FY2017 Report of Activities

Epidemiologic data on mortality and cancer incidence from the A-bomb survivors (the Life Span Study [LSS], the *in utero* study) and their children (the F₁ generation studies) have long been a primary basis for national and international estimates of the risks of cancer and other diseases from exposure to ionizing radiation. The unique importance of the LSS study stems from the combination of its large size, wide range of exposure levels, inclusion of all ages at exposure, and long, high-quality follow-up of mortality and cancer incidence. However, the LSS is only one facet of RERF's research activities. Clinical examinations and the collection of biosamples in the Adult Health Study (AHS, a subsample of the LSS) and the clinical, epidemiological and genetic studies of the children of A-bomb survivors provide more detailed information on health conditions of interest, including radiation-related non-cancer conditions, and the pathogenesis of those conditions in relation to radiation exposure, as well as the study of heritable mutations. Our basic science groups, in collaboration with the clinical studies and epidemiology departments, utilize the biosamples to further address the nature and extent of genetic (both heritable and somatic) effects, and molecular changes associated with health risks. These three components within the RERF research program provide an integrative approach into epidemiological, clinical, biological, and mechanistic aspects of human radiation risk. Such integrated opportunities are unique to RERF and demand the best possible science be conducted for the benefit of the survivors and the radiation research community. As we move forward, the primary focus of RERF studies will be on such integrated research programs through their development within the cancer, genetic and noncancer research clusters. An additional and essential component of our research program development is the expansion of collaborations with institutions outside of RERF both in Japan and internationally.

I. Report of Major Activities

1 Research Projects Examining A-bomb Survivors Health

1) Radiation and Cancer Risks

- Cancer incidence: A comprehensive analysis to update radiation risk estimates for cancer incidence through 2009 has been completed using updated individual doses and information of lifestyle factors such as smoking in collaboration with the US National Cancer Institute. Papers on all solid cancer (Grant EJ, et al. Radiat Res 2017; 187:513-537) and lung cancer (Cahoon EK, et al. Radiat Res 2017; 187:538-548) were published and a paper for the breast has been accepted by an international journal.
- Genomic study of thyroid cancer: Somatic mutations/genetic alterations that increase susceptibility to radiation-induced thyroid cancer and improve our understanding of radiation-induced carcinogenesis are of great interest because thyroid cancer has been the key disease risk for both Chernobyl and Fukushima. Therefore, a genomic study of papillary adenocarcinoma of the thyroid is underway in collaboration with the US National Cancer Institute and RIKEN of Japan as well as local hospitals in which those samples have been stored. In a pilot study, quality of extracted DNA/RNA from old formalin-fixed paraffin-embedded tissue samples was limited for genome sequencing, so whole exome sequence instead of whole genome sequence and RNA sequence were conducted. Although they were successfully sequenced, availability of those samples for a comprehensive investigation of somatic mutations of cancer is still inconclusive and further detailed

evaluation is required. If the results of evaluation are satisfactory, a full-scale study will commence in 2018.

- Liver cancer: Recent results from RERF showed that HBV and HCV infection and radiation exposure are associated independently with increased risk of HCC, and that radiation exposure was a significant risk factor for non-B, non-C HCC with no apparent confounding by alcohol consumption, smoking habit, or BMI. We are now conducting a study the objective of which is to examine whether chronic inflammation due to radiation exposure is involved in the development of HCC through insulin resistance or liver fibrosis, regardless of HBV/HCV infection and lifestyle-related factors. We have worked on a statistical model for inferring the latent factors (inflammation, insulin resistance, liver fibrosis, etc.) based on values of biomarkers such as CRP, TNF-α, IL-6, adiponectin, leptin, resistin, type 4 collagen, and platelet count in collaboration with the Statistics and Epidemiology Departments. Based on a joint structural-logistic model, we found significant associations between HCC and the latent factors; liver fibrosis, fatty liver and liver damage in general, but no evidence was seen of associations between HCC and the factors; steatohepatitis, insulin resistance, or chronic inflammation.
- Pathogenesis of Myelodysplastic Syndrome (MDS): This project has been developed in collaboration with the Nagasaki University and the Kyoto University. Radiation is one of the causes of the development of hematological malignancies. A-bomb survivors have a high risk of hematological malignancies, even 50 years after exposure, such as acute myeloid leukemia (AML) and MDS. Recent genome analyses of these diseases have demonstrated that most of samples contain several gene mutations, and that these mutations might be found before clinical diagnosis. We hypothesize that a hematopoietic progenitor or stem cell with a small number of gene mutation acquires additional gene mutations over time (more than several years) and causes hematological malignancies and that ionizing radiation increases the chance of such gene mutations occurring. Objectives are to determine dynamics of mutated clones before clinical diagnosis of MDS and to explore how it differs by exposed radiation dose. We have a plan to detect mutations in serially stored blood samples of AHS participants who developed MDS using nextgeneration genome analysis technology. This study will answer the very important question about how radiation-induced myeloid malignancies develop, which has never been tested. Furthermore, we will be able to obtain new knowledge of mechanisms of radiation-induced myeloid malignancies. A preliminary study on samples collected over a 25 year time span has demonstrated the feasibility of this study by identifying the evolution of several mutations over this time span.

2) Radiation and Risks of Circulatory Disease

• Cardiovascular disease: Recent LSS study have found a statistically significant association for radiation exposure and mortality for hypertensive heart disease, rheumatic or valvular heart disease and heart failure, but not for ischemic heart disease (IHD), including myocardial infarction. Studies of CVD mortality include the uncertainties in the diagnoses listed on death certificates. To determine the association between radiation exposure and CVD incidence, we conducted medical chart review to detect CVD with consistent diagnostic criteria during 1958 and 2011 in the AHS. A paper on detailed analysis of mortality risk and dose response of heart disease subtypes in separate observation periods from 1950 to 2008 was published (Takahashi I, et al Radiat Res 2017;187:319-332) in collaboration with the Departments of Epidemiology and Clinical Studies.

3) Activities to Enhance Ongoing and Future Analysis

i. Infrastructure

(1) Data Collection and Processing

- *Mortality surveillance:* A primary responsibility of the department. Mortality follow-up for all cohorts (LSS, F₁, *in utero*) continues on a 3-year cycle. Mortality data are complete through 2013 and include underlying cause of death as well as associated causes of death. Archiving early-time materials (scanning and digitization) including questionnaires of the major cohorts and other subjects in the early period has been conducted.
- Hiroshima and Nagasaki tumor/tissue registries: Case collection by notifications and death certificates is complete through 2014 in both Hiroshima and Nagasaki including case abstraction in Nagasaki. Annual reports of each registry were released. A paper of characteristics of bone tumors in the tissue registry of Hiroshima was submitted to an international journal. The cancer incidence information through 2011 in Hiroshima and 2012 in Nagasaki was summarized in the database of the LSS, in utero, and F₁. The Cancer Incidence in Five Continents, Vol. XI, and the International Incidence of Childhood Cancer, Vol. III, by the International Agency for Research on Cancer including recent data from Hiroshima and Nagasaki were released. A summary paper of the CONCORD-3 (a global comparison of population-based cancer survival) by the London School of Hygiene and Tropical Medicine including Hiroshima data was published. Works for transition from local cancer registries in Hiroshima and Nagasaki to the Japanese National Cancer Registry (cases diagnosed in 2016 and thereafter) are completed. Cooperative studies with the National Cancer Center of Japan are also being conducted to improve quality of data linkage between cohort studies and tumor registries in the national cancer registry system.
- Pathology studies: A database that indexes RERF specimens of formalin-fixed paraffinembedded tissues is being developed for future specimen utilization and storage in the Biosample Center of RERF. Preservation and utilization of pathological materials from the A-bomb survivors in Hiroshima and Nagasaki areas continues in collaboration with community hospitals and universities. Expanded collaboration is being organized.

