FY2021 report of activities

Radiation Effects Research Foundation

FY2021 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:

- A preliminary analysis has revealed evidence of possible mediation of radiation risk for HCC by HBV. We have examined the suitability of analytical methods and validity of model assumptions for the mediation model. Because of the presence of missing data, principled methods for dealing with missing need to be employed. We have therefore also investigated how best to conduct multiple imputation for this study given the nested case-control design. In particular, we are studying how best to account for the design parameters in the missing-data imputation model in collaboration with Department of Statistics.

- *Pathogenesis of Myelodysplastic Syndrome (MDS) (RP1-17, Miyazaki Y and Imaizumi M):* 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. We are conducting 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. MDS clones were detected 4-22 years before diagnosis and expanded during the development of MDS. There are two patterns in clonal evolution; 1) sustained expansion of MDS clones which had chronal-hematopoiesis related alterations (ex. *DNMT3A, TET2*) and 2) remarkable clonal shift and/or rapid expansion of MDS clones which had complex karyotypes and del11q including *ATM*. The former pattern was mostly observed in the less-exposed survivors (<1Gy) and the latter one was mostly observed in the high-exposed survivors (>=1Gy).

- *Updated cancer incidence (RPs 1-75, 18-61):* Periodic reporting on the radiation risks of cancer incidence is the highest prioritized for the Epidemiology department. A comprehensive analysis to update radiation risk estimates for cancer incidence through 2009 has been completed, in collaboration with the Dept. of 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, colon, rectum and central nervous system were published through 2020 and papers on 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;195:140-148) were published in 2021. A paper on comparison of cancer incidence and mortality (Brenner A, et al.) is in press and another paper on summary of those site-specific analyses (Brenner A, et al.) is 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.

  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. The observed non-linearity of dose response relationship for various outcomes highly concerns the radiation science community, but the reasons are complicated as indicated in the latest paper by Brenner, *et al*. 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.

- *Updated LSS mortality report (RP 1-75):* Analysis of mortality risk due to atomic bomb radiation among survivors is the most important in evaluation of late health effects due to exposure to atomic bomb radiation. It is because vital status and cause of death of cancer and noncancer diseases are the most essential for evaluation of health outcomes in epidemiology. Also information of vital status and cause of death is collected for LSS subjects living over the whole Japan whereas information on cancer incidence is collected

from those living in Hiroshima and Nagasaki prefectures. International risk assessment groups use the results of mortality risk as the primary basis for radiation-risk estimation. Since the first LSS report was published in 1962, the results have been published periodically and the latest 14th report was published in 2012 for the follow-up data during 1950-2003. Analysis for a new LSS mortality report (15th) has started using the data through 2017, updated dose estimates, and newly available information on lifestyle and residential factors in collaboration with the Dept. of Statistics. Those analyses include investigation of dose-response shape and radiation risk at low dose levels considering potential confounding by geospatial factors, lifestyle factors (smoking, alcohol drinking, body mass index), some indicators representing socioeconomic status, and so on, and also variation in baseline rates. Analysis of the same models that were used in the LSS 14 Report has been conducted for the data extended to 2017, and the results were substantially similar to the previous report. Currently, analysis is continued using various models including newly available variables, not-in-city subjects, and others (Sakata R, et al.).

- *Screening of fusion genes and genomic mutations in autopsied cases with CML (PI: N. Yoshida)*: Leukemia is one of the diseases caused by radiation dose. Especially, chronic myeloid leukemia (CML) was the most frequently developed type and CML which developed shortly after the bombing and may have produced characteristic genomic alterations. In this RP, we plan to extract DNA from the samples of autopsied CML participants and check the feasibility of applying high throughput sequencing analysis to FFPE tissue to detect fusion genes and genomic mutations. Dr. Kato estimated statistical power of the test of the relationship between radiation dose and prevalence of fusion gene in acute myeloid leukemia (AML) using a logistic regression model, under the guidance of Dr. Sposto.

2) Radiation and Non-Cancer Effects:

- Ophthalmologic examinations for our cataract study using 3 devices (slit-lamp, retro-illumination camera, and Scheimpflug camera with standardized method) 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 almost completed in collaboration with the Statistics Department.
  The presence or absence of cataracts was analyzed by inverse probability weighting logistic regression model (IPWLR) to account for possible missing data due to cataract surgery. The results of analysis suggested that cataract prevalence was significantly associated with age, sex, city, smoking, ultraviolet, and axial length. The significant association between radiation and posterior subcapsular cataracts was also shown. However, radiation effects on cortical cataracts and nuclear cataracts were not observed.

- *Atherosclerosis study, Part 1(RP7-09, Nakamizo T):* Past studies have reported an association between radiation exposure and cardiovascular disease mortality/morbidity. Although the mechanism is unclear, a plausible one is radiation-induced atherosclerosis. To examine the association between radiation and atherosclerosis, we measured a comprehensive set of indicators of atherosclerosis including ankle-brachial index, carotid

intima-media thickness, augmentation index, central systolic blood pressure, brachial-ankle pulse wave velocity, upstroke time, and aortic calcification evaluated from chest and lumbar X-rays among 3,775 AHS participants in 2010-2014. Data were analyzed by structural equation modeling with latent variables representing main atherosclerotic pathologies: 1) arterial stiffness, 2) aortic calcification, and 3) plaque.
Aortic calcification and plaque were linearly associated with radiation, but arterial stiffness was not related to radiation. The association was not so strong—comparable to about 2 years of aging per Gray of radiation exposure. The results of this cross-sectional study suggest a possible causative role of radiation on atherosclerosis, which should be confirmed by future longitudinal studies. A paper on the results has been published (*Eur J Epidemiol, 2021; 36*).

