

## FY2020 report of activities

Radiation Effects Research Foundation



## FY2020 Report of Activities

### I. Report of Major 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 non-cancer 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. We have recently developed in partnership with our Board of Councilors a strategic plan emphasizing integrative approaches in our future studies.

#### 1. Research Projects Examining A-bomb Survivors Health

##### 1) Radiation and Cancer:

- *Updated cancer incidence:* Periodic reporting on the radiation risks of cancer incidence is one of the highest priority effects for RERF. A comprehensive analysis to update radiation risk estimates for cancer incidence through 2009 has been completed, in collaborations between with the Depts. of Epidemiology and Statistics and the US National Cancer Institute, using updated individual doses and information on lifestyle factors such as smoking. Papers on all solid cancer, cancers of the lung, breast, uterus, upper digestive system including stomach colon and rectum, liver were published in 2018 and 2019 while papers on colorectal cancer (Sugiyama H, et al. *Int J Cancer* 2020;146:635-645), central nervous system tumors (Brenner A, et al. *Eur J Epidemiol* 2020;35:591-600) and cancers of the prostate (Mabuchi K, et al. *Radiat Res* 2021;195:66-76), ovary (Utada M, et al. *Radiat Res* 2021;195:60-65), and kidney and urinary tract (Grant E, et al. *Radiat Res* 2021, online ahead) were published. Papers on comparison of cancer incidence and mortality (Brenner A, et al.) and summary of those site-specific analyses (Brenner A, et al.) are being drafted. The series of recent papers focused on the shape of the dose-response curves, low-dose risk and risks among those young at exposure, while adjusting for relevant life-style factors. For the reliability of risk estimation, a paper investigating influence of misclassification of liver

cancer information was published by Dr. French of the Dept. of Statistics.

The updated risk estimates for cancer incidence of individual sites with adjustment for lifestyle factors were mostly similar to those previously reported although some variations were observed. Radiosensitive period, i.e., ages at exposure at which radiation risk is high, seems to be related to high activity of tissue stem cells, e.g., association between development of secondary sexual characteristics and radiation risk of breast cancer and uterine corpus cancer. The observed non-linearity of dose response relationship for various outcomes highly concerns the radiation science community, but the reasons are still under investigation. Since a majority of the subjects who were exposed at young ages are still alive and risk estimates for them are uncertain at this stage, further follow-up will provide more informative characterization of radiation risks.

A preliminary study to determine whether amplifying whole genomes using very small amounts of DNAs obtained from Wright-stained smears would make it possible to perform GWAS studies using the Toshiba Japonica SNP arrays. Genome analysis is considered important from the viewpoint of elucidating and evaluating genetic susceptibility to radiation-induced cancer. RERF holds several kinds of biological samples from the AHS cohort, including blood smears, which have been preserved since 1958. A potential large-scale genome study for all AHS subjects, consisting of approximately 20,000 A-bomb survivors, using old samples preserved after 1958, may enable us to examine genetic and gene-environmental interaction related to radiation exposure susceptibility. In order to conduct the genome analysis, it is necessary to determine whether SNP analysis that uses DNA samples extracted from smear samples is feasible. For initial studies a pool of RERF-employee volunteers, six subjects were randomly selected. DNAs (W-DNAs) were extracted from whole blood samples. Wright-stained smears were prepared from whole blood samples. DNAs extracted from Wright-stained smears were amplified using the QIAGEN REPLI-g DNA amplification kit (amplified-DNAs). W-DNAs and amplified-DNAs were genotyped using SNP arrays (Toshiba Japonica array). Result demonstrated that the amplified-DNA obtained from the smears was suitable for SNP analysis, with a high call rate of 97.0% for the amplified-DNA and a high concordance rate of 93.70% between the W-DNA and amplified-DNA. These results suggest that a whole-genome amplified DNA prepared from the stained smears represents a similar copy of the genomic DNA template and there are comparable call rates when used in high-throughput SNP genotyping assays, making it possible to use the stained smears for GWAS. (Hayashi, Yoshida K, Ohishi, Yoshida N, Kato, Sposto, Tokunaga, Ueki, and Ozasa). PI: Hayashi.

Two studies are being conducted using stored blood samples of myelodysplastic syndrome cases in the AHS and autopsy samples of chronic myeloid leukemia cases in the LSS. These studies will be able to provide us with new insight regarding the mechanisms of radiation-induced myeloid malignancies. We are working on the hematological malignancy studies in collaborations involving Clinical Studies, Statistics, and Epidemiology but also with outside investigators.

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. Three years ago, we initiated a study to detect mutations in serially stored blood samples of AHS participants who developed MDS using next-generation genome analysis technology. Objectives are to determine dynamics of mutated clones before clinical diagnosis of MDS and to explore how it differs by exposed radiation dose. This study will answer the very important question about how radiation-induced myeloid malignancies develop, which has never been tested.

Whole exome sequencing of blood samples serially collected before and after MDS diagnosis in 17 subjects were successfully conducted with average depth of 200-fold. In a preliminary analysis, 8-83 of candidate somatic mutations were detected for each sample. Clones with gene mutations or copy number alterations (CNAs) were detected and expanded several years before diagnosis. In some cases, decrease in mutated clones before diagnoses was also observed.

Leukemia is the only malignancy that developed shortly after the A-bomb, and it is widely recognized that radiation exposure can induce leukemia. A study of leukemia morphological classification (French-American British classification) among A-bomb survivors in 1950-1980 revealed that chronic myeloid leukemia (CML) most frequently developed during the period. CML is currently diagnosed based on the presence of the fusion gene BCR-ABL1. We have conducted a preliminary study to assess whether formalin-fixed paraffin-embedded (FFPE) samples of 3 CML autopsy cases are available for molecular analysis. We performed pathological analysis and extracted DNA and RNA from the unstained slides. Using the extracted DNA and RNA, we evaluated the existence of BCR-ABL1 and ABL1 mutation.

PCR /RT-PCR and pathological analyses indicated that extracted DNA and RNA from FFPE samples are suitable for traditional molecular analysis, but CML diagnosed using pathological criteria alone may result in misdiagnosis. A feasibility study for DNA/RNA analysis on early developing leukemia diagnosed as CML by targeted high-throughput sequencing is planned.

## **2) Radiation and Non-Cancer Effects:**

- Previous studies on A-bomb survivors suggest a relationship between radiation exposure and atherosclerotic diseases and inflammation. Recent evidence in studies involving radiation exposure suggests that clonal hematopoiesis (CH) can cause chronic inflammation leading to atherosclerotic diseases. To evaluate the hypothesis that CH caused by irradiation to hematopoietic stem cells is a cause of chronic inflammation and subsequent atherosclerosis in A-bomb survivors, we are initiating a study that analyzes stored AHS datasets relating hematological profiles with inflammatory and atherosclerotic indicators. A program project has recently approved following outside review and data collection has started.
- Clonal hematopoiesis (CH), potentially associated with radiation exposure and increased risks of inflammatory diseases, has not been evaluated in animal model studies. To develop strategies for assessments of CH linking to radiation-associated noncancer diseases, specifically arteriosclerosis, we conducted research to establish one or more mouse models that can test the hypothesis that CH in irradiated mice is involved in pro-inflammatory phenotypes and can promote atherosclerosis formation. Mouse models to be developed in this research may be useful for assessing the effects of a variety of environmental factors on somatic mutagenesis and CH development. Preliminary experiments conducted in FY2020 indicated that, deep whole-exome sequencing (WES) fully detected somatic mutations with

variant frequency exceeding 2% (a definition of CH in humans) in mouse bone marrow cells, and that the prevalence of CH was higher in 3-Gy whole-body irradiated mice than controls when examined 18 months after irradiation. Both pro-inflammatory monocytes and red blood cell distribution width (RDW) increased in the blood of irradiated mice, which is consistent with our recent findings in the AHS. Because these blood cell phenotypes are often observed in human populations exhibiting CH, these results validated the feasibilities of using WES-based CH detection and determining CH-related blood cell phenotypes for evaluating radiation-induced CH in mice as well as in humans. We have also planned clonality assessment of monocytes accumulating in atherosclerotic plaques that are formed in LDLR-KO mice irradiated and fed with a high-fat diet, which would be able to test the hypothesis that CH following radiation exposure promotes atherosclerosis through clonal accumulation of pro-inflammatory monocytes into atherosclerotic lesions. Publications; Yoshida et al, *British Journal of Haematology* (2021), in press.