(2) Research Resource Center

- The Research Resource Center (RRC) is a core RERF infrastructure to store, document, and index all RERF resources and to integrate research data with biosample data to promote research.
- Site visit by Dr. James Cuff: Dr. James Cuff, Assistant Dean and Distinguished Engineer for Research Computing, Harvard University visited RERF for a 3-day visit in May 2017. The meetings included tours of the biosample center and the current inventory system, the departments of Statistics, Epidemiology, MBS, and Clinical Studies. In addition, he toured the Archives section and viewed our current scanning system. He also had an extensive introduction to our ITD including a tour of the server room, discussion of RERF's S/W infrastructure, and service functions of ITD. Drs. Grant, Katayama (formerly, ITD), and Kodama worked with Dr. Cuff to develop and short White Paper on the steps to initiate the RRC. These included 3 primary steps:
 - 1. Protection—collect and protect all "at risk" assets within RERF
 - 2. Access Policies—develop policies for access to collected assets, including an "Informed Consent" database that scopes which Biosamples have been collected under which rules of use

- 3. Presentation Layer—develop a web-based system to access the RRC that integrates research data and biosamples
- Open Repositories Conference: Dr. Grant attended the Open Repositories conference, an international conference that focuses on the design of data infrastructures and access. This conference showed the current state of industry-standard data frameworks and roadmaps for future development. It is clear that a rich set of tools has already been created for this field of work. It is necessary for RERF to tap these resources to develop a quality product for RERF's internal collaboration and to facilitate future external collaboration.

ii. Activities for Promotion of Health and Welfare of Study Participants

The Adult Health Study (AHS) and the F1 clinical study contribute to the promotion of the health and welfare of the A-bomb survivors and their children through regular health examinations and health consultations via telephone contacts or home visits. At the health examinations physicians provide guidance for disease prevention to the study participants, report examination results to their attending physicians, or refer them to medical institutions when more detailed examinations or treatments are necessary. Continued support activities provided on occasions other than such medical examinations include health consultation by public health nurses, assistance for elderly or physical challenged in their hospital visits, advice on application procedures regarding governmental consultation services related to welfare benefits. In addition, educational brochures for health promotion are distributed to study participants on a regular basis.

iii. Research on Biological Mechanisms Related to Health Effects from Radiation among A-bomb Survivors

- Radiation and dendritic cells: Late effects of radiation on dendritic cells (DCs), key coordinators for activation and differentiation of T cells were investigated to test the hypothesis that A-bomb radiation exposure induced premature aging of DCs, resulting in reduced numbers and impaired functions of DCs. Numerical and functional changes related to age and radiation dose in conventional DCs (cDCs) and plasmacytoid DCs (pDCs) were analyzed among 229 A-bomb survivors. Investigators observed 1) a dose-dependent decreases in the number of plasmacytoid DCs (pDCs) in females; and 2) a hierarchical cluster of two distinct types in gene expression profiles of conventional DCs (cDCs), with different median values of age and cytokine production levels. This demonstrates that the numbers and functions of circulating DCs generally recovered to normal levels 65 years after A-bomb radiation exposure, i.e., levels typical for the unexposed group of the same generation.
- Animal model of stroke: The onset time of symptoms related to stroke was significantly earlier in spontaneously hypertensive stroke prone rat (SHRSP) irradiated with 0.1 Gy than in controls but not with 0.05 Gy. This suggested a threshold in the radiation dose effect between 0.05 and 0.1 Gy. Preliminary examinations, where SHRSP rats were chronically irradiated with an accumulated dose of 0.5 or 1 Gy (dose rate was 0.05 or 0.1 Gy/day, respectively), did not show any significant radiation effects. In addition, metabolome analyses demonstrated that the amounts of taurine and unsaturated fatty acids decreased and increased, respectively, with increasing dose. These data are useful to infer potential mechanisms underlying the radiation effect on circulatory disease.

2. Research Projects on the Health of A-bomb Survivors Children (F1)

1) F1 Mortality and Clinical Studies

• Radiation and multifactorial diseases: In a preliminary tabulation of the prevalence and incidence of individual multifactorial disease outcomes among about 10,000 FOCS participants between November 2010 and October 2015, no statistically significant evidence was observed for associations between increased risk of multifactorial disease (hypertension, hyper LDL-cholesterolemia, hypertriglyceridemia, and diabetes) and parental radiation exposure, in either the second round prevalence study (2010-2015) or incidence study (2002-2015).

2) Research on Biological Mechanisms Related to the Health of A-bomb Survivors Children

• Signature of radiation genetic effects: Radiation-induced deletions in mouse spermatogonia are usually large (over 200 kb) and contain little sequence similarity at the junctions (Kodaira, Radiat Res 2017; 187:722-31). This study aimed to characterize the structures and sequences of radiation-induced deletions occurring in mouse spermatogonia cells which are inherited to offspring. We analyzed the sequences of the regions around the rejoined junctions of 33 de novo copy-number mutations (27 deletions and 6 duplications) obtained from offspring sired by male mice that were irradiated at the spermatogonia stage and from non-irradiated controls. The deletions could be classified into three major groups. Group 1, deletion size 1kb to 1 Mb, sharing long blocks of similar sequences (200–6,000 bp) at the junctions (e.g., illegitimate recombination). Group 2, deletion size shorter than 200 kb, sharing only 0-7 bp homology (micro-homology-mediated). Group 3, deletion size longer than 200 kb, sharing 0-2 bp homology (typical NHEJ). The group 3 consisted primarily of deletions that occurred in the irradiated genomes. These data suggested that large size (>200 kb) with little sequence similarity around the rejoined sites are likely to be a hallmark of radiation-induced deletions in mice.

3. Research to Elucidate Individual Doses and Effects from the A-bomb

- Cytogenetics: To investigate the effect of A-bomb radiation to humans, a cytogenetic dosimetry study was conducted for A-bomb survivors in the AHS cohort. A total of 1,869 survivors (1,179 in Hiroshima and 690 in Nagasaki) were examined using 2-color-FISH for detection of translocations involving chromosomes 1, 2, and 4. The preliminary results are summarized as follows: (1) clear nonlinear dose responses were observed in both Hiroshima and Nagasaki; (2) a wide scatter of individual translocation frequencies against physical dose was observed in both cities as seen in the previous Giemsa staining study; (3) The city difference seen in previous studies using Giemsa staining became much smaller now with FISH; (4) Nagasaki factory workers had significantly lower dose responses than people who were exposed in Japanese houses; (5) the reduced intercity difference suggests that the previous city difference by the solid Giemsa method was mainly due to different aberration detection rates between Hiroshima and Nagasaki laboratories.
- Dose uncertainty: There were two major publications on dose uncertainty. First, investigators quantified the potential for bias in radiation risk estimates obtained from regression calibration correction for dose error, and proposed an alternative method (SIMEX) that avoided an assumption regarding the distribution of unobservable true doses, in contrast to the regression calibration method currently in use (Misumi). Second,

investigators provided an assessment of dosimetric uncertainty without parametric assumptions by using chromosomal aberration data available for a subset of the LSS as an instrumental variable, concluding that the attenuation of the radiation risk estimate in the LSS by dosimetric uncertainty (classical error) might be greater than previously assumed (Wang/Cullings). We continue to work both autonomously (Cullings, Misumi) and collaboratively with outside investigators (Cullings, with D. Pierce) in related areas.

We are continuing collaborations with external investigators in several areas related to new
radiation risk models, including mechanistic modeling of leukemia and multi-model
inference for circulatory disease outcomes, including a new collaboration with the German
Institute of Radiation Protection on mechanistic modeling studies of thyroid cancer after
childhood exposure and combined effects of radiation exposure and smoking on lung
cancer.

4. Projects to Release Research Results and to Collaborate with Other Scientific Organizations

Crucial to the mission of RERF is the dissemination of results of our studies to survivors and their children and to the international community. Toward that end we interact with local liaison councils representing the communities of Hiroshima and Nagasaki and provide information via public lectures and other activities. These will be described later in another section of this report. With respect to the international community there are a number of activities. These include seminars, workshops, participation at international scientific conferences, and international publication of results. This year 4 workshops and 14 seminars were held at RERF presented by national and international visitors to RERF, and published more than 30 scientific papers.

1) Collaborative Research Projects

Ongoing international collaborative research projects

In addition to the above activities the development of national and international collaborations is essential to help disseminate results and to enhance RERF research programs. A list of current collaborations is provided below:

- a. Partnership with the University of Washington
- b. Partnership with Kurume University
- c. Collaborations with the US National Cancer Institute
- d. Collaborations with the University of Florida
- e. Collaborations with Outside Investigators:
 - 42 Japanese Institutions
 - 14 North American Institutions
 - 13 European Institutions
 - 4 Asian, Oceanian Institutions

Nuclear Emergency Workers Study (NEWS): 10 Japanese Institutions

2) Workshops

- a. RERF-ICRP Joint Meeting: New RERF organ dose calculations for atomic bomb survivors
- b. ICRP-RERF-JHPS Joint Workshop "Recent progress in radiation dosimetry for epidemiology and radiological protection"

- c. RERF Workshop "Ethical considerations required in collaborative studies involving biosamples"
- d. International Workshop "Filling a gap between epidemiology and biology: Biologically-based modeling of radiation-induced carcinogenesis"

5. Training Programs for Domestic and Overseas Specialists

- 1) A "Training course for biologists: Let us learn more about epidemiology" was held to deepen biologists' understanding of RERF's epidemiological studies and to also promote exchanges among researchers working for radiation-related organizations (August 28–29, 2017; 32 participants in total).
- 2) RERF accepted overseas research trainees, either on their own initiative or in support of the activities of such organizations as the Hiroshima International Council for Health Care of the Radiation-exposed (HICARE), the Nagasaki Association for Hibakushas' Medical Care (NASHIM), and the Japan International Cooperation Agency (JICA) (140 trainees in total). A trainee, who was accepted by HICARE, received lectures on research methods and the results of past studies and took part in experiments and analyses to deepen their understanding of the health effects of radiation at RERF for about one month.
- 3) RERF cooperated in the international training course jointly held by the International Atomic Energy Agency (IAEA) and HICARE (February 19–21, 2018; approximately 30 participants in total), and provided lecturers and offered a venue for the training course on February 21, 2018.
- 4) RERF accepted visits by students from schools and universities in Japan for tours including research lectures (36 students in total).
- 5) RERF further reviewed future directions for its training activities, including an approach of publicly inviting overseas trainees in the International Exchange Research Program, and called for applications from researchers and others from abroad to receive training at RERF by posting an invitation and the guidelines for application on the RERF website. RERF received nine applications and accepted five trainees. RERF also accepted two trainees, who showed their interest in this training program in FY2017.
- 6) In addition to the above-mentioned programs, the Department of Molecular Biosciences and the Department of Epidemiology in Nagasaki accepted one visiting student fellow, respectively in FY2017.