- 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 as a part of CH program project, we conducted preliminary experiments 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. Preliminary mouse experiments using deep whole-exome sequencing (WES) and targeted amplicon sequencing ensured an extremely high prevalence of CH in 3-Gy whole-body irradiated mice, i.e., 16 months after irradiation recurrent somatic mutations with variant frequency exceeding 2% (a definition of CH in humans) were observed in 11 of 12 irradiated mice but in none of 6 controls. The mutations appeared almost specifically in hematopoietic tissues (bone marrow and spleen) and hematopoietic stem/progenitor single cell-derived colonies but not in non-hematopoietic organ (tail, brain, testis etc) cells. Moreover, CH in each of the irradiated mice contained multiple clones that expanded to collectively comprise 60-80% of a whole population of bone marrow nuclear cells, suggesting that high-dose radiation can induce massive hematopoietic cell generation and proliferation from a tiny number of stem/progenitor cells, which is somewhat concordant with our previous observation of clonal chromosome aberrations in blood cells among heavily exposed A-bomb survivors. The blood of irradiated mice exhibited elevated levels of both pro-inflammatory myeloid cells and red blood cell distribution width (RDW), which is often observed in human populations having CH. These results validated our experimental system involving WES-based CH detection and CH-related blood cell profiling for assessment of radiation-induced CH and associated proinflammatory phenotypes in mice as well as in humans. (K. Yoshida, Kusunoki et al., CR155). PI; Yoshida, a manuscript in preparation.

3) Genetic Effects of Radiation:

- The most important research initiative in the MBS 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 F_1 umbrella program. In FY2021, we have completed statistical calculations regarding the power estimates of detection of radiation induced mutations in F_1s. We had meetings with external collaborators to prepare a new RP and submitted it to the Genetics Research Cluster. Now, the RP is under review. In addition, we have prepared a human genome data analysis system consisting of an external cloud server and an on-premises server. One of the most important issues of the human WGS study is getting social agreement and treating with ethical problems. In this regard, last year (Dec. 2020), we held an international workshop entitled “ELSI workshop toward RERF future genome studies on atomic bomb survivors and their

children". In this year, we published the summaries of the discussions and their advice (Noda et al, 2021). Also, we have initiated a stakeholder meeting and discussed the aim of the study and related ethical issues. By the proceedings with the ethical examination of the research and the detailed examination of the scientific research plan in parallel, we plan to carry out appropriate research at an early stage. Uchimura, Satoh, Noda (MB) and Sposto (S) A part of CR162, PI; Uchimura.

- Radiation-induced mutations in mouse spermatogonia cells in culture. 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). 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 hold 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. These results are summarized for publication. Since large scale structural changes were scarcely detected in irradiated GS clones, we have initiated to introduce such changes by using gene editing technology. 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, RP-P3-17). PI: Noda, partially supported by MEXT grant No. 20K12179

2. Research Projects on the Health of A-bomb Survivors Children (F_1)

- *F_1 cohort study (RPs 4-75, 18-61):* Long-term studies of the F_1 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_1 cohort members will be updated to DS02R1 by May, 2022 (Sakata R). As residential information is essential for ascertainment of cancer incidence through the national cancer registry system, the information on participants in the F_1 Offspring Clinical Study (FOCS) has been collected and the record linkage will conduct (Sugiyama H, Kadowaki Y).

- *F_1 offspring clinical study (FOCS) RP4-10, Ohishi W, Tatsukawa Y, and Hida A:* The third round examination of the F_1 offspring clinical study (FOCS) that was initiated in November 2014 on a four-year cycle completed, 9,860 subjects participated by the end of September 2021 (participation rate of 75.3%). The fourth round was started in November 2018, 5,809 persons participated in the health examination by the end of November 2021 (participation rate of 58.4 %).

- We continued efforts to develop an integrated project in collaboration with Departments of Epidemiology, Molecular Biosciences, and Statistics. An umbrella project was organized

for investigation of genetic effects of atomic bomb radiation. We continued to be involved in the umbrella project through the role of obtaining clinical and epidemiological information or biosamples from FOCS participants in preparation for future linking genome information with clinical epidemiological information.