- Ophthalmologic examinations for our cataract study were initiated in Hiroshima and Nagasaki in collaboration with ophthalmologists in Hiroshima and Nagasaki Universities in April 2016. Supervision for this study is made by a cataract specialist in Kanazawa Medical University. Ophthalmologic examinations among 1048 AHS subjects who were <15 years of age at the time of bombings (including 115 in utero exposed subjects) were finished in March 2020 in Hiroshima and Nagasaki. Scoring of cataract severity using photographed images was completed by an ophthalmologist and a statistical analysis was started in collaboration with the Statistics Department.

The analysis using a generalized estimating equation (GEE) model suggests a significant association between posterior subcapsular opacities and radiation. However, the association between cortical opacities and radiation was not significant.

### 3) Genetic Effects of Radiation:

- *In utero cohort study:* The *in utero* cohort is small but important and unique then prioritized the highest, as there is no other extant study of radiation risk in mid- to-late life after *in utero* exposure. A paper on mortality risk was accepted by the *European Journal of Epidemiology* (Sugiyama H, et al.). An elevated radiation risk for solid cancer mortality among females was found, but among males was not. Microcephaly, low birth weight, and loss of father were suggested to be mediators of exposure to atomic bomb radiation on noncancer disease death and external causes of death. It is important to consider the mediating effects of those factors.
- The most important research initiative in the Department of Molecular Biosciences genetics program and for RERF in general is the whole genome sequencing (WGS) study focusing on human trios consisting of atomic bomb survivors and their offspring. This is a major part of the institutional-wide F1 umbrella program. In FY2020, statistical calculations regarding the power estimates of detection of radiation induced SNVs, small InDels, and multi-site mutations in F1s were conducted in collaboration with Department of Statistics. These were based on the results from our previous animal experiments and the data published by others. The statistical results provided the numbers of the trios needed for this project.
- To understand the effects of parental exposure on offspring, it is important to analyze the more complex types of mutations. Until FY2019, we had investigated de novo germline mutations (mainly base substitution and small size deletions) in the offspring born to irradiated parents. The results were reported as a paper (Satoh et al, 2020). The purpose of our new study is to uncover the incidence rate of the de novo mutations including complex structural variants in mouse germline and to establish a methodology for that purpose. For

detection of the de novo mutations, we used the following methodologies: short-read NGS (illumina), long-read NGS (Pacbio and Nanopore) and optical mapping methods (Bionano Saphyr). To characterize de novo spontaneous germline mutations efficiently, by using these methods, we analyzed the mutation accumulation (MA) mouse lines, which has been established by 14 years of breeding (passing more than 40 generations). We obtained sufficient WGS data both qualitatively and quantitatively in all sequencing platforms and got several new findings about de novo germline mutations. For instance, it has become possible to accurately detect mutations on short tandem repeat regions, and we found that the spontaneous incidence rate of indels is 40 times higher than previously reported our estimate (Uchimura et al. 2015). In addition, we identified 11 de novo retrotransposon mutations (mainly ~7 Kb LINE insertions) and at least 41 large size structural variants including a very complex mutation consisting of a combination of a segmental duplication (200 kb region) and its partial inversion. This incidence frequency was much higher than the previous estimates based on the conventional methods. Using state-of-the-art technologies, we have successfully developed several pipelines to detect various types of mutations. At the same time, the characteristics of spontaneous mutations in mice have been becoming clear. Our results are important for the future human trio WGS study. (Uchimura, Satoh). PI; Satoh. Satoh, 2020a, 2020b, and in press.

- To mechanistically understand how radiation exposure induces mutations in spermatogonia stem cells and how their mutations transmit to the next generation, we have initiated an in vitro culture approach to examine mouse spermatogonia cells (hereinafter GS, germline stem cells). This year in vitro GS cell mutagenesis experiments were conducted for in vivo transplantation studies in next year. The cultured GS cells were X-ray irradiated and surviving cell colonies were recovered. Structural changes of the genome were analyzed by aCGH (MacroGen/Agilent standard methods) for each 5 clones of control (unirradiated), 2-Gy-irradiated and 4-Gy-irradiated GS cells. For the entire genomic sequencing, short-read WGS was conducted in control and X-irradiated GS cell clones to detect radiation-induced SNVs and small InDels and multi-site mutations. aCGH analysis revealed only one deletion in irradiated clones which was supposed to be mediated by NHEJ. In the WGS, 4-Gy exposed clones showed apparent 2.5 and 4 fold increase of multi-site and deletion mutations, while SNVs and insertions showed only slight increase. Interestingly, while these InDels detected in the unexposed controls largely derived from repeat sequence, radiation-associated changes were largely occurred in the unique sequence, indicating the role of NHEJ in the radiation-associated mutagenesis in GS cells. We plan transplantation of these GS cells into male mice testes to examine the transmissibility of the individual mutations next year (Noda, Hamasaki, Satoh and Uchimura). PI: Noda, partially supported by MEXT grant No. 20K12179
- The Atomic Bomb Casualty Commission (ABCC) conducted a study of pregnancy outcomes of children of atomic bomb survivors, from 1948 to 1954. We have re-examined the risk of major congenital malformations and perinatal deaths using fully reconstructed data, with the DS02 gonadal dose and refined analytical methods. After long term discussions and revisions in partnership with Dr. Samet J, a member of our BOC, to respond to concerns by reviewers and contributors, the paper was endorsed by all contributors. Subsequently, the paper was accepted by the American Journal of Epidemiology. The analyses show that parental exposure is associated with increased risk for major congenital malformations and perinatal deaths, but most are not statistically significant. Although the reanalysis reinforced the results of the previous reports, the contribution of other than genetic effects by radiation, such as socioeconomic factor, might be substantial

(*Am J Epidemiol*, 2020).

## 2. Research Projects on the Health of A-bomb Survivors Children (F<sub>1</sub>)

- *F<sub>1</sub> cohort study*: Long-term studies of the F<sub>1</sub> cohort provide a framework for studying germline effects of radiation exposure and contribute important data to the largest study of its kind. After a major paper on mortality risk assessment was published in 2015, routine collection of case information is continuing. The individual doses of F<sub>1</sub> cohort members are being updated to DS02R1. As residential information is essential for ascertainment of cancer incidence through the national cancer registry system, the information on participants in the F<sub>1</sub> Offspring Clinical Study (FOCS) is being collected for use.
- *F<sub>1</sub> offspring clinical study (FOCS)* [Ohishi W, Tatsukawa Y, and Hida A]  
We have almost completed the third round examination of the F<sub>1</sub> offspring clinical study (FOCS) that was initiated in November 2014 on a four-year cycle. 9,815 subjects participated and participation rate during this cycle was 74.9%. The fourth round was started in November 2018.

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

- The Current work in this area is primarily related to our involvement in the organ dosimetry reevaluation project. Over this last year, a series of papers were published or in development.

