



## Message from the Chairman

### Toshiteru Okubo

In this introduction to the FY2009 Annual Report, I would like to summarize the major activities that took place during the one-year period.

#### **Research activities**

During FY2009, research activities were conducted smoothly because of the relatively stable condition in RERF's general operation, budget, and transfer of researchers.

##### 1. Scientific Council meeting

The 37th meeting of the Scientific Council was held at the Hiroshima Laboratory March 3–5, 2010. This meeting focused on evaluation of the Department of Clinical Studies, and detailed review was made of the department's research projects on such conditions as cataract, kidney disease, cardiovascular disease, and stroke. In addition, interdepartmental research projects conducted throughout the organization (research on circulatory disease, F<sub>1</sub> clinical study, and dosimetry) were also discussed.

##### 2. Transfer of researchers

###### **[Employment (appointment) and reappointment]**

- 1) On August 4, 2009, Dr. John Cologne was reappointed as a research scientist at the Department of Statistics with a fixed term of three years.
- 2) On September 1, Mr. Kanya Hamasaki, senior technician at the Department of Radiobiology/Molecular Epidemiology, obtained a Ph.D. in medicine, and was hired as a fixed-term research scientist at the Cytogenetics Laboratory of the Department of Genetics.
- 3) On November 1, Dr. Norio Takahashi was employed as a research scientist at the Biochemical Genetics Laboratory of the Department of Genetics with a fixed term of two years.

###### **[Retirement]**

- 1) Dr. Norman P. Ross retired as chief of the Department of Statistics as of October 13. Until his successor is appointed, Dr. Harry M. Cullings, assistant chief of the department, will serve as acting chief.
- 2) Dr. Nobuo Nishi retired as assistant chief of the Department of Epidemiology as of September 30.

##### 3. Standing committee on radiation dosimetry

The Dosimetry Committee was established as an ad hoc committee in April 2009. The responsibility of this committee is to resolve pending issues related to estimation of individual doses, including correction of distortion in the U.S. army maps and handling of the dose-unknown group, residual radiation, and medical radiation exposure. Thus, original records, such as interview survey sheets, will be reviewed in order to collect more information on exposure location and shielding. In this fiscal year, work was completed to include in the data set four-digit coordinates for all subjects for whom such records were available. Also, preparation has been made to correct for distortion of the U.S. army maps using orthorectified aerial photographs and to reconfirm coordinates of proximally exposed survivors based on neighborhood diagrams showing shielding histories. It has been decided that, instead of coordinates on the U.S. army maps, coordinates on the new city planning maps will be used to show exposure locations of A-bomb survivors.

##### 4. Workshops and meetings

A workshop titled "Epigenetics in Radiation Effects among A-bomb Survivors and Their Children" was held at the Hiroshima Laboratory March 17–18, 2010. Another meeting titled "Confounding and Modification of Radiation Effects by Lifestyle, etc." was held as a part of the partnership program on radiation research September 14–15.

#### 5. Sponsoring of a scientific meeting

The 52nd meeting of Japan Radiation Research Society was held at the Hiroshima City Minami-Ward Cultural Center for three days from November 11, 2009. I served as president, Dr. Kazunori Kodama as chairman of the working committee, and Dr. Nori Nakamura as chairman of the program committee. Because this meeting was held in the A-bombed city of Hiroshima, a unique program was held on peace, which received high marks from participants. With the cooperation of the entire RERF staff, careful preparations resulted in a successful event.

#### 6. Application for research grant

In response to a request for proposal (RFP) from the U.S. National Institute of Allergy and Infectious Diseases (NIAID), a contract for research on immunosenescence of A-bomb survivors was signed, with the five-year study initiated on September 30. With regard to this project, A-bomb survivors organizations expressed concerns about possible connections to anti-terrorism measures. Thus, an *ad hoc* meeting of the Hiroshima Local Liaison Council was held on April 28 to listen to the opinions of people in the local community. Further, at the regular meetings of the Hiroshima and Nagasaki Local Liaison Councils held in September, explanation was provided about the project being a basic immunological study for peaceful purposes and description to that effect was included in the preamble of the research contract. In this manner, we made every effort to seek the understanding of A-bomb survivors and those concerned in the local communities with respect to the study. The five-year budget for this research is to total about 9.6 million dollars, and nine U.S. and Japanese research institutions will cooperate.

#### **Senior Review Panel on Future Planning for RERF**

Since the panel's report was submitted in June 2008, RERF has continued discussion with the two governments concerning RERF's future after its mission is completed and about relocation of the Hiroshima facilities, but specific policies have yet to be decided. Based on the panel's recommendations for operational improvements within RERF, we have started promotion of project-based research activities.