- *Investigation of hereditable genetic effects of radiation base on F1 family trios (PI: Noda)*: Dr. Sposto, with the assistance of Ms. Funamoto and in collaboration with Drs. Noda and Uchimura of the Department of Molecular Biosciences, evaluated a study design and analytic plan for the proposed study of the relationship between parental radiation exposure and heritable mutations using parent/offspring trios. This work involved first assessing the existence of complete family trios with known DS02R1 estimated radiation doses and linking this to the inventory of specimens of the type required for sequencing of children and parents in order to identify the complete set of family trios that would be available for this study. Second, the distributional properties of the primary endpoints for this study, which are multi-site mutation, single nucleotide variants, and insertion/deletions, was derived from the existing literature, with particular attention to the expected extra-Poisson dispersion that will likely be encountered, leading to the adoption of a negative-binomial-based linear regression model of mutation rate on radiation dose. Simulations were performed based on the available trios and their associated DS02R1 doses to estimate the power of primary analyses that would be performed for each endpoint, including a subsampling scheme and sensitivity analyses in the event that cost prohibited assay of all possible trios, which would be the optimal approach. A detailed statistical analysis plan was written. The research proposal is now under review.

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

- *Coordinating of Organ Dosimetry Working Group (ODWG) activities:* 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. Dr. Harry Cullings, former chief of the Department of Statistics, and Ms. Sachiyo Funamoto, the member of the Department who is primarily responsible for overseeing the technical implementation of the dosimetry system at RERF, were and are ongoing contributors to this work.

- In order to evaluate the dose dependent effects of A-bomb radiation on humans, a cytogenetic biological dosimetry study was conducted for a subset of A-bomb survivors in the AHS cohort. A total of 1,868 survivors (1,179 in Hiroshima and 689 in Nagasaki) were examined using the 2-color-FISH method for detecting the frequency of stable translocations involving chromosomes 1, 2, and 4. The dose response from FISH data showed a wide scattering of individual translocation frequencies in both cities as we observed in the previous solid Giemsa staining study. Difference between two cities was remained significant but much reduced suggesting the large city difference in the past study was mainly due to different aberration detection rates between Hiroshima and Nagasaki laboratories. The city difference was not significant when Nagasaki factory workers were excluded from the analysis. The results suggest a shielding-related bias in physical dose estimates in some survivors. This FISH study also reconfirmed that our previous Giemsa staining had successfully detected about 70% of translocations. A manuscript will be submitted in 2022 (Kodama, Hamasaki, Cordova, Cullings, RP 8-93). PI; Kodama.

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 seminar were held at RERF presented by national visitor to RERF and published more than 60 scientific papers.

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:
   39 Japanese Institutions
   12 North American Institutions
   4 European Institutions
   1 Asian, Oceanian Institution

5. Training Programs for Domestic and Overseas Specialists

1) RERF held an online epidemiological training course for radiation biologists to deepen biologists' understanding of RERF's epidemiological research and to promote interaction among investigators working in radiation research institutes (August 26-27, 2021; 82 participants in total, including 54 and 28, respectively, from inside and outside RERF).

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 entering RERF premises with a view toward preventing COVID-19 in FY2021 as well, 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 the 30th anniversary Symposium of NASHIM's foundation sponsored by NASHIM (February 20, 2022) and sent lecturers. Furthermore, the symposium was held online.

4) There was no invitation for the MHLW-sponsored International Exchange and Research Program in FY2021 as well, so we did not recruit trainees from abroad.

5) The Department of Statistics recruited investigators who will participate in the International Fellowships for Research in Japan program, sponsored by the Japan Society for the

Promotion of Science (JSPS), on the RERF external website; since there was no applicant in FY2021, however, the department could not apply to the relevant program.

6. Public Information Programs

i) RERF public lecture series

RERF's new public lecture series, initiated in FY2019, targets peace volunteer guides among other such individuals, in partnership with external organizations such as the Hiroshima Peace Memorial Museum. In FY2021, this series was halted due to the coronavirus pandemic.

ii) RERF Open House events

RERF held the 26th and 24th Open House events at its Hiroshima and Nagasaki laboratories. For the first time, the event was held jointly by Hiroshima and Nagasaki, using a virtual, online format, out of consideration of the effects of the continued spread of the coronavirus. The number of viewers who accessed the videos made specifically for the Open House events was 1,824.

iii) Strengthening of social media-related activities

In FY2021, obtaining understanding from atomic bomb survivors, the second-generation of children, local communities, and the media was positioned as the most important task facing RERF, and social media was effectively used to reach that goal. RERF's Facebook page had 855 followers as of March 31, 2022. RERF's English and Japanese Twitter accounts had reached 573 followers in total by March 31, 2022. RERF paid particular attention to the creation of videos for posting on the website, Facebook page, and YouTube channel as part of our social media work. Videos made that year numbered 19 and were mainly designed for the Open House event.

Given the limited contact with the public due to the COVID-19 pandemic, social media such as Facebook and Twitter have become the most effective method of communicating with the outside world.

iv) Promotion of public relations activities targeting media

RERF planned gatherings and study sessions with the media in FY2021 to improve and strengthen relations, but such interactions were canceled due to the coronavirus. Based on RERF's continued efforts to fully engage with the media and provide story ideas, the number of published articles featuring RERF in FY2021 totaled 69 as of March 31, 2022.

v) Enhancement of RERF website

- During FY2021, the new homepage was regularly updated with revised information and the section on published scientific papers was reorganized for easier navigation and greater understanding of the RERF system of paper categorization.
- During FY2021, focus was placed on conveying readily understandable research-related and other information to the public through the utilization of more video and other methods, particularly at the time of the Open House events.
- Starting in FY2018, when papers are published in scientific journals, new easy-to-follow synopses have been posted on the public website. That synopses were further refined in FY2021 for timely dissemination of information.
- The total number of RERF website hits, or page views, between April 1, 2021, and March 31, 2022, was 609,602, with the daily average being 1, 670. The total number of

website visitors for the same period was 273,323, with the daily average being 749.*