### Papers published or in press

*Dosimetric influence of new computational phantoms*(Sato, Funamoto, Paulbeck 2020)

### Papers in development

*Paulbeck CJ, Sato T, Funamoto S, Lee C, Griffin K, Cullings HM, Egbert SD, Endo A, Hertel N, Bolch WE. Fetal and maternal atomic bomb survivor dosimetry using the J45 series of pregnant female phantoms. Part 1: Analysis using DS02 exposure scenarios. [Submitted - Radiation Environmental Biophysics]. 2020; In Development. [Dos]*

In this paper previous work [Radiat Res 192, 538-561 (2019) was extended using realistic angular fluences from the DS02 system for up to nine different radiation dose components and five shielding conditions.

*Paulbeck CJ, Sato T, Funamoto S, Lee C, Griffin K, Cullings HM, Egbert SD, Endo A, Hertel N, Bolch WE. Fetal and maternal atomic bomb survivor dosimetry using the J45 series of pregnant female phantoms. Part 2: Considerations of variations in fetal uterine position. [Target Journal - Radiation Environmental Biophysics]. 2020; In Development. [Dos]*

In this paper, the work in Part 1 (above) was extended to include additional models of the child both in a breach and in a transverse orientation at 15-weeks and 25-weeks post-conception.

*Griffin KT, Sato T, Funamoto S, Chizhov K, Domal S, Paulbeck C, Bolch W, Cullings H, Egbert S, Endo A, Hertel N, Lee C. Japanese pediatric and adult atomic bomb survivor dosimetry using the J45 phantom series: comprehensive source term modelling. [Target Journal - TBD]. 2021; In Development. [Dos]*

In this paper, in order to evaluate the potential dosimetry improvements that would arise from the use of the new phantoms in a Dosimetry System (DS) at RERF, organ doses in the J45 series



have been calculated using the environmental fluence data for twenty generalized survivor scenarios pulled directly from the current DS.

#### Completed and Ongoing work

The Department of Statistics has continued its coordination and collaboration activities in the binational working group that is tasked with developing an improved approach to organ dosimetry by using existing, DS02-calculated shielded radiation fields with new response function tables calculated from new and improved computational phantoms.

As part of this effort, a white paper was developed outlining a plan for adopting the new set of computational models of the human body (phantoms) for use with Dosimetry System DS02, with discussion of the models currently in use, the advantages of a newer set of phantoms that have been developed, the method for implementing the new phantoms, the anticipated cost and justification for the replacement of the current set of phantoms with the newer set, and a proposed timeline for implementation.

As part of the preparation for implementation of the revised organ dosimetry, current DS02 FORTRAN code from the obsolete Lahey FORTRAN compiler were converted to the modern Intel FORTRAN compiler. This code is used to integrate the response function tables generated from the computational phantom models with the source terms and leakage files generated from the transport model and shielding models, which apply to the individual survival data on location, shielding, and orientation. This conversion is necessary because a much larger volume of data from the computational model is required to implement the new dosimetry, and this cannot easily be accommodated by the Lahey compiler without significant structural changes to the established FORTRAN code. The conversion of existing code to Intel FORTRAN requires fewer code changes, which primarily consist of revising native function calls. The code revision and testing will be completed in early 2021. An additional module will be required to apply the response function tables, but this should also be completed during 2021.

#### **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, workshop, participation at international scientific conferences, and international publication of results. This year 1 workshop and 5 seminars were held at RERF presented by national and international researchers by Zoom, and published about 40 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:

- 44 Japanese Institutions
- 9 North American Institutions
- 8 European Institutions
- 1 Asian, Oceanian Institution

**2) Workshop**

International Workshop: ELSI workshop toward RERF future genome studies on atomic bomb survivors and their children

**5. Training Programs for Domestic and Overseas Specialists**

- 1) From the perspective of preventing the spread of COVID-19, the “Epidemiological Training Course for Radiation Biologists,” scheduled to be held in August 2020, was canceled.
- 2) Due to the effects of COVID-19, acceptance of trainees from overseas through the International Council for Health Care of Radiation-exposed (HICARE), the Nagasaki Association for Hibakushas’ Medical Care (NASHIM), and the like, was completely canceled. Additionally, because limits were placed on people’s entering RERF premises with a view toward preventing COVID-19 in FY2020, RERF could not fulfill an outside request for training. Instead, educational materials, such as an RERF introductory video and pamphlets were provided.
- 3) RERF cooperated in an International Symposium sponsored by HICARE (February 11, 2021) and sent lecturers. The symposium was held online attracting 206 participants.
- 4) RERF reviewed matters including an approach of publicly inviting overseas trainees in the International Exchange Research Program, and posted a public invitation and the guidelines for application on the RERF website. One person applied in FY2020, but because it was not possible to predict the state of COVID-19, at the time of actual training, a decision was reached in June 2020 to cancel the applicant’s training.

**6. Public Information Programs**

i) RERF Open House events

RERF canceled its Open House event in both Hiroshima and Nagasaki, due to the coronavirus pandemic. That rare situation this fiscal year led RERF to think of new ways to hold the event going forward.

ii) Strengthening of social media-related activities

By the end of FY2020, RERF’s Facebook page had 851 followers. RERF’s English and Japanese Twitter accounts together had surpassed 500 followers in total by the end of FY2020. During FY2020, RERF paid particular attention to the creation of videos for active posting on the website, Facebook page, and YouTube channel as part of our social media work. The videos included an introduction to RERF for a workshop held by ICAN (International Campaign to Abolish Nuclear Weapons), a video of a tour of RERF, and a series of video remarks by directors and scientists on the 75th year after the atomic bombings, and so on.

iii) Promotion of public relations activities targeting media

RERF planned gatherings and study sessions with the media in FY2020 to improve and strengthen relations, given that job transfers in that work are regular occurrences, resulting in a high degree of turnover in reporters that cover RERF as part of their beat, but such interactions were canceled due to the coronavirus pandemic. As a result of RERF's active efforts to propose story ideas to the media, local media concerns produced and aired several special and other broadcast programs about ABCC/RERF. In addition, based on RERF's continued efforts to fully engage with the media, the number of published articles covering RERF in FY2020 totaled 124 through the end of the fiscal year on March 31.

iv) Enhancement of RERF website

- During FY2020, the new homepage was regularly updated with revised information and the section on published scientific papers reorganized for easier navigation and greater understanding of our system of paper categorization.
- Starting in FY2018, when papers are published in scientific journals, new easy-to-follow synopses were posted on the public website. That effort was further refined in FY2020, with the synopses being further simplified.
- The total number of RERF website hits, or page views, between April 1, 2020, and March 31, 2021 was 606,324, with the daily average being 1,661. The total number of website visitors for the same period was 252,934, with the daily average 692.\*

\*These numbers are the result of a new system of assessment called Google Analytics, the use of which was initiated in June 2018.

v) Enhancement of online news-delivery system

RERF's email magazine system, distributed to subscribers, was enhanced during FY2020 by reducing complicated information and sometimes simply providing links to recently published news and information on our website. The email magazine idea was used to not only distribute the latest research results and information about RERF events and activities but also with the aim of attracting readers to RERF as "members," by offering a sense of "buy-in" with respect to RERF as an organization. The total number of subscribers to our email magazine by the end of March was 364 people.

vi) School Visit Program

The RERF School Visit Program—which is an attempt to teach radiation health effects to school children using readily understandable language—was scheduled to continue in FY2020 but had to be canceled due to the coronavirus pandemic.

vii) Internship (work experience) project

RERF has been accepting interns, mostly those with scientific backgrounds, for some time, and in early FY2020 a college student from the United States applied to RERF for an internship. Due to the coronavirus pandemic, the plan was put on hold.