6. Public Information Programs

1) RERF Open Houses

In fiscal 2017, RERF held its 23rd Open House on August 5–6 at the Hiroshima Laboratory and its 21st Open House on August 8–9 in Nagasaki. The events this year were held under the theme "This summer, discover RERF." The Open House event in Hiroshima featured the special exhibit "A scrapbook tells a story to the world: Hiroshima Diary." The Open House event in Nagasaki featured the special exhibit "Epidemiological Study of Health Effects in Fukushima Emergency Workers," which explained a research project entrusted to RERF on the emergency workers in the Fukushima nuclear power plant accident who were exposed to various radiation doses.

In addition, in Hiroshima, several science corners were established: "Liquid nitrogen: What is the world of –196° like?" and "Extracting DNA," among others, at which science experiments were conducted, with hands-on learning opportunities also provided. As

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usual, a "Quiz stamp rally" was featured, in which young visitors moved throughout the facilities to complete the quiz. In Nagasaki, several science corners were set up, including bone density testing, liquid nitrogen experiments, and arteriosclerosis screening.

The Open House lectures, which have become part of the regular program, were delivered on August 5 in Hiroshima, with Ms. Reiko Horimukai, Assistant Office Chief, Public Relations and Publications Office, giving a "School Visit Program" lecture, designed to model RERF's school lecture series that provides an understandable explanation about radiation for school children. The lecture on the next day, August 6, was "ABCC/RERF research and your everyday life," delivered by Dr. Ohtsura Niwa, Chairman, RERF, who explained how RERF research results contribute to the health and well-being of the general public. Dr. Niwa delivered the same lecture at Nagasaki RERF, on August 9.

The two-day Open House events attracted 1,383 and 608 visitors in Hiroshima and Nagasaki, respectively.

2) Enhanced RERF website

- A comprehensive overhaul of the RERF public website took place mostly over FY2017 and should be completed, with the homepage released, by the end of June FY2018.
- When papers were published in scientific journals, easy-to-follow short summary explanations continued to be posted in the "What's New" section on the public website; it is planned that those summary explanations will evolve into a new format including two kinds of explanations: one for specialists, and a shorter version for the general public or a video interview with the main authors. This change will take place sometime after the new website is launched.
- The total number of RERF website hits between April 1, 2017, and March 31, 2018, was about 35.62 million (compared to about 32.91 million in the corresponding period of the previous year), with the daily average being about 97,534 (compared to about 90,000 in the previous year). The total number of website visitors for the same period was about 863,403 (compared to about 872,000 in the previous year), with the daily average about 2,365 (compared to about 2,391 in the previous year).
- The RERF Facebook page continues to convey information to readers and now has more than 680 followers.

3) Press meeting in Tokyo

At the end of November, representatives of the International Commission on Radiological Protection (ICRP) visited Hiroshima and Tokyo over a period of several days for meetings, a workshop, and a press gathering.

First, on November 30, 2017, RERF held a joint meeting at its Hiroshima Laboratory together with ICRP.

Participants then traveled to the University of Tokyo campus to hold, on December 2, 2017, the "Joint ICRP-RERF-JHPS (Japan Health Physics Society) Workshop on Recent Progress in Radiation Dosimetry for Epidemiology and Radiological Protection."

The venue was moved to Tokyo from Hiroshima to accommodate the many radiation-protection and health-physics specialists in Tokyo, given the importance of the end-users of RERF data such as ICRP and JHPS, and to draw a larger audience for the event. The

Japanese Society of Radiation Safety Management (JRSM), along with JHPS, coorganized the workshop event.

In the RERF-organized press meeting held after the workshop, attending media had a chance to ask questions, with many of them involving the DS02R1 dosimetry system revisions and others relating to estimates of local radioactive fallout and soils made radioactive with bombardment by neutrons from the atomic bombs in Hiroshima and Nagasaki.

The press meeting also met RERF's goal of holding more events in the Tokyo area to interact with more media outside of the Hiroshima and Nagasaki local areas.

4) Media forums

RERF held its sixth round of media forums on April 21, 2017, at Hiroshima RERF, and on April 27 in Nagasaki. The Hiroshima forum gathered 17 media representatives, and the Nagasaki forum hosted six reporters. The purpose of this media gathering is to present new research achievements and increase understanding among media representatives about RERF studies. In this way, the forums provide knowledge that the media can use to better inform the public about the health effects caused by A-bomb radiation. At both the Nagasaki and Hiroshima forums in 2017, Dr. Eric J. Grant, Associate Chief of Research, opened the events by providing an explanation of his paper "Solid Cancer Incidence among the Life Span Study of Atomic Bomb Survivors: 1958-2009." Following Dr. Grant at both venues, Dr. Niwa spoke about RERF's future plans and direction.

5) School Visit Program

RERF scientists gave 12 lectures at four junior high and high schools in Hiroshima this year to further push forward a new project called the School Visit Program, in an attempt to broaden RERF's reach among school students in classroom settings and have young people and teachers understand the true risks and benefits of radiation.

6) Permanent exhibits

The Hiroshima Laboratory has upgraded its permanent exhibit space showing the history of ABCC-RERF, the organization's international collaborative activities, and basic information on radiation. The historical panel information was updated at the beginning of FY2017 so as to include both Japanese and English explanations, the latter of which was missing previously. Other more general information about RERF's organization/structure and funding, as well as an RERF message to the A-bomb survivors and a translation of a representative survivor's remarks, was added.

7) Updating public relations materials

The printed version of the RERF *Update* newsletter was discontinued at the end of 2016. However, a new electronic subscriber list newsletter will appear on the new homepage. The subscriber list will give the Public Relations and Publications Office access to user information and a way to achieve "buy-in" among a group of the general public that is interested in our research results and related news.

The Annual Report has been discontinued in its previous hard-copy format, with the FY2015 version of the new Report of Annual Activities being posted only online and the online FY2016 version to appear in conjunction with the launch of the new homepage.

8) Other public relations activities

• With the hiring of a PR expert, a former employee of a leading advertising firm,

progress is expected on RERF's public relations strategies from multiple dimensions. RERF will carry out strategic planning of its public relations activities utilizing his professional experience and know-how.

- As part of its public relations activities through the media, RERF held press conferences at the time of important functions and newsworthy events, as well as publication of topical papers. RERF also responded to inquiries and requests for interviews from many domestic and overseas media organizations.
- In addition to the Open House events, visitors are welcome to tour RERF's facilities upon request. Last fiscal year, as of the end of January 2018, 940 individuals from Japan, including students on school excursions, and 242 individuals from overseas toured the RERF facilities in Hiroshima and Nagasaki (as of the end of March 2018).
- As part of our effort to meet with smaller groups of stakeholders, including A-bomb survivors and their children, we invited three groups of citizens on three separate occasions to RERF to have them listen to a lecture from Dr. Niwa, engage in a dialogue with RERF staff, and participate in a tour of the facilities.
- As a first-time event, RERF received marketing and other students from the Think Global School, an international high school that travels the world to learn about different societies, to work with the school on a major marketing project. The result of their time at RERF was the creation of an RERF introductory video that can be potentially be posted on our new homepage and Facebook page to inform viewers of basic information about RERF.

FY2017 RERF International Collaborative Activities

I. Participation in international collaborative activities by RERF directors and staff members		II. Acceptance of visitors from overseas for briefing and training		
WHO-related activity	7 people	(Hiroshima)		
UNSCEAR-related activity	6 people	Visitors related to HICARE	35 people	
ICRP-related activity	5 people	Visitors related to JICA	8 people	
IAEA-related activity	5 people	Visitors related to RERF (International Exchange Research Program)	5 people	
Medical checkup for A-bomb survivors residing in South Korea-related activity	1 person	Visitors related to MEXT	15 people	
Others	9 people	Japan Atomic Energy Agency	44 people	
		Prefectural University of Hiroshima	5 person	
		Fulbright exchange program	1 person	
		(Nagasaki)		
		Visitors related to NASHIM	33 people	
Total: 33people		Total: 146 people (Hiroshima 113 people, Nagasaki 33 people)		

I. Participation in international collaborative activities by RERF directors and staff members (excluding participation in international scientific meetings)

In italics: Funding Organization

- 1. World Health Organization (WHO)-related activity (7 people)
 - 1) RERF (MHLW International Exchange Research Program) (hereinafter, all titles represent those at time of participation)

Kazunori Kodama, Executive Director, and Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki) and Acting Director of the Biosample Center, visited WHO headquarters to discuss collaboration between RERF and WHO. (Geneva, Switzerland, March 16, 2018)

