

## Departmental Overview

Responsibility of processing and storing biosamples at ABCC and RERF had been mostly assigned to individual research departments until recent years. To preserve precious biosamples such as blood (serum, plasma, and cells), urine, pathological specimens, blood smears, and teeth, in good condition, and to promote research use of those biosamples, it was essential to centralize their management and to generate a comprehensive biosample database. In 2013, the Biosample Research Center (formerly Biosample Center) was established to undertake this task. With the goal of clarifying late effects of ionizing radiation on medical conditions of A-bomb survivors and their children, and of elucidating their molecular mechanisms, the Center is arranging appropriate storage to ensure effective utilization of those invaluable materials, donated by A-bomb survivors, and their spouses and children. To achieve these objectives, biosamples and associated information previously collected by individual departments are being transferred to the Center, whereas most of the biosamples currently collected have been processed and stored by the Center with new standard operating procedures (SOPs) since 2015.

Because freezer rooms in Hiroshima Lab had been filled beyond the capacity with 51 upright deep freezers full of samples, RERF installed a robotic deep-freezer biorepository system (Brooks BioStore II) in 2015 to accommodate about 592,000 archived sample tubes compatible with the system and to efficiently manage future blood and urine samples. The transfer of the archived biosamples from conventional freezers to the robotic freezer was initiated in 2017, and almost finalized in 2020.

Quality assurance and quality control (QA/QC) of both aged and new biosamples is essential to ensure accuracy of data obtained by any analytical method. In 2020, the Center established SOPs for QA/QC of blood plasma with the assay methods endorsed by ISBER (International Society for Biological and Environmental Repositories).

Development of the Biosample Research Center and the Research Resource Center (RRC) is one of the top priorities of RERF to facilitate internal and external collaborative research. To make most of the precious biosamples, the RRC will link the inventory and quality information of biosamples with epidemiological and clinical information to construct an RERF integrated database, with which internal and external researchers can search for and find biosamples necessary for their research. Therefore, the Center needs to generate and constantly update a comprehensive biosample database and provide it to the RRC. In 2020, to record and manage all workflows and the inventory and quality information of biosamples, and to generate a biosample database, the Center designed and implemented a laboratory information management system (LIMS). Furthermore, to prepare for sample provision to both internal and outside researchers, the Center finalized drafts of detailed procedures and forms for sample request/provision.

As a future plan, the Center will develop a Sample Analytical Unit (SAU) with in-house capabilities in omics and image analysis to conduct QA/QC of biosamples and serve as a resource to drive both internal and external collaborative research, and to minimize consumption of precious biosamples.

## FY2020 Biosample Research Center Achievements

The Center designed and implemented a LIMS (Laboratory Information Management System)

for the management of its workflows and the biosample inventory and quality information.

***Inventory Management and Storage of Biosamples***

- During the past year (Dec. 2019 – Nov. 2020), the Center newly processed and stored blood and urine samples provided by 827 AHS subjects, of those 524 subjects at Hiroshima Lab (hereafter referred to as "H") and 303 at Nagasaki Lab (referred to as "N"), or provided by 2,034 FOCS subjects (H: 1,380, N: 654). A total of 50,966 tubes of blood samples were processed and stored; 33,963 tubes were by Hiroshima Center, of which 11,169 were transported to Nagasaki for backup storage, and 17,003 tubes were processed by Nagasaki Center, of which 5,480 were stored in Hiroshima. The Center also newly processed and stored 11,247 tubes of urine samples (H: 7,492, N: 3,755).
- Since 2015, the Center has processed and stored a total of 385,065 tubes of blood samples (H: 252,318, N: 132,747) and 80,716 tubes of urine samples (H: 53,623, N: 27,093), provided by 3,593 AHS subjects (H: 2,206, N: 1,387) and 9,804 FOCS subjects (H: 6,756, N: 3,048), as of Nov. 2020.
- As for archived samples, from 2014 to 2019, the Center inventoried and acquired archived blood and urine samples from AHS and FOCS subjects, which had been collected and preserved by the Departments of Clinical Studies or Molecular Biosciences (MBS). Currently, the Center holds a total of about 1,306,000 tubes of archived blood samples (H: 872,000, N: 435,000) and 157,000 tubes of archived urine samples (H: 100,000, N: 57,000), which had been provided by 16,803 AHS subjects (H: 11,263, N: 5,540) since 1969 and by 12,689 FOCS subjects (H: 8,489, N: 4,200) since 2002.
- As of Nov. 2020, the Center holds a grand total of 1,691,000 tubes of blood samples (H: 1,085,000, N: 607,000) and 238,000 tubes of urine samples (H: 154,000, N: 84,000), including both archived samples and those stored by the Center, which have been provided by 16,814 AHS subjects (H: 11,267, N: 5,547) and 12,786 FOCS subjects (H: 8,522, N: 4,264).
- Blood cells donated by Trio families have been preserved in liquid nitrogen tanks and deep freezers by MBS for genetic/genomic studies on trans-generational effects of parental radiation exposure. Last year, the Center and MBS jointly completed inventory of a total of 58,980 tubes of blood samples (fresh frozen mononuclear cells 11,109, EBV- transformed lymphocytes 41,426, and granulocytes 6,445), which were provided by 4,140 individuals accounting for 1,004 Trio families including A-bomb survivors and their spouses and 1,653 children. These samples have been transferred to the Center for centralized management and efficient research use.
- Since 2017, the Center of Hiroshima Lab has been transferring inventoried archived blood and urine samples from conventional upright freezers to the robotic deep-freezer biorepository system (Brooks BioStore II), and during the past year, transferred 80,923 tubes, bringing the total number of transferred tubes to 591,706 out of the 579,544 tubes that are compatible with the robotic system (to 98% completion)

- As of Nov. 2020, the Center holds a total of 5,822 DNA samples that the Center has extracted from blood clots provided by 3,800 AHS subjects.
- The Center designed, optimized, and implemented a commercially available LIMS, LabVantage®, to manage biosample workflows such as receipt, processing, storage, and transport of biosamples, to manage inventory and quality information of biosamples, to manage inventory of reagents and consumables, and to generate a comprehensive biosample database.

### ***Preparation for Biosample Provision***

- The Center established standard operating procedures (SOPs) for quality assurance and quality control (QA/QC) of blood plasma with assay methods endorsed by ISBER (International Society for Biological and Environmental Repositories). Those included measurement of plasma hemoglobin concentration by spectrophotometry as an indicator of hemolysis, and measurements of LacaScore (ratio of ascorbic and lactic acids) by enzymatic colorimetry and of interleukin 16 level by ELISA as indicators of delay in time from blood drawing to centrifugation.
- The Center finalized drafts of detailed regulations and procedures on sample provision and sample request forms and had them reviewed by the Committee on Biosamples and the Executive Committee.

### ***Other***

- The Center drafted Business Continuity Plans as a trouble shooting system to be well prepared against electric blackout, network failure, liquid nitrogen shortage, and the likes, caused by disasters including storm, earthquake, landslide, fire accident, and national or global pandemic that can cause sudden shortage of manpower and supplies.