the chiefs and assistant chiefs of the Departments of Genetics and Radiobiology/Molecular Epidemiology.
 - 7) On September 8, 2011, Mr. Atsuro Sasaki, Hiroshima Deputy Mayor, visited the Hiroshima Laboratory. Deputy Mayor Sasaki is a member of the RERF Hiroshima Local Liaison Council.

[V] Public relations activities

1. Open House event

RERF held its Open House events at the Hiroshima Laboratory for the 17th time on August 5 and 6, 2011 and at the Nagasaki Laboratory for the 15th time on August 8 and 9 under the theme "Radiation and health sciences." With enhanced public interest in radiation stemming from the Fukushima Dai-ichi nuclear power plant crisis, the Open House this year, in addition to the regular exhibitions of our latest research results, featured a special exhibition introducing the basics of radiation and its human health effects with a specialist's corner that attracted many visitors, including families with children, eager to ask questions. In the event's public lectures, which have become part of the regular program in Hiroshima, Dr. Asao Noda, Assistant Chief of the Department of Genetics, and Chief Scientist Nori Nakamura spoke about "What is radiation?" on the 5th and 6th, respectively, and on the 6th, Dr. Kotaro Ozasa, Chief of the Department of Epidemiology, spoke on the theme "What is radiation epidemiology?" Compared with the two lectures of last year's event, this year's Open House had three, with all lectures attended by large enthusiastic audiences who asked many questions even after the lectures were concluded. The events at the Hiroshima and Nagasaki Laboratories drew 1,375 and 390 visitors, respectively.

Visitors are welcome to tour RERF's facilities at other occasions besides the Open House events. During FY2011, 1,580 individuals from Japan including students on school excursions and 67 from overseas countries visited RERF to tour the facilities (as of March 31, 2012).

2. Public lecture

RERF held its first public lecture for citizens in Nagasaki on Saturday, July 16, 2011 for outreach and better public understanding of its research activities. The lecture comprised two talks, titled "Radiation and cancer risk" and "Studies on children of A-bomb survivors conducted thus far," and more than 180 people gathered in a hall of the Nagasaki Atomic Bomb Museum to attend. RERF held its second public lecture for citizens in Hiroshima on Saturday, December 10, 2011. The two talks, titled "Thinking about low-dose radiation exposure" and "Methods for radiation dose assessment," attracted more than 200 citizens to the Hiroshima lecture, which was held in the basement of the Hiroshima Peace Memorial Museum's East Building. With so many questions raised in the Q&A sessions, the lecture programs facilitated wide dissemination of accurate scientific knowledge regarding radiation risk. In a questionnaire survey conducted in conjunction with the lectures, 90% of the respondents expressed interest in attending similar events in the future.

RERF has been carrying out other public relations activities through the establishment of its permanent exhibition, updating of RERF's website, and holding of press conferences for the mass media. During FY2011, in response to the Fukushima Dai-ichi nuclear power plant crisis in particular, RERF established a special page on its website, providing a compilation of answers to frequently asked questions and RERF brochures about health effects of radiation, information on radiation emergency medical care facilities in Japan, and links to related information available in Japan and abroad. RERF also responded in timely fashion to numerous inquiries and requests for advice concerning the accident from both Japan and other countries through its website. The number of visits to RERF's website drastically increased immediately after the accident (the numbers increased to about two million hits and 30,000 visitors at the peak on March 15, 2011, from about 40,000 and 1,300, respectively, before the crisis). The total number of hits and visitors between April 1, 2011, and March 31, 2012, was about 47.7 million (daily average of 130,000) and 950,000 (daily average of 2,600), respectively.

[VI] Current status of biological sample (blood, serum and lymphocyte) storage facilities

Documents and papers in Unit G have been moved in order to make room for additional deep freezers (four or five freezer units are newly purchased each year) at the Hiroshima Laboratory. Through this and other efforts, we have managed to secure sufficient space to store a year's worth of samples. At the Nagasaki Laboratory, there should be enough room for storing specimens for at least nine years through such efforts as renovation of storage space.



Message from the Vice Chairman and Executive Director

Roy E. Shore

The data generated from the follow-up of A-bomb survivors and their children continue to be the principal basis for national and international estimates of cancer and other diseases associated with ionizing radiation. Our findings are being applied by international agencies, for instance, in estimating risk from the Fukushima reactor accident. We are also playing an advisory role regarding the planning and execution of a long-term health assessment study of Fukushima area residents.

A notable publication this year was a six-year update of cancer and noncancer mortality experience of the atomic bomb survivors. The report showed that excess rates of solid cancers are continuing to increase throughout the lifetime, cancer risk is greater for those exposed at younger ages, and the solid-cancer excess risk at low doses is approximately proportional to the dose.

This year marked progress on a number of important studies at RERF.