2) RERF

- (1) Hiroaki Katayama, Department Chief of Information Technology, and Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki), attended the WHO Cooperative meeting of WHO Collaborating. (Tokyo, April 23, 2017)
- (2) Kazunori Kodama, Chief Scientist, Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki), and Hiroko Kitamura, Associate Senior Scientist of Emergency Workers Health Study Office of Department of Clinical Studies

(Hiroshima), attended the WHO/REMPAN meeting. (Geneva, Switzerland, July 3–6, 2017)

2. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) -related collaborative activity (6 people)

1) UNSCEAR

Kyoji Furukawa, Associate Senior Scientist, Department of Statistics, attended a meeting on the project "Selected evaluations of health effects and inferred risk from radiation exposure." (Vienna, Austria, July 18–21 and December 12–15, 2017)

- 2) National Institute of Radiological Sciences
 - (1) Kazunori Kodama, Executive Director, and Kotaro Ozasa, Department Chief of Epidemiology, Hiroshima, attended the UNSCEAR domestic committee meeting. (Tokyo, September 8, 2017 and March 27, 2018)
 - (2) Kazunori Kodama, Chief Scientist, and Kotaro Ozasa, Department Chief of Epidemiology, Hiroshima, attended the UNSCEAR Fukushima accident report domestic JWG committee meeting. (Tokyo, November 24, 2017)

3) RERF

Kazunori Kodama, Chief Scientist, attended the 64th UNSCEAR meeting. (Vienna, Austria, May 28–June 2, 2017)

- 3. ICRP (International Commission on Radiological Protection)-related activity (5 people)
 - (1) Ohtsura Niwa, Chairman, participated as a member of the ICRP Main Commission in its meeting to discuss radiation protection. (Lima, Peru, May 6–14, 2017)
 - (2) Kotaro Ozasa, Department Chief of Epidemiology, Hiroshima, attended the committee meeting and symposium as a member of ICRP Committee 1. (Paris, France, October 8–16, 2017)
 - (3) Ohtsura Niwa, Chairman, attended an ICRP-sponsored dialogue seminar held in Yamakiya area of Kawamata-machi, Fukushima and discussed the activities toward reconstruction in this area one year after the evacuation order was lifted. (Kawamata-machi, Fukushima, November 24–26, 2017)
 - (4) Ohtsura Niwa, Chairman, and Harry M. Cullings, Department Chief of Statistics, attended An ICRP-RERF-Japan Health Physics Society (JHPS) joint workshop "Recent progress in radiation dosimetry for epidemiology and radiological protection." (Lecture room, Faculty of Engineering, the University of Tokyo, December 2, 2017)
- 4. International Atomic Energy Agency (IAEA)-related activity (5 people)

1) IAEA

Ohtsura Niwa, Chairman, and Kazunori Kodama, Chief Scientist, gave a lecture in IAEA-STS Consultancy Meeting. (Hiroshima, May 23, 2017)

2) RERF (MHLW International Exchange Research Program)

Kazunori Kodama, Executive Director, and Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki) and Acting Director of the Biosample Center, visited IAEA headquarters to discuss collaboration between RERF and IAEA. (Vienna, Austria, March 18–19, 2018)

3) Hiroshima International Council for the Radiation-exposed (HICARE) collaborative activities

Kanya Hamasaki, Research Scientist, Department of Molecular Biosciences, attended IAEA First Research Coordination Meeting on Clinical Applications of Biological Dosimetry Method (Vienna, Austria, October 28–November 6, 2017)

5. Medical checkup for A-bomb survivors residing in South Korea-related activity (1 person)

Nagasaki Prefectural Government's medical checkup project for A-bomb survivors residing in South Korea

Daisuke Haruta, Research Scientist, Department of Clinical Studies (Nagasaki), together with the physicians and others from Nagasaki University Hospital and the Nagasaki Genbaku Hospital participated in the medical checkup project for A-bomb survivors residing in South Korea sponsored by the Nagasaki Prefectural Government and provided health consultations for the A-bomb survivors in South Korea. (Seoul, South Korea, June 12–15, 2017 and Daegu, South Korea; October 30–November 2, 2017)

6. Others (9 people)

- (1) John Cologne, Senior Scientist, Department of Statistics, visited the University of Hawaii Cancer Center to provide a seminar and to conduct a collaborative study (RP P1-17: "Preliminary Project (RP-P) to Establish Capability for Integrated Analyses of Multiple Molecular [Omic] Endpoints") with a researcher—Dr. Gordon Okimoto—in bioinformatics at the center. (Hawaii, USA, May 3–10, 2017)
- (2) Robert Ullrich, Vice Chairman, chaired the plenary session and gave a presentation at the Columbia University CMCR (Center for Countermeasures against Radiation) U19 annual retreat. (New York, USA, May 8–9, 2017)
- (3) Ohtsura Niwa, Chairman, attended the 241st US Independence Day Reception. (Osaka, June 29, 2017)
- (4) Benjamin French, Assistant Department Chief of Statistics, visited the University of Washington as a lecturer in a short course on longitudinal data analysis at the 2017 Summer Institute for Statistics in Clinical Research. (Seattle, USA, July 25, 2017)
- (5) Ohtsura Niwa, Chairman, gave a lecture on the health effects of A-bombs and discussed how to eliminate gaps between science and public perception as a panelist at a workshop sponsored by Japan Chapter of IPPNW in the 22nd IPPNW World Congress. (York, UK, September 4–6, 2017)
- (6) Ohtsura Niwa, Chairman, has been appointed as external scientific councilor for MELODI Platform, a leading organization in the field of radiation effects research in Europe; he attended a MELODI-ICRP joint symposium in Paris and discussed the future radiation effects research in EU. (Paris, France, October 9–11, 2017)
- (7) Ohtsura Niwa, Chairman, led the Peace and Friendship Delegation to China by Hiroshima Citizens and visited Shanghai, Beijing, and Tianjin to promote Japan-China friendship and peace. (China, November 10–14, 2017)
- (8) Benjamin French, Assistant Department Chief of Statistics, visited Kyungpook National University and the Korean Radiation Epidemiology Group to provide a seminar and tutorial on joint regression modeling of longitudinal and survival data. (Daegu and Seoul, South Korea, November 29–December 1, 2017)
- (9) Ohtsura Niwa, Chairman, gave a lecture at the Annual Schull Institute Conference. (Houston, USA, March 17, 2018)

II. Acceptance of visitors from overseas for briefing and training (Total: 146 people)

[Hiroshima: 113 people] In italics: Funding Organization

- 1. Visitors related to *Hiroshima International Council for Health Care of the Radiation Exposed* (*HICARE*) (35 people)
 - 1) South Korea (25 people)
 - (1) June 22, 2017: 3 trainees from South Korea for the "A-bomb survivors residing in South Korea."
 - (2) July 4, 2017: 10 trainees from South Korea for the "A-bomb survivors residing in South Korea."
 - (3) September 28, 2017: 7 trainees from South Korea for the "A-bomb survivors residing in South Korea."
 - (4) October 25, 2017: 5 trainees from South Korea for the "A-bomb survivors residing in South Korea."
 - 2) United States (5 people)
 - (1) July 27, 2017: 3 trainees from United States
 - (2) November 28, 2017: 2 trainees from United States and Latvia
 - 3) Others (5 people)
 - (1) November 6-December 1, 2017: 1 trainee from Latvia
 - (2) February 16, 2018: 4 trainees from Brazil and United States
- 2. Visitors related to International Cooperation Agency (JICA) (8 people)

Japan Anti-Tuberculosis Association

November 8, 2017: 8 trainees from Kenya, Afghanistan, Philippines, Liberia, and East Timor for FY2017 JICA group training on "Management enhancement of Tuberculosis Laboratory examinations in UHC age" at the request of the Research Institute of Tuberculosis

- 3. RERF (MHLW International Exchange Research Program) (5 people)
 - (1) November 6–18, 2017: 1 trainee, National Cancer Center, South Korea
 - (2) November 6–18, 2017: 1 trainee, Department of Biochemistry, University Putra, Malaysia
 - (3) November 6–18, 2017: 1 trainee, Faculty of Medicine, Chiang Mai University, Thailand
 - (4) November 6–18, 2017: 2 trainees, College of Medicine, Korea University, South Korea
- 4. Ministry of Education, Culture, Sports, Science and Technology, MEXT (15 people)

November 14, 2017: 15 trainees from Mongolia, Malaysia, Myanmar, Cambodia, Afghanistan, and Kazakhstan for Nagoya University Graduate School of Medicine, Young Leaders' Program FY2017–2018

- 5. *Japan Atomic Energy Agency* (44 people)
 - (1) October 20, 2017: 24 trainees from Cambodia, India, Indonesia, Jordan, Kazakhstan, and others, for JAEA's Training Course on the Physical Protection of Nuclear Material and Facilities
 - (2) December 1, 2017: 20 trainees form Australia, Bangladesh, Bosnia and Herzegovina, India, and others, for JAEA's Training Course on State Systems of Accounting for and control of Nuclear Material
- 6. Prefectural University of Hiroshima (5 people)

December 8, 2017: 5 trainees, Nursing students from University of Canberra, Australia

7. *Fulbright* exchange program (1 person)

September 11, 2017–July 10, 2018: 1 visiting student (scholarship student) from the United States for the Fulbright exchange program

[Nagasaki: 33 people]

Visitors related to the Nagasaki Association for Hibakushas' Medical Care (NASHIM) (33 people)

- 1) Chernobyl and Kazakhstan (12 people)
 - (1) July 20, 2017: 6 trainees
 - (2) July 24, 2017: 6 trainees
- 2) South Korea (21 people)
 - (1) October 25, 2017: 9 trainees
 - (2) January 24, 2018: 12 trainees

FY2017 joint programs between RERF and overseas researchers/research organizations

In italics: Funding Organization

- 1. Collaborative studies between RERF and US National Cancer Institute (NCI)
 - (1) Under the research contract entered into by and between RERF and the US National Cancer Institute (NCI), in which Kotaro Ozasa, Department Chief of Epidemiology, Hiroshima, serves as a responsible person of the RERF side, he is working on analysis of solid cancer incidence risks in the LSS cohort, site-specific cancer studies based on histopathological diagnoses, and preliminary reviews for genomic analysis of thyroid cancer.