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

vi) Enhancement of online news-delivery system

In FY2021, RERF's email magazine system, E-News, which replaced the printed *Update* newsletter, was enhanced in terms of content and used to not only distribute the latest research results and information about RERF events and activities but also to attract 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 the RERF email magazine as of March 31, 2022, was 388 people.

vii) 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 FY2021 but had to be canceled due to the coronavirus pandemic.

viii) Facility tours

Each fiscal year, RERF tries to handle the many requests for facility tours that come in, with the aim of introducing the foundation's history and research activities. In FY2021, facility tours were canceled because of the coronavirus pandemic, but the Hiroshima Laboratory was able to use outside lecture venues and RERF's Hijiyama Hall during certain periods to introduce to the public RERF and its research work.

ix) Internship (work experience) project

RERF has been accepting interns, mostly those with scientific backgrounds, for some time. In FY2021, the plan was put on hold due to the coronavirus pandemic.

x) Other public relations activities

- RERF actively promoted the organization's important scientific papers to the media via press releases and remote press conferences, when it was possible to do so.
- RERF tried to conduct training for staff to be able to provide RERF facility tours in English, but due to its desire to protect the aging A-bomb survivor participants in RERF studies from COVID-19, RERF was unfortunately unable to provide practical experience to such staff.
- By increasing our effort at communicating RERF's research with the aim of improved transparency related to RERF research and establishment of good communication with the public, in particular A-bomb survivors, their children, and the media, the Public-Awareness Campaign (PAC) working group was formed in 2019. In FY2021, the PAC working group members formed the core of the RERF response to email inquiries from the public.
- RERF was unable 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.

（Attachment 1）

FY2021 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	4 people	(Hiroshima)	
UNSCEAR-related activity	7 people	Visitors related to HICARE	None
ICRP-related activity	4 people	Visitors related to RERF (International Exchange Research Program)	None
IAEA-related activity	1 person		
Medical checkup for A-bomb survivors residing in South Korea-related activity	None	Visitors related to MEXT	None
		Visitors related to JICA	None
Others	18 people		
		(Nagasaki)	
		Visitors related to NASHIM	None
Total: 34 people		**Total: 0 people (Hiroshima: 0 people, Nagasaki: 0 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 (4 people)

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

(1) Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki), attended the ConvEx-3 International Emergency Response Exercise in a part of activities of the WHO Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) (October 26-27, 2021, Online).

(2) At the request of the WHO, Kazunori Kodama, Executive Director, Misa Imaizumi, Assistant Department Chief of Clinical Studies (Nagasaki), and Kanya Hamasaki, Research Scientist, Department of Molecular Biosciences, conducted, with Ohtsura Niwa, Chairman's approval, administrative procedures for the re-designation as the WHO Collaborating Center (February 2022).

2. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) -related collaborative activity (7 people)

1) *National Institute of Radiological Sciences*

Kotaro Ozasa, Department Chief of Epidemiology, attended the UNSCEAR domestic committee meetings (September 13, 2021, and February 15, 2022, Online).

2) *RERF*

(1) Kotaro Ozasa, Department Chief of Epidemiology, attended meetings as a member of the Ad Hoc Working Group on Effects and Mechanisms (April 22, June 15, September 6, October 11, November 10, December 17, 2021, January 24, and February 15, 2022, 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 (May 17, July 26 and October 15, 2021, Online).

(3) Eric Grant, Associate Chief of Research, attended meetings as an expert writer for UNSCEAR Epidemiological studies of Radiation and Cancer (May 27, and June 18, 2021, Online).

(4) Alina Brenner, Senior Scientist, Department of Epidemiology, attended meetings as a lead writer for UNSCEAR Epidemiological studies of Radiation and Cancer (May 28, June 16, June 21-25, October 21-22, November 29, December 13, December 15-16, 2021, January 12, and February 24, 2022, Online).

(5) Kotaro Ozasa, Department Chief of Epidemiology, attended the 68th UNSCEAR meetings (June21-25, 2021, Online).

3. *ICRP (International Commission on Radiological Protection)*-related activity (4 people)

(1) Kotaro Ozasa, Department Chief of Epidemiology, attended meetings as a member of the ICRP Task Group 91 (Dose and Dose Rate Effectiveness Factor) (April 6, May 13, 2021, and March 1, 2022, Online).

(2) 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) (May 20, September 29, 2021, January 24 and March 4, 2022, Online).

(3) Tomoki Nakamizo, Division Chief of Radiology of the Department of Clinical Studies, Nagasaki, attended meetings as a member of the ICRP Task Group 119 (Radiation Effects on Diseases of the Circulatory System) (September 9, 2021, and March16, 2022, Online).

(4) Kotaro Ozasa, Department Chief of Epidemiology, attended annual conferences as a member of ICRP Committee 1 (November 2-5, and November 29, 2021, Online).