- ◆ Public attention recently has focused on whether radiation exposure from “black rain” fallout has materially increased rates of both acute (e.g., epilation) and chronic (e.g., cancer) conditions. We have finished computerizing the early data regarding the reported black rain and “early entrance” (to areas close to the bomb hypocenters where there would have been radioactive soil elements) exposures and plan to analyze those data to provide assessments of the risk. We are also performing geographic analyses to determine whether cancer excesses that correspond to the suggested paths of black rain exposure are evident.
- ◆ Breast cancer risk: A paper provides a new model to examine the shape of the dose-response curve for breast cancer using fewer assumptions; another examined the hypothesis that radiation exposure may have affected natural female sex-steroid hormone levels in ways that promote breast cancer risk.
- ◆ Publication on the joint effects of radiation, hepatitis virus infection and lifestyle factors on liver cancer risk. Although there are effects of lifestyle factors (e.g., alcohol consumption) and especially HBV/HCV infection on hepatocellular liver cancer risk, there is still an independent effect of radiation exposure on that risk.
- ◆ Publication providing some of the first documentation that doses of external radiation under several gray increase bone sarcoma risk.
- ◆ Researchers are attempting to understand molecular mechanisms behind radiation-related cancer, such as the role of certain types of genetic change (rearrangements in the *RET/PTC* and *ALK* genes) in radiation-related thyroid cancers, and the roles of cellular epigenetic changes (i.e., modification of genetic function by means other than through alterations in DNA) in radiation-induced cancer and other diseases.
- ◆ Radiation and circulatory disease risk: The risks of stroke and heart diseases increase at moderate-to-high doses, though the degree of risk at low doses is uncertain. Ongoing studies are aimed both at better assessments of the degree of risk for various subtypes of circulatory disease, and at examining the biological basis of the circulatory disease risks from radiation. Studies are underway on pathways of radiation effects on cardiovascular disease risk based on, for example, measurements of fat:muscle body composition, atherosclerosis and arterial stiffness, and various cytokines and cardiovascular risk biomarkers. A paper was published showing that radiation increases the incidence of hemorrhagic stroke but not ischemic stroke. Another suggested an association of radiation dose with chronic kidney dis-

ease mortality; a more detailed clinical study of radiation and kidney function is underway to better document associations among radiation, chronic kidney disease and hypertensive cardiovascular disease.

- ◆ An experimental animal study of radiation and the risk of elevated blood pressure and stroke found excess early mortality from stroke at doses of 4, 2 and 1 Gy. There are plans to extend that study to determine if yet lower doses confer risk for hypertension and stroke, measuring biomarkers to determine what circulatory disease pathways may be implicated.
- ◆ Closer examination of the apparent association of radiation with nonmalignant respiratory and digestive diseases is being conducted to clarify whether there are genuine radiation risks for various noncancer diseases, and, if so, their magnitude.
- ◆ Past RERF immunology studies determined that both immune cell counts and immune function were compromised by radiation in a manner substantially similar to immune changes associated with aging. Research currently underway aims to determine the mechanisms of radiation-derived immune aging—how radiation affects the stem cells, dendritic cells and thymus that give rise to or activate the mature immune cells.
- ◆ Measurements of a large number of cytokine and immune markers to develop a robust immune-aging scoring system are being conducted for over 3,000 A-bomb survivors in our clinical study. It will then be possible to relate radiation dose to immune status after adjusting for other factors that affect immune function, and to determine the impact of radiogenic immune effects on the incidence of various diseases.
- ◆ Trans-generational genetic effects of radiation: Since many diseases besides cancer have a strong genetic component, a unique study was developed to establish whether there are radiation-associated inherited risks for common adult noncancer diseases. Approximately 12,000 offspring of atomic-bomb survivors, children conceived after the bomb, have participated in a health examination to evaluate the possible association between parental radiation exposure dose and the prevalence of various common diseases in the offspring (such as, heart disease, stroke, hypertension, and diabetes). A paper on the prevalence of various diseases among those offspring in relation to parental radiation doses has been submitted for publication. The second round of examinations is underway, with plans to repeat examinations every four years to determine whether development of subclinical and clinical disease in offspring is related to parental dose.
- ◆ An innovative system was developed with a genetically modified mouse that has highly fluorescing cells when certain mutations occur in them, potentially permitting the monitoring of large numbers of cells in solid tissues of irradiated animals, including the assessment of hereditary mutations.
- ◆ An international workshop was held at RERF this year on the role of stem cells in the biology of radiation effects. The workshop brought RERF scientists together with four international and five Japanese experts on this topic and provided new insights.

Our research provides benefits to A-bomb survivors and to the world at large as we learn more about the types and magnitude of risks from radiation exposure. Such knowledge is important because of the many uses of radiation in today's world. We want to thank our sponsors who have provided continued support as we address important radiation questions in the best ways we know how. We especially want to thank the many A-bomb survivors and their children who have selflessly participated in studies over the years that provide a fund of knowledge of benefit to all mankind.