viii) RERF public lecture series

RERF's new public lecture series, initiated in 2019, targeted peace volunteer guides among other such individuals, in partnership with external organizations such as the Hiroshima Peace Memorial Museum. In FY2020, this program was limited because of the pandemic, but RERF did hold two events outside of RERF at the Hiroshima Peace Memorial Museum for groups of students who had come to Hiroshima on peace-study trips.

ix) Science Club

RERF had plans to provide a venue for science students at junior-high and senior-high schools to learn about RERF's science. However, out of concern for public health during the coronavirus pandemic, RERF canceled this plan.

x) Other public relations activities

- 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 when topical papers were published, mostly through online teleconferencing apps. RERF also responded to inquiries and requests for interviews from numerous domestic and overseas media organizations.
- With the aim of improving public understanding of our research, RERF initiated in FY2018 a new series of paper synopses that explain research with simpler prose and smaller word counts than used previously in our "summary explanation" series for specialists. In FY2020, the synopses were further refined, achieving improved understanding by the public and media of RERF's work.
- RERF had no visitors for RERF facility tours, due to its desire to protect the aging A-bomb survivor participants in RERF studies from COVID-19, and thus had no opportunity to train personnel to handle facility tours in English in preparation for visitors from overseas.
- By enhancing our efforts at communicating RERF's research with the aim of increasing transparency related to RERF research and establishment of good communication with the public, in particular A-bomb survivors and their children, the Public-Awareness Campaign (PAC) working group was formed in January 2019. In FY2020, several of the PAC members led RERF's efforts to respond to email inquiries, as well as media requests for interviews about genomic testing and other plans at RERF and in reports about ABCC/RERF.
- RERF was not able to target small public groups of A-bomb survivors and their children to come to RERF and speak with directors and staff about ABCC/RERF history and research results, with the aim of achieving greater understanding about RERF, due to the coronavirus pandemic.

**FY2020 RERF International Collaborative Activities**

<b>I. Participation in international collaborative activities by RERF directors and staff members</b>		<b>II. Acceptance of visitors from overseas for briefing and training</b>	
WHO-related activity	2 people	(Hiroshima)	
UNSCEAR-related activity	6 people	Visitors related to HICARE	None
ICRP-related activity	3 people	Visitors related to RERF (International Exchange Research Program)	None
IAEA-related activity	1 person	Visitors related to MEXT	None
Medical checkup for A-bomb survivors residing in South Korea-related activity	None	Visitors related to JICA	None
Others	14 people		
		(Nagasaki) Visitors related to NASHIM	None
<b>Total: 26 people</b>		<b>Total: 0 people (Hiroshima 0 people, Nagasaki 0 people)</b>	

**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 (2 people)***RERF* (hereinafter, all titles represent those at time of participation)

Kazunori Kodama, Executive Director, and Misa Imaizumi, Assistant Department Chief, Department of Clinical Studies, Nagasaki, attended The 16th WHO Radiation Emergency Medical Preparedness and Assistance Network (REMPAN). (March 22-24, 2021, Online)

**2. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR)-related collaborative activity (6 people)****1) *National Institute of Radiological Sciences***

Kotaro Ozasa, Department Chief of Epidemiology, attended the UNSCEAR domestic committee meetings. (October 12 and December 22, 2020, Online)

**2) *RERF***

- (1) Alina Brenner, Senior Scientist, Department of Epidemiology, attended meetings as a lead writer for UNSCEAR Epidemiological studies of Radiation and Cancer. (May 18, June 4, July 23, 2020 and January 20, March 18 and March 31, 2021, Online)
- (2) Kazunori Kodama, Executive Director, and Kotaro Ozasa, Department Chief of Epidemiology, attended meetings of the Fukushima Follow-up Program as a former Senior Technical Advisor and a member of the Japanese Working Group, respectively. (July 2 and October 28, 2020, Online)
- (3) Kotaro Ozasa, Department Chief of Epidemiology, attended the 67th UNSCEAR

meetings. (November 2-6, 2020, Online)

- (4) Kotaro Ozasa, Department Chief of Epidemiology, attended meetings as a member of the Ad Hoc Working Group on Effects and Mechanisms. (December 14, 2020, January 25, February 25, and March 23, 2021, Online)

3. *ICRP (International Commission on Radiological Protection)*-related activity (3 people)

- (1) Kotaro Ozasa, Department Chief of Epidemiology, attended meetings as a member of the ICRP Task Group 115 (Risk and Dose Assessment for Radiological Protection of Astronauts). (July 28, 2020 and March 22, 2021, Online)
- (2) Kotaro Ozasa Department Chief of Epidemiology, attended meetings as a member of the ICRP Task Group 91 (Dose and Dose Rate Effectiveness Factor). (July 29, 2020, Online)
- (3) Kotaro Ozasa, Department Chief of Epidemiology, attended annual conferences as a member of ICRP Committee 1. (August 31- September 2, 2020, Online)

4. *IAEA (International Atomic Energy Agency)*-related activity (1 person)

*HICARE (Hiroshima International Council for Health Care of the Radiation-exposed)* collaborative activities

Kanya Hamasaki, Research Scientist, Department of Molecular Biosciences attended and made an oral presentation at IAEA Third Research Coordination Meeting (RCM) of the Coordinated Research Project (CRP) E35010 “Applications of Biological Dosimetry Methods in Radiation Oncology, Nuclear Medicine, Diagnostic and Interventional Radiology (MEDBIODOSE)” (February 12, 2021, Vienna, Austria, Online).

5. Medical checkup for A-bomb survivors residing in South Korea-related activity (0 person)

This activity was not done in FY2020.

6. Others (14 people)

- (1) Eric Grant, Associate Chief of Research, attended the “Scientific Committee 1-27” of the National Council on Radiation Protection and Measurements (NCRP). (April 1-2, 2020, Online)
- (2) Robert Ullrich, Vice Chairman, and Eric Grant, Associate Chief of Research, attended the Radiation Research Society Virtual Meetings. (October 18-21, 2020, USA, Online)
- (3) Robert Ullrich, Vice Chairman, Osamu Tanabe, Chief Scientist/Director of Biosample Research Center, Alina Brenner and Hiromi Sugiyama, Senior Scientists, Department of Epidemiology gave seminars at the Gilbert W. Beebe Webinar Series “Commemorating the 75th Anniversary of the Atomic Bombings—Studies on Radiation Health Effects at the Radiation Effects Research Foundation”. (November 11, 2020, USA, Online)
- (4) Kotaro Ozasa, Department Chief of Epidemiology, attended the conference of 15th International Congress of the International Radiation Protection Association. (January 18-27, 2021, Online)
- (5) Ohtsura Niwa, Chairman, and Kazunori Kodama, Executive Director, attended the HICARE International Symposium, “75 years since the atomic bombings, 30 years since the establishment of HICARE and 10 years since Fukushima Daiichi nuclear power plant accident,” as a chair of the keynote speech and a chair/panelist, respectively. (February 11, 2021, Online).
- (6) Ohtsura Niwa, Chairman, Kazunori Kodama, Executive Director, and Eric Grant, Associate Chief of Research, attended the 2021 Fukushima Medical University International Symposium on the Fukushima Health Management Survey (February

13-14, 2021, Online).

## **II. Acceptance of visitors from overseas for briefing and training**

International Council for Health Care of Radiation-exposed (HICARE), the Nagasaki Association for Hibakushas' Medical Care (NASHIM), and the like, was completely canceled in FY2020.