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

Ohtsura Niwa, Chairman, gave a lecture at the Technical Meeting on Radiation in Medicine Communications and Methodologies – International Perspectives and the Role of Science, Technology and Society in Low-Dose Radiation Settings (Online seminar, November 9, 2021).

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

This activity was not done in FY2021.

6. Others (18 people)

(1) Kazunori Kodama, Executive Director, took the lead in various administrative procedures for redesignating HICARE (Hiroshima International Council for Health Care of the Radiation- Exposed) a collaborating center of the IAEA (International Atomic Energy Association) (August 2021).

(2) Robert Ullrich, Vice Chairman, and Eric Grant, Associate Chief of Research, attended the Radiation Research Society（RRS）'s virtual meeting, and Alina Brenner, Senior Scientist, Department of Epidemiology, gave a presentation (October 3-6, 2021, Puerto Rico, Online).

(3) Eric Grant, Associate Chief of Research, gave a lecture to Radiation Effects Association (REA) (November 4, 2021).

(4) Eric Grant, Associate Chief of Research, attended the meetings as a member of the 2022 Radiation Research Society (RRS) Program Committee (December 16, 2021,

January 20, February 23, March 14, 2022, Online).

(5) Kotaro Ozasa, Department Chief, Alina Brenner, Senior Scientist, and Hiromi Sugiyama, Senior Scientist, Department of Epidemiology, gave presentations at the IsoRed Webinar Series featuring Radiation Epidemiology and Dosimetry at RERF (January 12, 2022, Online).

(6) Eric Grant, Associate Chief of Research, attended the National Council on Radiation Protection and Measurements (NCRP) meetings as a Program Committee Chairman for the 2023 NCRP meeting (January 13 and 26, 2022, Online).

(7) Robert Ullrich, Vice Chairman, gave a seminar at the Public Meeting of the National Academies of Sciences, Engineering, and Medicine - Developing a Long-Term Strategy for Low-Dose Radiation Research in the United States (January 24-25, 2022, USA, Online).

(8) Ohtsura Niwa, Chairman, participated in a lecture at the 6th International Symposium of the Network-type Joint Usage/Research Center for Radiation Disaster Medical Science (February 7, 2022, Online).

(9) Kazunori Kodama, Executive Director, attended the NASHIM (Nagasaki Association for Hibakushas' Medical Care) 30th Anniversary Symposium as a panelist (February 20, 2022, Online).

(10) Eric Grant, Associate Chief of Research, attended the meetings as a member of the Radiation Research Society (RRS) Finance Committee (February 23, 2022, Online).

(11) Ohtsura Niwa, Chairman, gave a lecture in person, and Kazunori Kodama, Executive Director, remotely attended the 2022 Fukushima Medical University's International Symposium on the Fukushima Health Management Survey (March 5, 2022, Online).

(12) Eric Grant, Associate Chief of Research, attended the "Scientific Committee 1-27" of the National Council on Radiation Protection and Measurements (NCRP) (March 28-29, 2022, Online).

(13) Kanya Hamasaki, Research Scientist, Department of Molecular Biosciences, attended EPR Biodose 2022 conference (March 28-30, 2022, 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 FY2021.

(Attachment 2)

FY2021

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, served as a responsible person of the RERF side, 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 were conducted based on this contract.

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

   Fujihara M, Sakata R, Yoshida N, Ozasa K, Preston DL, Mabuchi K. Incidence of lymphoid neoplasms among atomic bomb survivors by histological subtype: 1950-1994. *Blood* 2022; 139(2):217-27

   Brenner AV, Preston DL, Sakata R, Cologne JB, Sugiyama H, Utada M, Cahoon EK, Grant EJ, Mabuchi K, Ozasa K. Comparison of all solid cancer mortality and incidence dose-response in the Life Span Study of atomic bomb survivors, 1958-2009. *Radiat Res* 2022; [Epub]:1-18 [RP1-75, RP18-61]

   Sugiyama H, Misumi M, Sakata R, Brenner AV, Utada M, Ozasa K. Mortality among individuals exposed to atomic bomb radiation in utero; 1950-2012. *Eur J Epidemiol* 2021; 36(4):415-28 [RP2-61]

   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 [RP1-75, RP18-61]

   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 cancers: 1958-2009. *Radiat Res* 2021; 195(2):140-8 [RP1-75, RP18-61]

   (2) Ritsu Sakata, Assistant Department 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.

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 served as coordinator. Under this contract, RERF supported the training and education of MS and PhD students in epidemiology and biostatistics and conducted collaborative research with students and their advisors. Research projects focused 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):

   Hu A, French B, Sakata R, Bhatti P, Bockwoldt B, Grant EJ, Phipps A. The possible impact of passive smoke exposure on radiation-related risk estimates for lung cancer among women: The Life Span Study of atomic bomb survivors. *Int J Radiat Biol* 2021; 97(11):1548-54

   Note: The contract research agreement between RERF and the University of Washington, dated September 16, 2017, expired on December 31, 2021.

5. *RERF* international collaborative studies on statistical analyses

   Munechika Misumi, Assistant Department Chief of Statistics, continued a collaboration study with the investigators at Helmholtz München on the mechanistic modeling of carcinogenesis having online meeting.

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.

7. *University of Bern* international multi-institutional 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).