The following papers have been published (RERF authors underlined):

<u>Grant EJ</u>, <u>Brenner A</u>, <u>Sugiyama H</u>, <u>Sakata R</u>, <u>Sadakane A</u>, <u>Utada M</u>, Cahoon EK, Milder CM, <u>Soda M</u>, <u>Cullings HM</u>, Preston DL, Mabuchi K, <u>Ozasa K</u>. Solid Cancer Incidence among the Life Span Study of Atomic Bomb Survivors: 1958–2009. Radiat Res 2017;187(5):513-37.

Cahoon EK, Preston DL, Pierce DA, <u>Grant E, Brenner AV</u>, Mabuchi K, <u>Utada M, Ozasa K</u>. Lung, Laryngeal and Other Respiratory Cancer Incidence among Japanese Atomic Bomb Survivors: An Updated Analysis from 1958 through 2009. Radiat Res 2017;187(5):538-48.

- Grant EJ, Cologne JB, Sharp GB, Eguchi H, Stevens RG, Izumi S, Kim YM, Berrington de González A, Ohishi W, Nakachi K. Bioavailable serum estradiol may alter radiation risk of postmenopausal breast cancer: a nested case-control study. Int J Radiat Biol 2018;94(2):97-105.
- (2) Dr. Dale Preston, Principal Scientist from Hirosoft International Corporation, visited RERF to conduct collaborative studies including a solid cancer incidence risks study of A-bomb survivors. (May 28–June 13, 2017 and January 5–20, 2018)
- (3) Dr. Kiyohiko Mabuchi of Radiation Epidemiology Branch, NCI, visited RERF to conduct NCI-funded collaborative studies including a site-specific cancer study. (July 3–14, 2017)
- (4) Ritsu Sakata, Assistant Chief, and Alina Brenner, Senior Scientist, Department of Epidemiology, Hiroshima are joining with the data of tumor of the central nervous system from RERF as a part of the pooled analysis conducted by the scientist of Radiation Epidemiology Branch, NCI.
- (5) Ritsu Sakata, Assistant Department Chief of Epidemiology, Hiroshima is joining with the data of tumor of the central nervous system from RERF as a part of the pooled analysis of radiation-associated thyroid cancers conducted by the scientist of Radiation Epidemiology Branch, NCI.
 - The following paper has been published (RERF authors underlined):
 - Lubin JH et al. (RERF: <u>Sakata R</u>). Thyroid cancer following childhood low dose radiation exposure: a pooled analysis of nine cohorts. J Clin Endocrinol Metab, July 2017, 102(7):2575–2583
- (6) Harry M. Cullings, Chief, Benjamin French, Assistant Chief, John Cologne, Senior Scientist, and Munechika Misumi, Research Scientist, Department of Statistics, collaborated with the RERF Department of Epidemiology and the US NCI in preparation of data and methods for a series of upcoming papers on improved analyses of solid cancer incidence and mortality.
- (7) John Cologne, Senior Scientist, Department of Statistics, collaborated with the

RERF Department of Epidemiology and the US NCI in the preparation of two papers dealing with methodological aspects of Life Span Study cancer incidence and mortality risk analyses: one published in 2018 in the journal *Radiation and Environmental Biophysics* (RERF RR 2-17: "Effect of follow-up period on minimal-significant dose in the atomic-bomb survivor studies"), the other currently under RERF internal review ("Background-rate heterogeneity as a source of nonlinearity in the solid-cancer radiation dose response among male atomic-bomb survivors").

2. Research exchange between RERF and ICRP

A workshop "RERF's new calculation of organ doses for the atomic bomb survivors" was held to coincide with an ICRP task-group meeting at RERF. (Hiroshima, November 30, 2017)

3. Collaboration between RERF and the/Asia Cohort Consortium (ACC)

Atsuko Sadakane, Senior Scientist, Department of Epidemiology, Hiroshima, is joining the collaborative project with the ACC entitled: *Tobacco smoking, alcohol drinking, body mass index and risk of rare cancers*.

4. Collaboration between RERF and London School of Hygiene & Tropical Medicine

Hiromi Sugiyama, Senior Scientist, Department of Epidemiology, Hiroshima, and Hiroshima Prefecture cancer registry, are joining the working group of CONCORD-3, global surveillance of cancer survival, conducted by Dr. Michel Coleman of London School of Hygiene & Tropical Medicine.

5. Collaboration between RERF and Institute of Cancer Research, UK and US National Institute of Environmental

Atsuko Sadakane, Senior Scientist, Department of Epidemiology, Hiroshima, is joining with premenopausal breast cancer data from RERF as a part of the pooled analysis conducted by Dr. Anthony Swerdlow of Institute of Cancer Research, UK, and Dr. Hazel Nichols of US National Institute of Environmental.

The following paper has been published (RERF authors underlined):

Nichols HB, Schoemaker MJ, Wright LB, McGowan C, Brook MN, McClain KM, Jones ME, Adami HO, Agnoli C, Baglietto L, Bernstein L, Bertrand KA, Blot WJ, Boutron-Ruault MC, Butler L, Chen Y, Doody MM, Dossus L, Eliassen AH, Giles GG, Gram IT, Hankinson SE, Hoffman-Bolton J, Kaaks R, Key TJ, Kirsh VA, Kitahara CM, Koh WP, Larsson SC, Lund E, Ma H, Merritt MA, Milne RL, Navarro C, Overvad K, Ozasa K, Palmer JR, Peeters PH, Riboli E, Rohan TE, Sadakane A, Sund M, Tamimi RM, Trichopoulou A, Vatten L, Visvanathan K, Weiderpass E, Willett WC, Wolk A, Zeleniuch-Jacquotte A, Zheng W, Sandler DP, Swerdlow AJ. The Premenopausal Breast Cancer Collaboration: A Pooling Project of Studies Participating in the National Cancer Institute Cohort Consortium. Cancer Epidemiol Biomarkers Prev. 2017;26:1360–1369

- 6. *RERF* international collaborative studies on statistical analysis
 - (1) Kyoji Furukawa, Associate Senior Scientist, Department of Statistics, visited the Institute of Radiation Protection, Helmholtz Zentrum in Germany to discuss a collaborated project with researchers from Helmholtz Zentrum on mechanistic modelling of radiation-induced cancer. (Munich, Germany, July 16–17, 2017).
 - (2) Benjamin French, Assistant Department Chief of Statistics, collaborated with researchers at the University of Pennsylvania, Philadelphia, Pennsylvania, US, on statistical methods for conducting sensitivity analyses of multiple dependent comparisons in a single observational study.

平成29年度 外部資金研究一覧表 FY2017 External Research Funds

外部機関名称 Name of Outside Organization	件数 Number of Grants	研究資金 (資金拠出機関からの入金額) Research funds (amount of funds from funding organizations)
厚生労働省 Ministry of Health, Labour and Welfare (MHLW)	2	¥2,170,000
文部科学省 Ministry of Education, Culture, Sports, Science and Technology (MEXT)	~	¥200,000
独立行政法人 日本学術振興会 (文部科学省所管の独立行政法人) Japan Society for the Promotion of Science (JSPS) [Independent administrative entity under the jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology (MEXT)]	ത	¥47,440,000
国立研究開発法人国立がん研究センター National Cancer Center	~	_* 0*
総合計 Grand total	13	¥49,810,000

- These amounts include indirect cost.

 These amounts may include subsidies allocated to collaborators.

 No research fund is allocated because the RERF researcher takes part in the research as an associate investigator.