**FY2020**

**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, 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):

Brenner AV, Sugiyama H, Preston DL, Sakata R, French B, Sadakane A, Cahoon EK, Utada M, Mabuchi K, Ozasa K. Radiation risk of central nervous system tumors in the Life Span Study of atomic bomb survivors, 1958-2009. *Eur J Epidemiol* 2020; 35(6):591-600

Grant EJ, Yamamura M, Brenner AV, Preston DL, Utada M, Sugiyama H, Sakata R, Mabuchi K, Ozasa K. Radiation risks for the incidence of kidney, bladder and other urinary tract cancer: 1958-2009. *Radiat Res* 2020 (Epub); 195:1-9

Mabuchi K, Preston DL, Brenner AV, Sugiyama H, Utada M, Sakata R, Sadakane A, Grant EJ, French B, Cahoon EK, Ozasa K. Risk of prostate cancer incidence among atomic bomb survivors: 1958-2009. *Radiat Res* 2021; 195(1):66-76

Sugiyama H, Misumi M, Brenner AV, Grant EJ, Sakata R, Sadakane A, Utada M, Preston DL, Mabuchi K and Ozasa K, "Radiation risk of incident colorectal cancer by anatomical site among atomic bomb survivors: 1958–2009", *Int J Cancer* 2020; 146(3):635-45

Utada M, Brenner AV, Preston DL, Cologne JB, Sakata R, Sugiyama H, Kato N, Grant EJ, Cahoon EK, Mabuchi K, Ozasa K. Radiation risk of ovarian cancer in atomic bomb survivors: 1958-2009. *Radiat Res* 2021; 195(1):60-65

- (2) Ritsu Sakata, Assistant Chief, and Alina Brenner, Senior Scientist, Department of Epidemiology, are joining with the data of tumor of the central nervous system from RERF as a part of the pooled analysis conducted by the scientists of Radiation Epidemiology Branch, NCI.
- (3) Ritsu Sakata, Assistant Department Chief of Epidemiology, is joining with the data of radiation-associated thyroid cancers from RERF as a part of the pooled analysis conducted by the scientists of Radiation Epidemiology Branch, NCI.

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

Ritsu Sakata, Assistant Department Chief of Epidemiology, is joining the collaborative project with the ACC entitled: *Tobacco smoking, alcohol drinking, body mass index and risk of rare cancers*.

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

Alina Brenner, Senior Scientist, Department of Epidemiology, 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):

Schoemaker MJ, Nichols HB, Wright LB, Brook MN, Jones ME, O'Brien KM, Adami HO, Baglietto L, Bernstein L, Bertrand KA, Boutron-Ruault MC, Chen Y, Connor AE, Dossus L, Eliassen AH, Giles GG, Gram IT, Hankinson SE, Kaaks R, Key TJ, Kirsh VA, Kitahara CM, Larsson SC, Linet M, Ma H, Milne RL, Ozasa K, Palmer JR, Riboli E, Rohan TE, Sacerdote C, Sadakane A, Sund M, Tamimi RM, Trichopoulou A, Ursin G, Visvanathan K, Weiderpass E, Willett WC, Wolk A, Zeleniuch-Jacquotte A, Sandler DP, Swerdlow AJ. Adult weight change and premenopausal breast cancer risk: A prospective pooled analysis of data from 628,463 women. *Int J Cancer*. 2020; 147(5):1306-14

4. Collaboration between *RERF* and University of Washington

RERF entered into a research contract with the University of Washington (Department of Epidemiology and Department of Biostatistics), for which Richard Sposto, Department Chief of Statistics serves as coordinator. Under this contract, RERF supports the training and education of MS and PhD students in epidemiology and biostatistics, and conducts collaborative research with students and their advisors. Research projects focus on analyses of cancer incidence and mortality outcomes in the LSS, as well as the development of new statistical methods for analyzing LSS cohort data.

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

Bockwoldt B, Sugiyama H, Tsai K, Bhatti P, Brenner AV, Hu A, Kerr K, Morenz E, French B, Phipps A. Gastrointestinal cancer survival and radiation exposure among atomic bomb survivors: The Life Span Study. *Cancer Epidemiol Biomarkers Prev* 2020 (Epub):1-19

5. *RERF* international collaborative studies on statistical analyses

- (1) Munechika Misumi, Assistant Department Chief of Statistics, collaborated with the investigators at Helmholtz München resulted in the following publication (RERF authors underlined):

Kaiser JC, Misumi M, Furukawa K. Biologically-based modeling of radiation risk and biomarker prevalence for papillary thyroid cancer in Japanese a-bomb survivors 1958 - 2005. *Int J Radiat Biol*. 2020; 1-12.

- (2) John Cologne, Senior Scientist, and Harry Cullings, Consultant, Department of Statistics collaborated with Dr. Yong-Min Kim of Kyungpook National University in South Korea resulted in the following publication (RERF authors underlined):

Kim YM, Cologne JB, Jang E, Lange T, Tatsukawa Y, Ohishi W, Utada M, Cullings HM. Causal mediation analysis in nested case-control studies using conditional logistic regression. *Biometrical J*. 2020; 1-21.

6. *RERF* international collaborative studies on radiation dosimetry.

Harry Cullings, Consultant, and Sachiyo Funamoto, Section Chief, Department of Statistics, collaborated with an international group of dosimetry experts in work to update RERF radiation dosimetry resulted in the following publication:

Sato T, Funamoto S, Paulbeck C, Griffin K, Lee C, Cullings HM, Egbert SD, Endo A, Hertel N, Bolch WE. Dosimetric impact of a new computational voxel phantom series for the Japanese atomic bomb survivors: Methodological improvements and organ dose response functions. *Radiat Res*. 2020; 194(1-13).

7. *RERF* international collaborative studies on thyroid

Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki), Waka Ohishi, Department Chief of Clinical studies and Michiko Yamada, Division Chief of Radiology of Department of Clinical Studies are joining with Adult Health Study data from RERF as a part of the pooled analysis of thyroid conducted by Dr. Rodondi of University of Bern, Switzerland (Thyroid Studies Collaboration).

#### 8. *RERF* Other

“International workshop: ELSI workshop toward RERF future genome studies on atomic bomb survivors and their children” was held in December 10 and 11, 2020 by online conference. We invited 6 domestic and 3 American experts of genome study ELSI. Total participants were 78.

令和2年度 外部資金研究一覧表  
FY2020 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	¥1,450,000
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)]	10	¥13,845,000
一般社団法人 日本血液学会 Japanese Society of Hematology	1	¥300,000
一般財団法人 土谷記念医学振興基金 Tsuchiya Memorial Medical Foundation	1	¥1,000,000
国立研究開発法人 国立がん研究センター National Cancer Center	1	¥0 *
総合計 Grand total	15	¥16,595,000

注)

- ・ 間接費を含む。
- ・ 研究分担者の配分額を含む。
- \* 研究協力者として研究参画のため、配分資金の配分なし。

Notes)

- ・ These amounts include indirect cost.
- ・ These amounts include subsidies allocated to collaborators.