#### **Preparation for reform of the public-interest corporation system**

In preparation for RERF's transition to a new public-interest corporation, the Committee for Selection of First Councilors met at the Hiroshima Laboratory on March 6, 2010, resulting in the appointment of eight councilors.

#### **Liaison with local communities and related organizations**

##### 1. Local Liaison Councils

The 15th meeting of the Hiroshima Local Liaison Council was held on September 8, and the 18th meeting of the Nagasaki Local Liaison Council on September 11. For details, please see "6. Application for research grant" above.

##### 2. Council of Radiation Effects Research Organizations

The 4th meeting of the Council of Radiation Effects Research Organizations was held at the National Institute of Radiological Sciences on December 14, where it was decided that RERF would sponsor an epidemiological training session for researchers in basic biology in September 2010.

##### 3. Cooperation with the International Atomic Energy Agency (IAEA)

In response to recommendations from the Scientific Council and the Senior Review Panel, we have started preparations to apply for designation as an IAEA collaborative center and have begun discussions on specific issues with the IAEA officials in charge.

#### **Public relations activities**

##### Open House

Open House events were held August 5–6 at the Hiroshima Laboratory and August 8–9 at the Nagasaki Laboratory. The number of visitors during the two days in Hiroshima was 617, which was about half of last year's 1,355, but there were more visitors than usual eager to learn about RERF. The number of visitors in Nagasaki was 566, which was 46% more than last year. We believe that this increase was due to the efforts made in the area of public relations.

#### **Employee training**

##### 1. Outsourced training program for employees

The employee training program, which was conducted over a one-and-a-half-year period starting in November 2008, was completed on April 21. The number of sessions and total number of trainees in each category were as follows: 1) Policy issue review meetings: 12 sessions/107 trainees, 2) Manager training: 12 sessions/345 trainees, and 3) General employee training: 16 sessions/403 trainees. In addition, 134 employees were personally interviewed.

In the training sessions for managerial staff, proposals for specific improvements were made concerning three current issues at RERF: 1) Project to make basic policies related to personnel transfer and reassignment,

2) Project to improve the personnel evaluation system, and 3) Reorganization project. Through these training sessions and interviews, employees identified various problems and proposed possible solutions. We plan to address these issues one by one, starting with those having the most potential for realization.

2. Training on medical research ethics/protection of study participants

A training session was held at the Nagasaki Laboratory on March 23 (scheduled for the next fiscal year at the Hiroshima Laboratory) with Permanent Director Takanobu Teramoto (chairman of the Human Investigation Committee and chairman of the Ethics Committee for Genome Research) as lecturer. Because RERF is a joint U.S.-Japan research institute and has to observe the laws and guidelines of both countries, high-level training sessions will continue to be held.

**Status of storage facilities of biological samples (blood, serum, and lymphocytes)**

By moving the documents stored in Unit G of the Hiroshima Laboratory and thereby creating space for installation of deep freezers, we secured a one-year storage space for such samples. On the other hand, at the Nagasaki Laboratory, renovation of the storage room will create additional storage space that will be sufficient for the next several years.

**External evaluation of ethics program**

The U.S. Department of Energy (DOE) reviewed for the first time RERF's research ethics program for three days starting June 29, 2009, and sent us a report titled "Review of RERF's Human Subjects Protection Program" in September. It was stated in the report that "RERF demonstrates an extremely high level of commitment to protecting the rights and welfare of its unique research participant population." The report also pointed out the need for employee training. RERF's responses to this report were sent to DOE on December 22.

## Message from the Vice Chairman and Chief of Research

### Roy E. Shore



The international radiation risk-assessment and protection communities rely heavily on RERF data in making their judgments as to the nature and magnitude of radiation risks. We are currently in a time of some changes in risk assessments, brought about in part by our recent data. In 2008 the UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) published a report on cardiovascular disease (CVD) risk that featured RERF findings, and the ICRP (International Commission on Radiological Protection) is now working on a report with a major section on CVD risk that will rely heavily on our newest data on that topic. Although long-term studies of patients who received radiotherapy for cancer provide information on CVD risks after high-dose irradiation, both the UNSCEAR and ICRP reports regard the RERF results as the primary source of information on CVD risk in the lower dose range (<4 gray).