関連性 Relationship to RERF's mission	被爆者のがん罹患調査 Study of cancer incidence among A-bomb survivors	日本人のがんの疫学研究 Epidemiological study of cancer in Japanese population	原爆放射線の被爆者およびその子供への健康影響に関する 知見の教育普及活動の一環 Activity of education and distribution on the findings of health effects of atomic bomb radiation on survivors and their
関連RP F	RP 18-61 被爆 amon	RP-A2-15 日本) Epidemi in Ji	No RP 原爆放射 の子供・ 知見の Activ distribu health t
終了日 Termination Date	March 31, 2018 R	March 31, 2018 R	March 31, 2018
開始日 Initiation Date	April 1, 2017 N	April 1, 2017	April 1, 2017 N
研究資金 (資金拠出機関からの入金額) Research funds (amount of funds from funding organizations)	¥550,000	連携研究者のため、 研究資金の配分なも Since this person is an associate investigator, research funds were not allocated to her.	¥200,000
放影研における研究者の名前 Investigator(s) at RERF	研究分担者 (Collaborator) 杉山 裕美 Hiromi Sugiyama	連携研究者 (Associate Investigator) 定金、敦子 Arsuko Sadakane	研究者 (Investigator) 小笹 晃太郎 Kotaro Ozasa
委託組織の名前と場所及び研究 グループのチーフスは担当の主任研究者 Name and location of entrusting outside organization Chief of research group or principal investigator in charge	厚生労働省・厚生労働科学研究費補助金 「がん対策推進総合研究事業」 研究代表者、松田 智大 国立研究開発法人が研究センター がん対策情報センターが心でを設センター を国がん登録センター Health and Labour Sciences Research Grants (MHLW) Promotion of Comprehensive Research Project for Cancer Control Tomohiro Masuda Section Head, Registry Section, National Cancer Registry, Center for Cancer Registries, Center for Cancer Centrol and Information Services, National Cancer Control	国立がん研究センター・国立がん研究センター研究 開発費 研究代表者 島津 太一 国立研究開発法人国立がん研究センター 社会と健康研究センター 予防研究部 室長 National Cancer Center Funds for Cancer Research and Related Technology Development Taichi Shimazu Section Head, Division of Prevention, Epidemiology and Prevention Group, Center for Public Health Sciences,	文部科学省「博士課程教育リーディングプログラム」 国立大学法人広島大学 学長 越智 光夫 Ministry of Education, Culture, Sports, Science and Technology Program for Leading Graduate Schools Mitsuo Ochi President, Hiroshima University
研究のタイトル Title of Research	接学部 Department of Epidemiology 1 都道府県が心登録の全国集計データと診療情報等との併用・突合によるがん統計整備及び活用促進の研究。 Study to promote the usage and the maintenance of the cancer statistics by merging data of prefecture-based cancer registries and national cancer registry	2 科学的根拠に基づく発がん性・がん予防効果の 評価とがん予防ガイドライン提言に関する研究 Study for proposal of cancer prevention guidelines and evaluation of carcinogenetic and cancer preventing effects based on scientific evidences	3 博士課程教育リーディングブログラム「放射線 災害復興を推進するフェニックスリーダー育成 ブログラム」 Program for Leading Graduate Schools "Phoenix Leader Education Program (Hiroshima Initiative) for Renaissance from Radiation Disaster"

関連性 Relationship to RERF's mission	広範囲な医学的調査 (生活習慣病) Broad-based medical research (Lifestyle disease)	広範囲な医学的調査 (生活習慣病) Broad-based medical research (Lifestyle disease)
関連RP Related RPs	RP 2-75	RP 2-75 RP 5-92
終了日 Termination Date	March 31, 2018	March 31, 2018
開始日 Initiation Date	April 1, 2017	April 1, 2017
研究資金 (資金拠出機関からの入金額) Research funds (amount of funds from funding organizations)	¥1,620,000	直接経費 (Direct cost) ¥200,000 間接経費 (Indirect cost) ¥60,000
放影研にあける研究者の名前 Investigator(s) at RERF	研究分担者 (Collaborator) 山田 美智子 Michiko Yamada	研究分担者 (Collaborator) 山田 美智子 Michiko Yamada
委託組織の名前と場所及び研究 グループのチーフ又は担当の主任研究者 Name and location of entrusting outside organization Chief of research group or principal investigator in charge	厚生労働省・厚生労働科学研究費補助金 「循環器疾患・糖尿病等生活習債病対策総合研究事業」 研究代表者 岡村 智教 慶應義塾大学医学部 教授 Health and Labour Sciences Research Grants (MHLW) Comprehensive Research on Life-Style Related Diseases including Cardiovascular Diseases and Diabetes Mellitus Tomonori Okamura Professor,	日本学術振興会・科学研究費助成事業 「基盤研究(B)」 研究代表者 大久保 孝義 帝京大学医学部 教授 Scientific Research Scientific Research (B) Takayoshi Okubo Professor, School of Medicine, Teikyo University
研究のタイトル Title of Research	臨床研究部 Department of Clinical Studies 1 生涯にわたる循環器疾患の個人リスクおよび 集団のリスク評価ツールの開発を目的とした 大規模コホートの統合研究 A large-scale integrated cohort study to develop tools to assess life-long individual/group risk of circulatory diseases	2 現代の後期高齢者における循環器疾患リスク 要因の検証 Inspection of the circulatory disease risk factors in the modern old-old

関連性 Relationship to RERF's mission	放射線影響研究所 免疫学研究 免疫プレム研究 RERF Immunology and Immunogenome Study	放射線被曝の遺伝的影響 Genetic effects of radiation exposure	放射線被暖の遺伝的影響 Genetic effects of radiation exposure
関連RP Related RPs	RP 4-02 RP 4-04	RP 2-13	RP 1-08
終了日 Termination Date	March 31, 2018 館の研究分 に含まれて cated to the o and Saga-	March 31, 2018	March 31, 2018 の研究分担者 ままれている。 ceated to the binn of Tokyo, hima Univ.).
開始日 Initiation Date	直接経費 April1,2017 March 31, W4,100,000 間接経費 間接経費 間接経費 Indirect cost) ¥1,230,000 東京大学と佐賀県医療センター好生館の研究分担者への配分額は、上記の研究資金に含まれている。	April 1, 2017	直接経費 April 1, 2017 March 31, 20 (Direct cost) April 1, 2017 March 31, 32 (Direct cost) 情接経費 Indirect cost) Y7,470,000 Y7,470,000 April 2, E記の研究資金に含まれている。 The above amount includes funds allocated to the Univ. of Tokyo, Osaka Univ., Ibaraki Univ. and Hiroshima Univ.).
研究資金 (資金拠出機関からの入金額) Research funds (amount of funds from funding organizations)	直接経費 April I, (Direct cost) ¥4,100,000 間接経費 (Indirect cost) ¥1,230,000 東京大学と佐賀県医療センタ担者への配分額は、上記の取いる。 The above amount includes fu collaborator at the University ken Medical Center Koseikan.	直接経費 (Direct cost) ¥300,000 間接経費 (Indirect cost) ¥90,000	直接経費 (Direct cost) ¥24,900,000 間接経費 (Indirect cost) ¥7,470,000 他機関(東大、阪 一の配分額は、上 The above amount colla borators at orl Osaka Univ., Ibara
放影研における研究者の名前 Investigator(s) at RERF	研究代表者 (P.1.) 林 奉権 Tomonori Hayashi 連携研究者 (Associate Investigators) 吉田 健吾 Kengo Yoshida John B. Cologne (統計部) (Dept. Statistics)	研究代表者 (P.1.) 佐藤 康成 Yasunari Satoh	研究代表者 (P.I.) 野田 朝男 Asao Noda 研究分担者 (Collaborator) 濱崎 幹也 Kanya Hamasaki
委託組織の名前と場所及び研究 グループのチーフ又は担当の主任研究者 Name and location of entrusting outside organization Chief of research group or principal investigator in charge	日本学術振興会・科学研究費助成事業 「基盤研究(B)」 研究代表者 林 奉権 JSPS Grant-in-Aid for Scientific Research Scientific Research (B) Tomonori Hayashi	日本学術振興会・科学研究費助成事業 「基盤研究(C)」 研究代表者 佐藤 康成 JSPS Grant-in-Aid for Scientific Research Scientific Research(C) Yasunari Satoh	日本学術振興会・科学研究費助成事業 「基盤研究(S)」 研究代表者 野田 朝男 JSPS Grant-in-Aid for Scientific Research Scientific Research (S) Asao Noda
研究のタイトル Title of Research	分子生物科学部 Department of Molecular Biosciences 1 原爆被爆者集団における放射線関連がん発生の分 子疫学研究 Molecular epidemiology study of inflammation- associated disease development on the basis of long- term follow-up of atomic-bomb survivors	2 全ゲノムシークエンス法による放射線のマウス精 原細胞に及ぼす遺伝的影響評価 Estimation of genetic risk of radiation on mouse spermatogonia by whole genome sequencing	3 In vivo, in siu突然変異検出系を用いた環境および 放射線リスク評価 In vivo, in situ mutagenic risk evaluation of radiation and environmental chemicals using newly developed knock-in mouse systems