令和2年度 外部資金研究一覧表  
FY2020 External Research Funds

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)	令和2年度 開始日 First project date in FY2020	令和2年度 終了日 Last project date in FY2020	関連性 Relationship to RERF's mission
疫学部 Department of Epidemiology						
1 国際比較可能ながん登録データの精度管理および他の統計を併用したがん対策への効果的活用の研究 Studies on the quality control of internationally comparable cancer registry data and on the effective usage for cancer control using other statistics	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 国立研究開発法人国立がん研究センター がん対策情報センターがん登録センター 全国がん登録室長 Health and Labour Sciences Research Grants (MHLW) Promotion of Comprehensive Research Project for Cancer Control Tomohiro Matsuda Section Head, Registry Section, National Cancer Registry, Center for Cancer Registries, Center for Cancer Control and Information Services, National Cancer Center	研究分担者 (Collaborator) 杉山 裕美 Hiromi Sugiyama	¥650,000	June 1, 2020	March 31, 2021	日本人のがんの疫学研究 Epidemiological study of cancer in Japanese population
2 国内外研究連携基盤の積極的活用によるがんリスク評価及び予防ガイドライン提言に関する研究 Study of evaluation of carcinogenetic effects based on active utilization of domestic and international research consortia and proposal of cancer prevention guidelines	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 井上 真奈美 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 部長 National Cancer Center Funds for Cancer Research and Related Technology Development Manami Inoue Chief, Division of Cohort Consortium Research, Epidemiology and Prevention Group, Center for Public Health Sciences, National Cancer Center	研究協力者 (Cooperative Investigator) 歌田 真依 Mai Utada	研究協力者のため、 研究資金の配分なし Since this person is a cooperative investigator, research funds were not allocated to her	April 1, 2020	March 31, 2021	日本人のがんの疫学研究 Epidemiological study of cancer in Japanese population

令和2年度 外部資金研究一覧表  
FY2020 External Research Funds

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)	令和2年度 開始日 First project date in FY2020	令和2年度 終了日 Last project date in FY2020	関連性 Relationship to RERF's mission
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 集団リスクの評価ツールの開発及び臨床応用 のための研究 Assessments and clinical application of long-term predictability of cardiovascular risk factors in both individual and population levels	厚生労働省・厚生労働科学研究費補助金 「循環器疾患・糖尿病等生活習慣病対策総合研究事業」 研究代表者 村上 義孝 東邦大学医学部 教授 Health and Labour Sciences Research Grants (MHLW) Comprehensive Research on Life-Style Related Diseases including Cardiovascular Diseases and Diabetes Mellitus Yoshitaka Murakami Professor, Graduate School of Medicine, Toho University	研究分担者 (Collaborator) 山田 美智子 Michiko Yamada  研究協力者 (Cooperative Investigator) 立川 佳美 Yoshimi Tatsukawa	¥800,000	April 1, 2020	March 31, 2021	広範囲な医学的調査 (生活習慣病) Broad-based medical research (Lifestyle disease)
2 被爆による造血器腫瘍発症に関与する分子機構 の解明と今後への展望 Identification of molecular mechanisms related to development of hematological malignancies by atomic-bomb	日本学術振興会・科学研究費助成事業 「若手研究」 研究代表者 吉田 稚明 JSPS Grant-in-Aid for Scientific Research Early-Career Scientists Noriaki Yoshida	研究代表者 (P.I.) 吉田 稚明 Noriaki Yoshida	直接経費 (Direct cost) ¥1,800,000  間接経費 (Indirect cost) ¥540,000	April 1, 2020	March 31, 2021	がん研究 (被爆者ががん研究への応用) Cancer research (Application to cancer research among A-bomb survivors)
3 被爆後早期に発症した白血病症例でのゲノム異常 スクリーニング Screening of genomic alterations in leukemia shortly development after A-bomb radiation	一般社団法人 日本血液学会研究助成 研究代表者 吉田 稚明 Research Grant for Japanese Society of Hematology Noriaki Yoshida	研究代表者 (P.I.) 吉田 稚明 Noriaki Yoshida	¥300,000	April 1, 2020	March 31, 2021	がん研究 (被爆者ががん研究への応用) Cancer research (Application to cancer research among A-bomb survivors)
4 被爆後早期に発症した白血病症例の分子病理学 的解析 Pathological and molecular characterization of leukemia developed shortly after A-bomb radiation exposure	一般財団法人 土谷記念医学振興基金 研究代表者 吉田 稚明 Tsuchiya Memorial Medical Foundation Noriaki Yoshida	研究代表者 (P.I.) 吉田 稚明 Noriaki Yoshida	¥1,000,000	December 1, 2020	March 31, 2021	がん研究 (被爆者ががん研究への応用) Cancer research (Application to cancer research among A-bomb survivors)

令和2年度 外部資金研究一覧表  
FY2020 External Research Funds

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統計部 Department of Statistics  1 測定誤差を考慮した低線量被曝影響の統計的評価 Project to investigate effects of measurement errors in low dose range	日本学術振興会・科学研究費助成事業 「若手研究」 研究代表者 三角 宗近 JSPS Grant-in-Aid for Scientific Research Early-Career Scientists Munechika Misumi	研究代表者 (P.I.) 三角 宗近 Munechika Misumi	直接経費 (Direct cost) ¥0  間接経費 (Indirect cost) ¥0	April 1, 2020  補助事業期間延長により、令和元年度の未執行額(87,777円)を使用。 令和2年度に新たな助成金の交付はなし。 With extension of the funded term, the unexecuted amount for FY2019 (87,777yen) was used No grant was provided for FY2020	March 31, 2021		LSS、遮蔽調査、線量調査 LSS, Shielding survey and dosimetry study
2 Fused-lassoによる広島・長崎の被爆に関する時空間リスク推定モデルの開発 Development of a spatio-temporal risk estimation model for Hiroshima and Nagasaki exposures by Fused-lasso	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 山村 麻理子 JSPS Grant-in-Aid for Scientific Research Scientific Research (B) Mariko Yamamura	研究代表者 (P.I.) 山村 麻理子 Mariko Yamamura  研究分担者 (Collaborator) 坂田 律 Ritsu Sakata	直接経費 (Direct cost) ¥2,600,000  間接経費 (Indirect cost) ¥780,000  広島大学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。 The above amount includes funds allocated to the collaborator at Hiroshima University	April 1, 2020	March 31, 2021		LSS LSS

令和2年度 外部資金研究一覧表  
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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)	令和2年度 開始日 First project date in FY2020	令和2年度 終了日 Last project date in FY2020	関連性 Relationship to RERF's mission
分子生物科学部 Department of Molecular Biosciences						
1 放射線の遺伝影響研究を目的として、マウス精原細胞の染色体に構造変異を持ち込む Introduction of chromosome structural changes into mouse spermatogonia cells for the analysis of their transmission to next generation	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 野田 朝男 JSPS Grant-in-Aid for Scientific Research Scientific Research (C) Asao Noda	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	直接経費 (Direct cost) ¥1,300,000  間接経費 (Indirect cost) ¥390,000	April 1, 2020	March 31, 2021	GS細胞染色体への構造変異導入 Introduction of chromosome structural changes by gene editing technology
2 胚発生の自然発生変異に注目した高解像度な細胞系譜の解析 High resolution analysis of cell lineage by using post-zygotic spontaneous mutations	日本学術振興会・科学研究費助成事業 「挑戦的研究(萌芽)」 研究代表者 内村 有邦 JSPS Grant-in-Aid for Scientific Research Grant-in-Aid for Challenging Research (Exploratory) Arikuni Uchimura	研究代表者 (P.I.) 内村 有邦 Arikuni Uchimura	直接経費 (Direct cost) ¥0  間接経費 (Indirect cost) ¥0  大阪大学の招へい教員の立場で研究代表者として研究全体に従事。当該科研費の管理および係る交付申請、実績報告書等の提出事務はすべて大阪大学が行う。 Engage whole work as PI and perform in Osaka University, and all management of this funds and submission of reports, etc are done by Osaka University  補助事業期間延長により、令和元年度の未執行額(200万円)を使用。令和2年度に新たな助成金の交付はなし。 With extension of the funded term, the unexecuted amount for FY2019 (2,000,000yen) was used No grant was provided for FY2020	April 1, 2020	March 31, 2021	放射線被曝の遺伝的影響 Genetic effects of radiation exposure
3 微量変異原評価を可能とする全ゲノム解読に基づく網羅的自然発生突然変異検出系の開発 Development of comprehensive identification of spontaneous mutations based on whole genome sequencing applicable for the assessment of low-dose 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 榎藤 洋一 東海大学 医学部基礎医学系 分子生命科学 教授 JSPS Grant-in-Aid for Scientific Research Scientific Research (A) Yoichi Gondo Professor, Department of Molecular Life Sciences, Tokai University School of Medicine	研究協力者 (Cooperative Investigator) 内村 有邦 Arikuni Uchimura	研究協力者のため、研究資金の配分なし Since this person is a cooperative investigator, research funds were not allocated to him	April 1, 2020	March 31, 2021	放射線被曝の遺伝的影響 Genetic effects of radiation exposure