It is fair to say that the recent RERF data on radiation dose and cataract risk have been the major impetus for the radiation community to reassess its assumptions about cataract induction at low-to-moderate doses. For instance, till recently the ICRP had assumed that there was no radiation risk for clinically-significant cataracts below an eye lens dose of about 5 Gy. However, the new RERF data showing an excess of vision-limiting cataracts (i.e., cataract surgeries) at <1 Gy has spurred a reconsideration, and the ICRP is now working on a report that probably will consider the dose threshold to be more like 0.5 Gy rather than 5 Gy for clinically-significant cataracts. In early 2009, RERF held an international conference on the frontiers of radiation research on cataract risk and mechanisms, and an extended summary of that conference will soon be published in *Radiation Research* (2010).

One of the highlights of RERF work this year was the publication of findings on radiation exposure and mortality from CVD (Shimizu et al., *British Medical Journal*, 2010). For heart disease, the dose response was approximately linear, and there was a clear excess risk at doses above about 0.5 Gy. The estimate of excess relative risk (ERR) was 14% per Gy. For stroke the ERR was 9% per Gy for a linear model, but the data suggested there was little radiation risk for stroke at low doses. Though the heart disease and stroke ERR estimates are smaller than the one for solid cancer (namely, 47% per Gy), CVD nevertheless accounts for about one-third as many radiation-related excess deaths as does cancer. Compared with other studies of CVD risk in the dose range under 3–4 Gy, the A-bomb survivor study has a number of advantages, including the large population, wide dose range, and complete mortality ascertainment. But an especially notable feature is that, unlike most other studies, we have data on other potential risk factors for CVD (e.g., smoking, obesity, history of diabetes mellitus), so as to evaluate whether there may be substantial biases in the data (which there are not).

We also are developing additional research protocols to investigate the pathways and mechanisms by which radiation damage to the circulatory system may affect CVD risk. Those include studies of whether radiation effects on CVD risk are mediated via atherosclerosis, arterial stiffness, inflammation-related factors, the growth-hormone pathway, or kidney dysfunction. Our CVD working group is considering how to measure further potential aspects of CVD-related radiation damage.

Two other new developments during FY2009 are especially notable. The Genetics Department is beginning new studies using high-density arrays (>1.8 million probes) to determine the frequency of inherited mutations in the offspring of A-bomb survivors that may be attributable to parental radiation exposure. This will provide much better answers than previously available as to how much radiation-induced genetic damage is passed on to offspring. The Department of Radiobiology/Molecular Epidemiology received funding for a project on the effects of radiation exposure upon the “aging” of the immune system and its relationship with

health outcomes. The studies in the project include ones to examine the mechanisms of radiation-associated immune aging, to define networks of immune function that are affected by radiation, and to determine the degree to which radiation impacts the immune response to vaccination. This is a complex and highly collaborative research project in which RERF is supplementing its own research capacity with collaborative efforts by four Japanese and five U.S. research groups.

Under our Chairman Dr. Okubo's leadership, much progress is being made in refining the individual information on which the atomic-bomb doses are calculated for survivors. Included are: checking the precision and accuracy of the individual data on location and shielding at the time of the bomb; correcting the 1945 U.S. army map that was used to chart locations, but which has been found to have inaccuracies; making further exposure adjustments for terrain-shielding; and using pre-bombing aerial photos to precisely locate survivors' houses. Although we do not expect the refinements to have a large impact on future risk estimates, as changes will tend to average out, the enhancements should improve both estimates of individual doses and the precision of risk estimates.

We held an international conference on radiation and epigenetics in March 2010 at which papers were presented by recognized epigenetics experts from both Japan and abroad. (Epigenetics refers to inherited changes in gene expression or function of a cell that are caused by mechanisms other than an altered DNA sequence.) The historical biosamples and special populations (for example, those exposed *in utero* and the offspring of A-bomb survivors) at RERF are of great value for studies of epigenetic effects of radiation, and such studies are currently being planned.

Since RERF research data and biosamples will continue to be unparalleled resources for the radiation community, we recently began a systematic review of our procedures for data documentation, quality control, and management. The aim is to evaluate the quality control and documentation of source data, the documentation and replicability of data analyses, and the comprehensiveness, integration, and user-accessibility of databases. Similar assessments are being made of the biosamples and their attendant databases. Plans will be formulated to make improvements and to establish updated policies where needed.

Our research provides benefits to the world at large as we learn more about the range and magnitude of risks from radiation exposure. Such knowledge is becoming increasingly important in this era when radiation exposures from modern medical imaging techniques (computed tomography [CT], fluoroscopically-guided medical procedures, etc.) deliver larger doses than conventional radiography did in the past, so that average population radiation exposures have increased sharply. Much of our research would not be possible without the gracious participation of many atomic-bomb survivors and their offspring in our clinical studies. Although those studies provide benefits to the participants in the form of early disease detection and health maintenance, we can hardly begin to repay them for their assistance in our research. We owe them a deep debt of gratitude.