   Van Vliet AN, van Heemst D, Almeida OP, Åsvold BO, Aubert CE, Bae JB, Barnes LE, Bauer DC, Blauw GJ, Brayne C, Cappola AR, Ceresini G, Comijs HC, Dartigues JF, Degryse JM, Dullaart RPF, van Eersel MEA, den Elzen WPJ, Ferrucchi L, Fink HA, Ficker L, Grabe HJ, Han JW, Helmer C, Huisman M, Ikram MA, Imaizumi M, de Jongh RT, Jukema JW, Kim KW, Kuller LH, Lopez OL, Mooijaart SP, Moon JH, Moutzouri E, Nauck M, Parle J, Peeters RP, Samuels MH, Schmidt CO, Schminke U, Slagboom PE, Stordal E, Vaes B, Völzke H, Westendorp RGJ, Yamada M, Yeap BB, Rodondi N, Gussekloo J, Trompet S. Association of thyroid dysfunction with cognitive function: An individual participant data analysis. JAMA Intern Med, 2021; 181(11): 1440-50

   Syrogiannouli L, Wildisen L, Meuwese C, Bauer DC, Cappola AR, Gussekloo J, den Elzen W, Trompet S, Westendorp R, Jukema JW, Ferrucci L, Ceresini G, Åsvold BO, Chaker L, Peeters RP, Imaizumi M, Ohishi W, Vaes B, Völzke H, Sgarbi JA, Walsh JP, Dullaart RPF, Bakker SJL, Iacoviello M, Rodondi N, Giovane CD for the Thyroid Studies Collaboration. Incorporating baseline outcome data in individual participant data meta-analysis of non-randomized studies. Front Psychiatry, 2022; 13: 774251

令和3年度　外部資金研究一覧表
FY2021 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
厚生労働省 Ministry of Health, Labour and Welfare (MHLW)	2	¥1,320,000
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)]	9	¥8,710,000
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	13	¥11,030,000

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.
＊ No research funds are allocated, because the RERF researcher takes part in the research as a cooperative investigator.

令和3年度 外部資金研究一覧表
FY2021 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3年度 開始日 First project date in FY2021	令和3年度 終了日 Last project date in FY2021	関連RP Related RPs	関連性 Relationship to RERF's mission
疫学部 Department of Epidemiology								
1	社会経済的格差に着目したがん対策に資する空間疫学的ビッグデータ解析研究 Spatial epidemiological big data analysis research that contributes to cancer control focusing on socio-economic disparities	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　伊藤 秀美 JSPS Grant-in-Aid for Scientific Research Scientific Research (B) Hidemi Ito	**研究分担者** (Collaborator) 杉山　裕美 Hiromi Sugiyama	直接経費 (Direct cost) ¥200,000 間接経費 (Indirect cost) ¥60,000	April 1, 2021	March 31, 2022	RP-S2-17	日本人のがんの疫学研究 Epidemiological study of cancer in Japanese population
2	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	¥600,000	April 1, 2021	March 31, 2022	RP-S2-17	日本人のがんの疫学研究 Epidemiological study of cancer in Japanese population
3	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) 坂田　律 Ritsu Sakata	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, 2021	March 31, 2022	RP-A2-15	日本人のがんの疫学研究 Epidemiological study of cancer in Japanese population

令和3年度 外部資金研究一覧表
FY2021 External Research Funds

	研究のタイトル Ti le 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3年度 開始日 First project date in FY2021	令和3年度 終了日 Last project date in FY2021	関連RP Related RPs	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	¥720,000	April 1, 2021	March 31, 2022	RP 2-75 RP 6-08 RP 1-15	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) ¥300,000 間接経費 (Indirect cost) ¥90,000	April 1, 2021	March 31, 2022	RP 6-70 RP 5-90 RP-S2-15 RP 5-02 RP-P2-19	がん研究 （被爆者がん研究への応用） 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	April 1, 2021	March 31, 2022	RP 6-70 RP 5-90 RP-S2-15 RP 5-02	がん研究 （被爆者がん研究への応用） Cancer research (Application to cancer research among A-bomb survivors)

令和3年度 外部資金研究一覧表
FY2021 External Research Funds

研究のタイトル Ti le 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3年度 開始日 First project date in FY2021	令和3年度 終了日 Last project date in FY2021	関連RP Related RPs	関連性 Relationship to RERF's mission
統計部 Department of Statistics							
1 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) ¥2,400,000 間接経費 (Indirect cost) ¥720,000 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 collaborators at Hiroshima University	April 1, 2021	March 31, 2022	RP 1-75	LSS LSS

令和3年度 外部資金研究一覧表
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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) ¥1,000,000 間接経費 (Indirect cost) ¥300,000	April 1, 2021	March 31, 2022	RP-P3-17	GS細胞染色体への構造変異導入 Introduction of chromosome structural changes by gene editing technology
2 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　権藤　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, 2021	March 31, 2022	No RP	放射線被曝の遺伝的影響 Genetic effects of radiation exposure
3 放射線発癌と体細胞変異に対する抗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　田邉　修 JSPS Grant-in-Aid for Scientific Research Scientific Research (C) Osamu Tanabe	**研究代表者** (P.I.) 田邉　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) ¥200,000 間接経費 (Indirect cost) ¥60,000	April 1, 2021	March 31, 2022	RP-P3-19	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