令和2年度 外部資金研究一覧表  
FY2020 External Research Funds

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分子生物科学部 Department of Molecular Biosciences  4 放射線発癌と体細胞変異に対する酸化ストレス転写 因子NRF2による防御作用の検討 Possible Roles of Oxidative Stress Response in Protection against Radiation-induced Mutagenesis and Oncogenesis	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 田邊 修 JSPS Grant-in-Aid for Scientific Research Scientific Research (C) Osamu Tanabe	研究代表者 (P.I.) 田邊 修 Osamu Tanabe 研究分担者 (Collaborator) 松田 由喜子(分子生物科学部) Yukiko Matsuda (Dept Molecular Biosciences) 吉田 稚明(臨床研究部) Noriaki Yoshida (Dept Clinical Studies)	直接経費 (Direct cost) ¥2,100,000  間接経費 (Indirect cost) ¥630,000	April 1, 2020	March 31, 2021	放射線による発がんメカニズムの 解明とその予防法の開発に貢献 Contribution to the elucidation of mechanisms of radiation oncogenesis and to the development of methods to prevent it
5 脊髄小脳変性症モデルマウスを用いたCRISPR/Cas13 による新しい核酸医療 New oligonucleotide therapy using CRISPR/Cas13 in spinocerebellar ataxia model 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 松田 由喜子 JSPS Grant-in-Aid for Scientific Research Scientific Research (C) Yukiko Matsuda	研究代表者 (P.I.) 松田 由喜子 Yukiko Matsuda	直接経費 (Direct cost) ¥1,690,000  間接経費 (Indirect cost) ¥0  広島大学原爆放射線医科学研究所の研究員(非常 勤)の立場で研究代表者として当研究所の就業時間 外に広島大学において行われる。当該科研費の管 理および係る交付申請、実績報告書等の提出事務 はすべて広島大学が行う。  As the part-time researcher of RIRBM in Hiroshima University, this project is performed at Hiroshima University outside working hours All management of this funds and submission of reprot, etc are done by Hiroshima University	April 1, 2020	March 31, 2021	なし None



令和2年度 外部資金研究一覧表  
FY2020 External Research Funds

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)	令和2年度 開始日 First project date in FY2020	令和2年度 終了日 Last project date in FY2020	関連性 Relationship to RERF's mission
<b>情報技術部</b> <b>Department of Information Technology</b> <b>1</b> ワイヤレスセンシングと機械学習による猟師向けリアル タイム獣流推定に関する研究 Study concerning the use of wireless sensing and machine learning by hunters to estimate the movements of wildlife real-time	日本学術振興会・科学研究費助成事業 「若手研究」 研究代表者 小野 悟 JSPS Grant-in-Aid for Scientific Research Early-Career Scientists Satoru Ono	<b>研究代表者 (P.I.)</b> 小野 悟 Satoru Ono	直接経費 (Direct cost) ¥1,500,000  間接経費 (Indirect cost) ¥450,000	April 1, 2020	March 31, 2021	診療録を始めとする紙媒体のス キャンデータを分類するための 手法の構築には、本研究で用 いる機械学習を用いた行動情 報の分類に関する研究が有用 に機能すると思われる。  This research which will examine machine-learning-based dog's movement data classification, will expect to contribute to the creation of a best-fit classification method for medical charts and other paper documents
<b>2</b> 情報空間による都市空間強化のためのワイヤレス神 経網の実証的研究 Practical Study on Wireless Neural Network for Strengthening Urban Space by Informatic Space	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 猿渡 俊介 大阪大学 准教授 JSPS Grant-in-Aid for Scientific Research Scientific Research (B) Shunsuke Saruwatari Associate Professor, Osaka University	<b>研究分担者 (Collaborator)</b> 小野 悟 Satoru Ono	直接経費 (Direct cost) ¥50,000  間接経費 (Indirect cost) ¥15,000	April 1, 2020	March 31, 2021	広域に展開する複数の研究拠 点間で効果的な大容量データ の共有を可能とするコンテンツ マネジメントシステムの構築に係 る汎用的な知見の取得。  Versatile knowledge will be gained that is related to constructing a content- management system able to effectively share voluminous data between multiple research centers that span a large area



令和2年度 特別会計一覧表  
FY2020 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)	2	¥24,566,597
米国国立がん研究所(NCI)契約 U.S. National Cancer Institute (NCI) Contract	1	¥6,853,083
広島県 Hiroshima Prefecture	1	¥13,731,928
長崎県 Nagasaki Prefecture	1	¥8,713,000
総合計    Grand total	5	¥53,864,608

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.

令和2年度 特別会計一覧表  
FY2020 Special Funds

	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	放影研における契約者/ 研究者の名前 Investigator(s) at RERF	資金拠出機関か らの入金額 Amount of Funds from Funding Agencies	開始日 Initiation Date	終了日 Termination Date	関連性 Relationship to RERF's mission
1	放射線業務従事者の健康影響に関する疫学 研究 Epidemiological Study on Health Effects among Radiation Workers	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 独立行政法人労働者健康安全機構 労働安 全衛生総合研究所 労働者放射線障害防止 研究センター センター長 Research Grant for Clinical Studies of Work-Related Illness (MHLW) Toshiteru Okubo Director, Research Center for Prevention from Radiation Hazards of Workers, National Institute of Occupational Safety and Health, Japan Organization of Occupational Health and Safety	研究分担者 (Collaborative Investigators) 大石 和佳 Waka Ohishi	¥22,692,597	April 1, 2020	March 31, 2021	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 epidemiological study on emergency workers of TEPCO, Fukushima 1F Nuclear Power Plant accident.
2	原爆被爆者の生物試料の保管及び活用に関 する研究事業 Research Program on preservation and use of the A-bomb survivors' biosamples	厚生労働省・委託事業 丹羽 太貴 MHLW Entrustment Ohtsura Niwa	受託者 (Contractor) 丹羽 太貴 Ohtsura Niwa	¥1,874,000	December 15, 2020	March 31, 2021	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
3	原爆被爆者のがん罹患データの更新 Updated cancer incidence data in the atomic- bomb survivors.	米国国立がん研究所 (NCI) 契約 米国メリーランド州ベセスダ、 米国国立がん研究所 NCI契約 75N91019P00167 主任研究者 小笹 晃太郎 U.S. National Cancer Institute (NCI) Contract National Cancer Institute, Bethesda, Maryland, USA NCI Contract 75N91019P00167 Kotaro Ozasa	主任研究者 (Program Director) 小笹 晃太郎 Kotaro Ozasa 研究管理者 (Project Managers) エリック グラント Eric J. Grant リチャード スポスト Richard Sposto	直接経費 (Direct cost) ¥4,568,723  間接経費 (Indirect cost) ¥2,284,360	August 1, 2019	July 31, 2021	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
4	がん登録推進事業 Cancer Registry Promotional Project	広島県・委託事業 丹羽 太貴 Hiroshima Prefecture Ohtsura Niwa	受託者 (Contractor) 丹羽 太貴 Ohtsura Niwa	¥13,731,928	April 1, 2020	March 31, 2021	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
5	長崎県がん登録・評価事業 Nagasaki Prefecture Cancer Registry Program	長崎県・委託事業 丹羽 太貴 Nagasaki Prefecture Ohtsura Niwa	受託者 (Contractor) 丹羽 太貴 Ohtsura Niwa	¥8,713,000	April 1, 2020	March 31, 2021	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

## **II. Operation and management of RERF**

### **1. Research Resource Center**

The Research Resource Center (RRC) is envisioned to be a core component of RERF's infrastructure. The successful implementation and execution of the RRC is a necessary component to advance RERF's strategic plans.