研究のタイトル Title of Research	委託組織の名前と場所及び研究 グループのチーフ又は担当の主任研究者 Name and location of entrusting outside organization Chief of research group or principal investigator in charge	放影研における研究者の名前 Investigator(s) at RERF	研究資金 (資金拠出機関からの入金額) Research funds (amount of funds from funding organizations)	開始日 Initiation Date	終了日 Termination Date	関連RP Related RPs	尉連性 Relationship to RERF's mission
分子生物科学部 Department of Molecular Biosciences 4 胎生期に被ばくしたマウス造血幹細胞の放射線感受性に関する研究 A study for radiation-sensitivity in hematopoietic stem cells (HSCs) following fetal irradiation mice	日本学術振興会・科学研究費助成事業 「基盤研究(C)」 研究代表者 濱崎 幹也 JSPS Grant-in-Aid for Scientific Research Scientific Research (C) Kanya Hamasaki	研究代表者 (P.I.) 濱崎 幹也 Kanya Hamasaki	直接経費 (Direct cost) ¥1,300,000 間接経費 (Indirect cost) ¥390,000	April 1, 2017	March 31, 2018	RP 6-11	生物学的線量推定 Biodosimetry
5 生殖細胞変異の1分子解析と後世代影響のリスク 評価 Single molecular analysis of germline mutagenesis and risk assessment for future generation	日本学術振興会・科学研究費助成事業 「若手研究(A)」 研究代表者 内村 有邦 JSPS Grant-in-Aid for Scientific Research Young Scientist (A) Arikuni Uchimura	研究代表者 (P.I.) 内村 有邦 Arikuni Uchimura	直接経費 April 1, 2017 March 31, 3 (Direct cost) ¥6,100,000 間接経費 (Indirect cost) ¥0 ×0 大阪大学の招へ、教員として阪大で研究を継続。 Dr. Uchimura continues this research project as a visiting researcher at Osaka University.	April1,2017 労員として阪大で t Osaka University	March 31, 2018 T究を継続。 roject as a		なし None
6 モザイク変異を指標とした生殖細胞遺伝毒性試験 の開発 In vivo genotoxicity test using mosaic mutations in germline cells	日本学術振興会・科学研究費助成事業 「挑戦的萌芽研究」 研究代表者 内村 有邦 JSPS Grant-in-Aid for Scientific Research Grant-in-Aid for Challenging Exploratory Research Arikuni Uchimura	研究代表者 (P.1.) 内村 有邦 Arikuni Uchimura	直接経費 April 1, 2017 March 31, 2 (Direct cost) ¥0 間接経費 (Indirect cost) ¥0 大阪大学の和へい教員として阪大で研究を継続。補助事業期間延長により、平成29年度に新たな助成金の交付はなし。Dr. Uchimura continues this research project as a visiting researcher at Osaka University. With extension of the funded term, no grant was provided for FY2017.	April 1,2017 X員として阪大でを こより、平成29年度 ues this research p Osaka University, led term, no grant **	March 31, 2018 F究を継続。 (乙新たな助 coject as a With		ない None
7 極微量変異原評価のための全ゲノム解読に基づく 網羅的自然発生突然変異検出系と標準化 New detection system of spontaneous mutations with whole genome sequencing for evaluation of infinitesimal mutagens	日本学術振興会・科学研究費助成事業 「基盤研究(A)」 研究代表者 権藤 洋一 JJSPS Grant-in-Ad for Scientific Research Scientific Research (A) Yoichi Gondo	連携研究者 (Associate Investigator) 内村 有邦 Arikuni Uchimura	連携研究者のため、 研究資金の配分なし Since this person is an associate investigator, research funds were not allocated to him.	April 1, 2017	March 31, 2018		なし None

平成29年度 外部資金研究一覧表 FY2017 External Research Funds

関連性 Relationship to RERF's mission	循環器疾患研究 RERF Circulatory Disease Study
関連RP Related RPs	RP 1-11 RP 2-12
終了日 Termination Date	March 31, 2018
開始日 Initiation Date	April 1, 2017
研究資金 (資金拠出機関からの入金額) Research funds (amount of funds from funding organizations)	直接経費 (Direct cost) ¥1,000,000 間接経費 (Indirect cost) ¥300,000
放影研における研究者の名前 Investigator(s) at RERF	研究代表者 (P.1.) 高橋 規郎 Norio Takahashi 研究分担者 (Collaborators) 大石 和佳(臨床研究部) Waka Ohishi (Dept. Clinical Studies) 三角 宗近(統計部) Munechika Misumi (Dept. Statistics)
委託組織の名前と場所及び研究 グルーブのチーフ又は担当の主任研究者 Name and location of entrusting outside organization Chief of research group or principal investigator in charge	日本学術振興会・科学研究費助成事業 「基盤研究(C)」 研究代表者 高橋 規郎 JSPS Grant-in-Aid for Scientific Research Scientific Research (C) Norio Takahashi
研究のタイトル Title of Research	その他 Other Office 1 どの程度低い放射線被曝、どの程度低い線量率 被曝が循環器疾患と相関するか? How lower radiation dose and how lower radiation dose rate associate with circulatory diseases?

平成29年度 特別会計一覧表 FY2017 Special Funds

資金拠出機関名称 Name of Funding Agency	件数 Number of Funds	資金合計 Amount of Funding Total
厚生労働省 Ministry of Health, Labour and Welfare (MHLW)	3	¥548,157,000
米国国立がん研究所(NCI)契約 U.S. National Cancer Institute (NCI) Contract	-	¥23,220,042
広島県 Hiroshima Prefecture	-	¥14,400,000
長崎県 Nagasaki Prefecture	-	¥8,370,457
エム・アール・アイリサーチアソシエイツ株式会社(環境省委託事業の受託機関) MRI Research Associates Inc. [Contract project organization commissioned by the Ministry of the Environment (MOE)]	-	¥6,951,720
国立大学法人 京都大学(国立研究開発法人 日本医療研究開発機構委託事業の受託機関) Kyoto University [Contract project organization commissioned by the Japan Agency for Medical Research and Development (AMED)]	-	¥1,000,000
総合計 Grand total	8	¥602,099,219

- 注) ・間接費を含む。 ・研究分担者の配分額を含む。

- Notes)
 These amounts include indirect cost.
 These amounts may include subsidies allocated to collaborators.

平成29年度 特別会計一覧表 FY2017 Special Funds

関連性 Relationship to RERF's mission	東電福島第一原発事故処理緊急作業従事者の長期疫学調査 Long term follow-up epidmeiological study on emergency workers of TEPCO, Fukushima IF Nuclear Power Plant accident.	放射線の人に及ぼす影響及び これによる疾病に関する調査 研究の成果の管理、報告及び 公表並びに研修を行うこと To report and publicize the results of research and studies, and to provide training on the effects of radiation and associated diseases in humans	原爆被爆者の生物試料の保管 及び活用 Preservation and use of the A- bomb survivors' biosamples	がんの疫学研究、 LSS、胎内被爆者、 F.集団 Epidemiological study of cancer, LSS, <i>in utero</i> , and F, populations
関連RP Related RPs	RP 6-15 RP 2-17 RP 1-18			RP 1-75 RP 18-61 RP 3-94 RP 6-02 RP 1-06 RP 4-07 RP 5-08 RP 6-10 RP-S2-15 RP-S2-16 RP-S2-16
終了日 Termination Date	March 31, 2018	March 31, 2018	March 31, 2018	July 31, 2019
開始日 Initiation Date	April 1, 2017	April 19, 2017	March 1, 2018	April 1, 2014
資金拠出機関からの入金額 トの入金額 Amount of Funds from Funding Agencies	直接経費 (Direct cost) ¥468,151,000 間接経費 (Indirect cost) ¥74,402,000	¥3,730,000	¥1,874,000	直接経費 (Direct cost) ¥16,579,309 間接経費 (Indirect cost) ¥6,640,733
放影研における契約者/ 研究者の名前 Investigator(s) at RERF	研究代表者 (Principle Investigator) 大人保 利晃 Toshiteru Okubo 研究分担者 (Collaborative Investigator) 児玉 和紀 Razunori Kodama 小笹 是太郎 Kotaro Ozasa 大石 和佳 Waka Oishi 喜多村 紘子	受託者 (Contractor) 丹羽 太貴 Ohtsura Niwa	受託者 (Contractor) 丹羽 太貴 Ohtsura Niwa	主任研究者 (Program Director) 小笹 是太郎 Kotaro Ozasa 研究管理者 (Project Managers) エリック グラント Eric J. Grant ハリー カリングス Harry M. Cullings
委託組織の名前と場所及び研究 グループのチーフ又は担当の主任研究者 Name and location of entrusting outside organization/Chief of research group or principal investigator in charge	厚生労働省・労災疾病臨床研究事業費補 助金 研究代表者 大久保 利晃 Research Grant for Clinical Studies of Work- Related Illness (MHLW) Toshiteru Okubo	厚生労働省・委託事業 丹羽 太貴 MHLW Entrustment Ohisura Niwa	厚生労働省・委託事業 丹羽 太貴 MHLW Entrustment Ohtsura Niwa	米国国立がん研究所 (NCI) 契約 米国メリーランド州ペセスダ、 米国国立がん研究所 NCI契約 HHSN261201400009C 主任研究者 小笹 是太郎 U.S. National Cancer Institute (NCI) Contract National Cancer Institute, Bethesda, Maryland, USA NCI Contract HHSN261201400009C Kotaro Ozasa
研究のタイトル Title of Research	東電福島第一原発緊急作業従事者に対する 疫学的研究 Epidemiological Study of Health Effects in Fukushima Emergency Workers	原爆放射線による健康影響に関する国際交 流調査研究業務 International Exchange Program on Health Effects of the Atomic Bomb Radiation	原機被爆者の生物試料の保管及び活用に関する する 研究事業 Research Program on preservation and use of the A-bomb survivors' biosamples	原爆被爆者におけるがんの疫学的研究支援 Support for Epidemiological studies of cancer among atomic bomb survivors 4