令和3年度 外部資金研究一覧表
FY2021 External Research Funds

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分子生物科学部 **Department of Molecular Biosciences**							
4 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) ¥700,000 間接経費 (Indirect cost) ¥210,000 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 reprots, etc are done by Hiroshima University	April 1, 2021	March 31, 2022	No RP	なし None
5 がん細胞の力学モデルの構築と病理診断への応用 Mechanical model of cancer cells and its application to pathology	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　今井　正幸 JSPS Grant-in-Aid for Scientific Research Challenging Research (Exploratory) Masayuki Imai	**研究分担者** (Collaborator) 鶴山　竜昭 Tatsuaki Tsuruyama	直接経費 (Direct cost) ¥1,000,000 間接経費 (Indirect cost) ¥300,000	April 1, 2021	March 31, 2022	No RP	原爆被爆者におけるがん細胞像の生物物理学メカニズムの解明 Understand biophysical mechanism of cancer cell imaging in A-bomb survivors

令和3年度 外部資金研究一覧表
FY2021 External Research Funds

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情報技術部 Department of Information Technology							
1 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	**研究代表者** (P.I.) 小野　悟 Satoru Ono	直接経費 (Direct cost) ¥900,000 間接経費 (Indirect cost) ¥270,000	April 1, 2021	March 31, 2022	No RP	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考えられる。 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

令和3年度　特別会計一覧表
FY2021 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	¥17,837,000
米国国立がん研究所(NCI)契約 U.S. National Cancer Institute (NCI) Contract	1	¥3,701,335
広島県 Hiroshima Prefecture	1	¥15,739,885
長崎県 Nagasaki Prefecture	1	¥8,700,000
総合計　Grand total	5	¥45,978,220

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3年度　特別会計一覧表
FY2021 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RP Related RPs	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 of health effects in 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 Iccupational Safety and Health, Japan Organization of Occupational Health and Safety	研究分担者 (Collaborative Investigators) 大石　和佳 Waka Ohishi	¥15,963,000	April 1, 2021	March 31, 2022	RP 6-15 RP 2-20	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　太貫 MHLW Entrustment Ohtsura Niwa	受託者 (Contractor) 丹羽　太貫 Ohtsura Niwa	¥1,874,000	December 20, 2021	March 31, 2022		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) ¥2,467,559 間接経費 (Indirect cost) ¥1,233,776	August 1, 2019	July 31, 2021	RP 1-75 RP 18-61 RP 3-94 RP 1-06 RP 4-07 RP 5-08 RP 6-10 RP-S5-19 RP-S2-20 RP-S1-21 RP-S2-21	がんの疫学研究、 LSS、胎内被爆者、 F_1集団 Epidemiological study of cancer, LSS, *in utero* , and F_1 populations
4	がん登録推進事業 Cancer Registry Promotional Project	広島県・委託事業 丹羽　太貫 Hiroshima Prefecture Ohtsura Niwa	受託者 (Contractor) 丹羽　太貫 Ohtsura Niwa	¥15,739,885	April 1, 2021	March 31, 2022	RP18-61 RP29-60 RPs18-61& 29-60附属書	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　太貫 Nagasaki Prefecture Ohtsura Niwa	受託者 (Contractor) 丹羽　太貫 Ohtsura Niwa	¥8,700,000	April 1, 2021	March 31, 2022	RP18-61 RP29-60 RPs18-61& 29-60附属書	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:

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.

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.

Provide an administrative framework to use and share RERF resources and facilitate contracts and grants via a new office (Office of Research Support).

As part of a "two-step" process to initiate the RRC, a new ad hoc committee was created by RERF's Executive Committee under the recommendation of the Preparatory Committee for the Establishment of the Research Resource Center. The new committee (The Research Resource Operating Committee), chaired by Dr. Grant will advise on steps and priorities to establish the RRC. Immediate actions identified include expanding the ITD by creating a new section (the Research Resource Section) to oversee technical development; expand the Library and Archives Section to aid in the development and implementation of a Content Management System (CMS) to centralize and protect all text and paper-based materials; to initiate the Office of Research Support in the Secretariat to begin to identify and automate administrative procedures for research. All activities in the ITD will be managed by the Chief of ITD. Activities over the past year include initiating a pilot project of a CMS using contract help from a firm in Tokyo. Applying for an academic grant to allow CMS technical development and build a collaboration with the Medical Archives group at the University of Hiroshima. Initiating the Scanning Center at the Hiroshima laboratory to allow individual researchers or sections to scan and upload local materials for long-term storage. The Gen3 Data Commons framework pilot project was discontinued as of March 2021, largely due to the COVID pandemic precluding an internship of a visiting engineer. A small RRC "Technical Team" met throughout the year to specify technical requirements and functionality of our vision of the RRC.

2. Review on the relocation of the Hiroshima Laboratory

We proceeded with deliberations on the two candidate relocation sites to achieve RERF's strategic plans: The Hiroshima Comprehensive Health Center and Hiroshima University's Kasumi Campus.