The RRC's mission is 3-fold. The mission includes:

1. Protect, index, and integrate RERF's research assets. These include data, biosample inventories, paper records, artifacts, manuscripts, datasets and programming scripts, as well as other historically important articles. Access to research data will be made through a web portal with clear accessibility rules that protect the privacy of our subjects.
2. Enhance RERF's ability to perform research by integrating all data and biosample inventories. Tools for data visualization, data assembly, and analysis will simplify and standardize access, and facilitate research.
3. Provide an administrative framework to use and share RERF resources and facilitate contracts and grants via a new office (Office of Collaborative Research).

Activities over the past year include the hiring of a new chief of ITD (and two new programmers), a MEXT grant application in collaboration with RIRBM, meetings of the "Subcommittee for Drafting Guidelines of the Establishment of the RRC", significant progress by the Inventory and Digitization subcommittees, and bi-weekly Technical Team meetings by Dr. Grant and key personnel from ITD. Another important activity was the completion of a pilot project to scope the effort involved to scan all of the medical records housed in the Clinical Studies department in Hiroshima. The pilot project estimated that there were 10,000,000 sheets of paper contained in the medical charts. The vendors concluded that digitizing all of the materials in the medical charts would cost roughly \$5M dollars. A 25-member team could complete the job in 3 years. A pilot project using the Gen3 Data Commons software platform developed by the University of Chicago and presented to RERF by Dr. Robert Grossman was initiated. An intern from the University of Texas Medical Center was recruited and scheduled to travel to Chicago for training and then to Hiroshima to spend the summer working on site. Unfortunately, the COVID pandemic blocked his trip. The intern worked remotely on the project until January 2021 and a decision needs to be made whether to continue the pilot project.

### **2. Review on the relocation of the Hiroshima Laboratory**

Up to now, we have considered the proposal for RERF Hiroshima Laboratory's relocation to the Hiroshima Comprehensive Health Center. Nevertheless, Hiroshima University's Kasumi Campus was newly added as a candidate relocation site. Therefore, we will consider two candidate relocation sites in the future.

### **3. Introduction of an attendance and work management system**

Following the enforcement of the work-style reform law enacted in June 2018, RERF began procedures to procure an attendance and work management system with the primary goal of monitoring employee work hours objectively. Based on a previous unsuccessful comprehensive evaluation bidding, the specifications were narrowed down to a necessary

minimum. Team Spirit Inc won the tender as a result of an open tendering held in February 2021. Therefore, a contract was signed with them to introduce the attendance and work management system.

#### **4. Facility upgrades**

##### **(1) Facility upgrades to the Hiroshima Laboratory**

The air conditioners that had been markedly deteriorated and had failed repeatedly were replaced. Since the production of R22 refrigerant ended in December 2019, it was expected that maintenance would become difficult in the event of failure, making it necessary to replace the air conditioners as soon as possible. In FY2020, the air conditioners were replaced in Units C, D, E, H, and I (construction cost: 17,490,000 yen), completing the three-year project to replace the air conditioners in the Hiroshima Laboratory.

In addition, the access control system in the Departments of Clinical Studies, Epidemiology, and Information Technology, and the RI facility to protect personal information had been in place for 14 years, and the IC card reader terminals were no longer eligible for maintenance, so the system was upgraded (construction cost: 8,369,000yen).

The above two projects were funded by FY2020 subsidy for the maintenance of health and hygiene facilities from the Ministry of Health, Labour and Welfare (39,807,000 yen).

##### **(2) Facility upgrades to the Nagasaki Laboratory**

As a measure to prevent incidents and accidents among the aging study participants and to ensure the safety of wheelchair users, tiles were replaced on the entrance slope, additional handrails were installed in the walkways at the Nursing Section, and the two entrance doors at the Nursing Section and one entrance door at the Division of Radiology were changed from single swing doors to sliding doors (construction cost: 1,768,000 yen).

In addition, the access control system for the Department of Epidemiology and server room, which was installed at the same time as the Hiroshima Laboratory, was upgraded (construction cost: 3,850,000 yen).

#### **5. Revision of the rules and regulations**

The following regulations were revised to enhance this public interest incorporated foundation's operational framework:

- **Work-Related Ethics Regulations for Employees [Effective date: April 1, 2020]**  
Provisions were added to have the ethics supervisor review the justification for the amounts of remuneration paid by the interested parties.
- **Supplementary Regulations Concerning Application of Accounting Regulations [Effective date: April 1, 2020]**  
A revision was made to the amount of office expenses that can be handled as petty cash; and provisions for purchases of goods over the internet were added.
- **Guidelines for Purchase of Goods [Effective date: April 1, 2020]**  
Regarding the determination of target tender prices, revisions were made in a manner to be consistent with and reflect laws and regulations and the actual situations.
- **Regulations Regarding Management of Conflict of Interest [Effective date: April 1, 2020]**

These regulations were revised to require that economic interests and the likes obtained from outside corporations and other entities be reported and reviewed for all research activities, not only for research that requires reporting of conflicts of interest.

- Regulations Concerning Prevention of and Response to Improper Use of Research Funds [Effective date: April 1, 2020]  
Regulations Concerning Prevention of and Response to Research Misconduct [Effective date: April 1, 2020]  
To comply with the national guidelines, independent regulations respectively were established for "misuse of research funds" and "misconduct related to research activities."
- Detailed Regulations on Handling of Personal Information [Effective date: June 1, 2020]  
Detailed provisions on the safety management of information systems and the proper management and handling of personal information stored at RERF were stipulated.
- Administrative Procedures for the Travel Expenses of Research Study Participants [Effective date: July 1, 2020]  
The criteria for the payment of transportation expenses for research study participants who take a taxi to visit the Foundation were clarified. In addition, special measures for the prevention of new coronavirus infection were stipulated.
- Regulations Concerning Handling of Donations [Effective date: Oct. 20, 2020]  
As a result of our investigation to be re-certified as a tax-deductible corporation, we found that our financial situation and past donations did not meet the requirements for such a corporation. Therefore, provisions regarding preferential tax treatment have been deleted from these regulations.
- Guidelines for Animal Experiments, Regulations for Experimental Animal Care Committee and Procedures for the Care, and Maintenance of Experimental Animals [Effective date: January 22, 2021]  
The Experimental Animal Care Committee conducted a comprehensive review of the guidelines, regulations, and procedures on the occasion of the establishment of Experimental Animal Care Room in 2019.
- Guidelines Concerning Administrative Procedures for Remuneration for Councilors, Auditors and Scientific Advisors [Effective date: February 8, 2021]  
The procedures for payment of remuneration to Councilors, Auditors, and Scientific Advisors were clarified and the provisions to deal with special situations were added.
- Guidelines for Use of Corporate Card [Effective date: March 1, 2021]  
These guidelines were revised to make the use of the corporate card (a credit card for which RERF as a juristic person contracts) more efficient and exact.

## Appended documents to FY2020 report of activities

There were no items considered to be important matters for supplementing the contents of the FY2020 report of activities.