平成29年度 特別会計一覧表 FY2017 Special Funds

関連性 Relationship to RERF's mission	がんの疫学研究、 LSS、胎内被爆者、 F1集団 Epidemiological study of cancer, LSS, in utero, and F1 populations	がんの疫学研究、 LSS、胎内被爆者、 F1集団 Epidemiological study of cancer, LSS, in utero, and F1 populations	循環器疾患研究 RERF Circulatory Disease Study	被爆者のがん研究 Cancer research in atomic bomb survivors
関連RP Related RPs	RP18-61 RP29-60 RPs18-61& 29-60附属書	RP18-61 RP29-60 RPs18-61& 29-60附属書	RP 1-11 RP 2-12 RP-S1-15	RP 1-17
終了日 Termination Date	March 31, 2018	March 31, 2018	March 31, 2018	March 31, 2018
開始日 Initiation Date	April 1, 2017	April 1, 2017	April 1, 2017	April 1, 2017
資金拠出機関からの入金額 らの入金額 Amount of Funds from Funding Agencies	¥14,400,000	¥8,370,457	¥6,951,720	直接経費 (Direct cost) ¥769,231 間接経費 (Indirect cost) ¥230,769
放影研における契約者/ 研究者の名前 Investigator(s) at RERF	受託者 (Contractor) 丹羽 太貴 Ohtsura Niwa	受託者 (Contractor) 丹羽 太賞 Ohtsura Niwa	主任研究者 (P.I.) 高橋 規郎 Norio Takahashi 研究協力者 (Cooperative Investigators) 大石 和佳 Waka Ohishi 三角 宗近 Mumechika Misumi 村上 秀子 Hideko Murakami	研究分祖者 (Collaborator) 今泉 美彩 Misa Imaizumi 研究協力者 (Cooperative Investigators) 飛田 あゆみ Ayumi Hida ベンジャミンフレンチ Benjamin French 三角 宗近 Munechika Misumi
委託組織の名前と場所及び研究 グループのチーフ又は担当の主任研究者 Name and location of entrusting outside organization/Chief of research group or principal investigator in charge	広島県・委託事業 丹羽 太賞 Hiroshima Prefecture Ohtsura Niwa	長崎県・委託事業 丹羽 太貴 Nagasaki Prefecture Ohtsura Niwa	エム・アール・アイ・リサーチアソシエ イツ株式会社 環境省「平成29年度放射線健康管理・健 康不宏対策事業(放射線の健康影響に係 る研究調査事業)」 研究代表者 高橋規郎 MRI Research Associates MOE Research Associates MOE Research on the Health Effects of Radiation in FY2017 (Study of the Health Effects of Radiation) Norio Takahashi	日本医療研究開発機構 (AMED) 研究費 「革新的がん医療実用化研究事業」 研究代表者 小川 誠司 京都大学大学院医学研究科 教授 Japan Agency for Medical Research and Development (AMED) Grants Practical Research for Innovative Cancer Control Seishi Ogawa Professor, Kyoto University Graduate School of Medicine
研究のタイトル Title of Research	が心登録推進事業 Cancer Registry Promotional Project 5	長崎県がん登録・評価事業 Nagasaki Prefecture Cancer Registry Program 6	低線量放射線は循環器疾患のリスクを上げるか? 低線量率放射線は? 放射線関連循環器疾患の機序の解明 Can low-dose radiation exposure increase the risk of circulatory diseases? How about low-dose rate radiation? Inferring potential mechanisms underlying the radiation associated circulatory diseases.	骨髄異形成症候群(MDS)のオミックス解析による治療反応性および海型進展の新たなペイオマーカーの同定とその実用化に関する研究 Study for identification of new biomarkers for predicting therapeutic responsiveness and disease type progression of myelodysplastic syndrome (MDS) by omics analyses and the practical use

II. Activities necessary for the above projects

1. Review of the job performance evaluation system and its implementation

We have reviewed the current job performance evaluation system so that employees can maintain high morale. For this, we have considered revising the regulations to use job-performance evaluations for promotions, salary grade increases, and human resource development and to increase salaries across the board. However, we decided to suspend the revisions in light of our financial basis as a Public Interest Incorporated Foundation run using government subsidies and due to social conditions. From now on, we will strive to enhance the credibility of, and satisfaction with, the job evaluation system.

2. Multi-year personnel plan for the Secretariat

The majority of management-level personnel in the Secretariat will reach mandatory retirement age within five years. Some sections will find it challenging to put capable successors in place due to mandatory retirements and a shrinking personnel cap. In the future, the Secretariat will need to select competent management-level personnel from a limited number of employees. Also, we need to establish a system in which a limited number of employees can perform current duties. We considered the merger of sections and offices within the Secretariat to cope with this situation. As a result, the Accounting Section physically moved to the Supply and Property Section's office in January 2018 so that staff at the two sections of the Hiroshima Laboratory can collaborate from April 2018.

3. Converting temporary employees to permanent staff members

The temporary employee to permanent staff member hiring process enables us to evaluate temporary employees regarding work morale and attitudes, work performance and accuracy, and cooperativeness with other staff members while they work as temporary employees. We expect to hire employees who fit RERF's culture using the job status conversion process. We converted four temporary employees to permanent staff members in FY2017, after considering the necessity of their duties, RERF's financial situation, and our personnel cap.

4. Planning to motivate staff to aspire to management-level positions

We have created a training program to foster supervisory skills in employees with potential to assume managerial positions in the future. The training is for general employees whose present positions are assistant section chiefs or lower and who are at the age of 50 years or younger. The training will be conducted one to two times a year over a three year period. In February 2018, 47 employees participated in the first training course initiated this fiscal year.

5. Continuation of internal audit process

A contract with Deloitte Touche Tohmatsu LLC was signed on July 7, 2017, to perform an internal audit of RERF. The internal audit has been conducted from the date of the contract and will continue through June 30, 2018. The specifics of the internal audit, as of the end of January 2018, are as follows:

- First-round audit, July 12–14, 2017
 - Re: finance and accounting, purchase and payment, contract process, entrustment contract, provision of salaries, external research grants, following up on items identified in FY2016 (finance and accounting, settlement of accounts).
- Second-round audit, August 22–24, 2017

Re: external research grants

• Third-round audit, January 16–18, 2018

Re: finance and accounting, purchase and payment, contract process, entrustment contract, personnel-cost allocation, following up on items identified in FY2016 (purchase and payment, contract process, entrustment contract).

Regarding the results of the internal audit, the interim report was sent to the Auditors on October 26, 2017. Upon completion of the internal audit, the final report will be submitted to the Auditors by the regular meeting of the Board of Directors in June 2018.

6. Facility upgrades

- (1) Facility upgrades to the Hiroshima Laboratory
 - i. Completed the installation of emergency power generator no. 5.
 - ii. Completed repairs of emergency power generators no. 1, no.3, and no. 4.
 - iii. Replacement of the fire hydrant pumps in Hijiyama Hall began from December 2017 and was completed in February 2018.
 - iv. The relocation of the Animal Facility to the first floor of Building B began from January 2018 and is set to be completed May 2018.
 - v. In conjunction with various office relocations, related interior walls are presently being painted.

7. Revision of the rules and regulations

The following regulations were revised with the aim of enhancing RERF's operational framework as a Public Interest Incorporated Foundation (PIIF):

- ➤ The Regulations Concerning Documents and the Internal Regulations for Handling of Decision-making Authority (Effective date: May 1, 2017)
 - The revisions clarify the definitions of "decision-making by a designated person" and "approval by proxy." Also, provisions were added for review and approval by proxy so that authorized or designated decision-makers' duties are not delayed if they are absent from work for an extended period.
- ➤ The Travel Reimbursement Regulations and the Travel Reimbursement Regulations Details of Application (Effective date: November 1, 2017)
 - Given that RERF is a PIIF that operates using government subsidies, the revisions clarify who is responsible regarding the purpose of business trips and the justification of expenses.
- ➤ Internal Regulations Concerning Management of Visiting Student Fellows (Effective date: October 23, 2017)
 - An increasing number of students and research scientists are seeking to come to RERF to receive training and acquire knowledge of the effects of radiation exposure. As a result, RERF expects to receive more visiting fellows than the allowed maximum number stipulated in the existing internal regulations. Accordingly, we have abolished the numerical limit on visiting student fellows.

Appended documents to FY2017 report of activities

There were no items considered to be important matters for supplementing the contents of the FY2017 report of activities.