3. Transition to a full audit

RERF is aiming to obtain a full audit by an external auditing firm to supplement the audit by the Auditors. For the full audit, we have selected Deloitte Touch Tohmatsu LLC, which has been providing us with Agreed Upon Procedures services since FY2007 and since FY2016 internal audit assistance services. In October 2021, we signed a contract for

performing investigation services for the audit. The preliminary investigation for the audit was conducted in November 2021, and the investigation report was received in December of the same year. We are currently responding to the findings and suggestions for improvements in the investigation report.

4. Introduction of an attendance and work management system

RERF was required to monitor employee work hours objectively, following the enforcement of the work-style reform law. RERF decided to introduce an attendance and work management system because it not only allows employee work hours to be monitored objectively but it also saves labor by having applications for leave filed electronically. Based on a contract with Team Spirit Inc. signed on April 13, 2021, following an open bidding, the system was introduced on January 1, 2022.

5. Revision of the rules and regulations

RERF in FY2021 reviewed its regulations to enhance the public interest incorporated foundation's operational framework. The following are main regulations revised or established:

- Framework Concerning Plans for Prevention of Misuse of Research Funds, Regulations Concerning Prevention of and Response to Misuse of Research Funds [Effective date: April 1, 2021]
  The regulations prepared in compliance with the guidelines of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) were revised so that they could be consistent with the reality of the operational system of RERF.

- Regulations Concerning Prevention of and Response to Research Misconduct [Effective date: April 1, 2021]
  The regulations were revised to comply with the MEXT's Guidelines for Responding to Misconduct in Research.

- Regulations Concerning Rules/Regulations Management [Effective date: April 30, 2021]
  Procedures for establishment, revision/abolition, and promulgation of the rules/regulations were clarified.

- Regulations of Management Authority of Directors [Effective date: June 3, 2021]
  Control system of chemical substances was reevaluated to change the general supervisor, and as a consequence, change was made to the Director in charge of the environment management (toxic and chemical substances) defined in the appended table related to Article 7 (Duties of Directors).

- Regulations for Protection of Study Subjects and Regulations for Protection of Personal Information [Effective date: June 3, 2021]
  The Ethical Guidelines for Medical and Health Research Involving Human Subjects and the Ethics Guidelines for Human Genome/Gene Analysis Research were unified to establish the Ethical Guidelines for Life-Science and Medical Research Involving Human Subjects; as a result, the names of guidelines in the Regulations for Protection of Study Subjects and the Regulations for Protection of Personal Information were changed.

- Operational Procedures of the Biosample Research Center and Detailed Regulations for Provision of Samples and Sample Information from the Biosample Research Center

[Established on June 8, 2021]
The operational procedures and the detailed regulations were established.

- Regulations Concerning Handling of Official Seals [Effective date: July 1, 2021]
  The rules on the omission of official seals and digital certificates were added, and the Nagasaki Laboratory's bank-registered seals were revised to fit the reality.

- Procedures for Computation of Project-Specific Expenses [Effective date: Aug. 1, 2021]
  The procedures were revised to comply with the change made to how to distribute the indirect costs.

- Supplementary Regulations Concerning Organization of the Secretariat [Effective date: Aug. 1, 2021]
  The Secretariat's sections (offices) reevaluated and revised their duties to fit the reality.

- Internal Regulations for Handling of Decision-making Authority [Effective dates: October 1, 2021, and January 1, 2022]
  The classification table of the documents to be approved and the authorized decision-makers was reevaluated and revised to fit the reality. In addition, the authorized decision-makers for accounting clerical work were partially changed in response to the findings of the Deloitte Touche Tohmatsu's preliminary investigation report.

- Regulations Concerning Documents [Effective date: October 14, 2021]
  The rules on the omission of draft documents and change or withdrawal of approved draft documents were added.

- Standards Concerning Appointment and Payment of Salaries of Fixed-term Research Scientists, Procedures to partially revise the Procedures for Application of Article 2-4, 2-5 of the Procedural Standards Concerning Hiring of Research Scientists (Interim policy for hiring of research scientists) [Effective date: October 26, 2021]
  The standards and the procedures on fixed-term research scientists were revised as the term of appointment for those who serve as a department chief or the equivalent was changed to five years.

- Regulations for Management of Books [Effective date: December 23, 2021]
  The regulations on use of the RERF Library's books were established.

- Regulations for Management of Employee IC Cards [Effective date: January 1, 2022]
  The regulations on management and handling of IC cards required for the attendance management system and the like were established.

- Supplementary Regulations for Administering Contracts [Effective date: January 1, 2022]
  The rules on tender deposit and contract guarantee were added.

- Internal Regulations for Handling of Preserved Documents at the Secretariat [Effective date: January 1, 2022]
  The Secretariat's sections reevaluated the classification and period of preserved documents, and a rule on electronic documents was added.

- Regulations Concerning Administrative Procedures for Prevention of Correction or Deletion of Electronic Transaction Data [Effective date: January 1, 2022]

The regulations on administrative procedures for preserving and administrating electronic books and documents were implemented in accordance with the enactment of the Electronic Books/Documents Preservation Act.

Appended documents to FY2021 report of activities

There were no items considered to be important matters for supplementing the contents of the FY2021 report of activities.