CANCER RESEARCH INSTITUTE

The Research Institute for Radiation Biology and Medicine, RIRBM, Hiroshima University

Background and Scope

The Institute was founded in April 1961with the aim of conducting basic and applied studies into injuries, therapy and prevention of radiation-damage from atomic bombs and other sources, impacting upon human beings and societies. For these purposes, basic research in biological, epidemiological and clinical sciences related to radiation and the A-bomb are being conducted. To meet changes in both biological sciences and social demands of A-bomb and radiation victims, the institute was reorganized and expanded in 1994. In 2002 there were further changes implemented and one department and two visiting professorships were newly created. It is now composed of four divisions covering Environmental, Radiation Biology, Molecular Biology, Social Medicine and Clinical Research (see the Table and Figure 1).

Table. Organization of the Research Institute for Radiation Biology and Medicine

Research Divisions	Division of Genome Biology	Department of Radiation Biology
		Department of Human Genetics
		Department of Molecular Radiobiology
		Department of Experimental Oncology
	Division of Clinical and Experimental Oncology	Department of Molecular Oncology
		Department of Translational Cancer Research
		Department of Hematology and Oncology
		Department of Surgical Oncology
	Division of Radiation and Regeneration Control	Department of Cellular Biology
		Department of Developmental Biology
		Department of Stem Cell Biology
		Department of Radiation Medicine
	Division of Bio-Medical Informatics	Department of Epidemiology
		Department of Environmetrics and Biometrics
		Department of Genome Informatics
Research Centers	International Radiation Information Center	
	Radiation Research Center for Frontier Science	
Technical Office		
Administration Office		
University Hospital	Internal Medicine	
	Surgery	

Figure 1. The Research Institute for Radiation Biology and Medicine Buildings

Organization

The RIRBM is composed of four divisions, Genome Biology, Clinical and Experimental Oncology, Radiation and Regeneration Control and Bio-Medical Informative In addition, the International Radiation Information Center (June 1994) and one attached Radiation Research Center for Frontier Science (June 1998) were organized by uniting the facilities for radiation, radioisotopes, radiation exposure of experimental animals and newly established gene technology. The division of clinical research provides accommodation with 90 beds at the University Hospital, and has been operating clinics for A-bomb survivors since April 1962. There are a total of

Research Projects

Radiation induced effects, included cancers, are considered to begin with injury at the DNA level, and develop depending on many modifications such as genome repair, cell responses and host genetic and environmental factors. Genome science has been increasing at a rapid rate and is now opening the way for exhaustive analysis of disease-associated genes based on decoding of the human genome. We are studying the mechanisms underlying radiation induced diseases by introducing genome medical concepts in order to develop order-made medicine.

At the time of the Tokai critical accident, bone marrow transplantation and skin grafting proved to be of very great assistance. The success of cloning of the sheep 'Dolly' and use of embryonic stem cells has facilitated regeneration of various tissues so that this area will be of major importance in the 21st century. Therefore, we are now concentrating attention on therapy of acute radiation injury with introduction of advances in radiation regenerative medicine.

Furthermore, since the possible social problems with low dose radiation are presently unclear, the direct relevance of Japanese energy policy needs to be assessed. For this purpose basics of genome science, including bioinformatics, molecular epidemiology and new dosimetry approaches, with reference to the indvidual exposure level, are being researched in detail. New facets of radiation biology are being explored from different aspects, marrying new concepts with well-established ideas. We hope that the coming generations of young scientists will play a major role in developing this field, working productively together to generate a world center of excellence for research and generation of new therapeutic approaches to radiation damage.

Radiation Research Center for Frontier Science

This is composed of facilities for radiation experiments, animal experiments and gene technology. Included are animal care rooms, various radiation sources, radioisotope laboratories and high-technology equipment (see Fig 3). The center is designed to contribute to studies of radiation, cellular and molecular biology in radiation exposed gene

Figure 2. R for Radiation, R for Research. Dr Kenji Kamiya, the Director is pictured Front Row, Third from the Right and Dr Hiromitsu Watanabe, a Member of the APJCP Editorial Board, Front Row, Fourth from the Left

Figure 3. State of the Art Facilities for Analysis of Human Specimens

modified animals.

For radiation experiments, X-ray generators, ^{60}Co and ^{127}Cs gamma-ray sources, a ^{252}Cf fission neutron source, and a neutron generator are all available. Basic research on the effects of various types of radiation both in vivo and in vitro, simulation experiments to evaluate the Hiroshima atomic bomb doses, and other biological work requiring labeling of unsealed radioisotopes are also performed with the help of computers. Calibulation and maintenance of radiation equipment and safety requirements are followed strictly. Since these facilities are among the most advanced and sophisticated in Japan, they are also used by many visiting researchers from other universities.

Facilities for animal experiments were established in 1984 to perform in vivo studies on radiation effects from the viewpoints of experimental pathology, oncology, toxicology, teratology and genetics. There are 17 animal rooms in total, divided into two categories according to the pathogen free quality: thirteen conventional rooms and 4 for SPF usage. The animals introduced into the facilies must be proven SPF. Genetically engineered mutant mice as well as knockout mice are being generated and maintained in the facilities. Operations and autopsies are performed in a specialized experiment room.Animals are moved through a specific pathway between the animal rooms and the radiation exposure facilities. Researchers in the Institute and others made extensive use of the facilities for their experiments.

Facilities for gene technology were established in 1999 for the promotion of research in the field of radiation effects at the molecular level. The central laboratory is open to qualified facility members and students in the Institute, and features high-technology equipment including laser scanning microscopy (Carl Zeiss), a flow cytometer (Orthodiagnostic), a cryostat (Carl Zeiss), a system for UV laser microdissection (Nikon), a high performance liquid chromatograph (Shimadzu), a peptide synthesizer (Appled Biosystems), an automatic DNA isolation (Kurabo), DNA sequencers (Applied Biocystems) , a sequence detection system (Applied Biosystems), a bioimaging analyzer (FujiFirm, BioLab), and a microplate reader (Lab System). In 2002 additional equipment was purchased as follows: a DNA Microarray Spotter (Hitachi Software Engineering), a Gene TAC Hybridization Station, a Microarray Scanner (Agilent Technologies), a MALDI-TOF Mass Spectrometry (Bruker), a Protein purification system, a FACS Calibur HG flow cytometer (Beckton Dickinson), a Three Dimentional Time-laps Imaging System (Carl Zeiss), an ABI PRISM 310NT Genetic analyzer (Applied Biosystems), a Two Dimentional Electrophoresis System (Amersham Bioscience), an Automatic Nucleic acid Purification System MFX-6100 (TOYOBO),a Lumino Imaging Analyzer FAS1000 (TOYOBO), and a Real-time Bio-molecular Interaction Detector (Biacore).

Departments Conducting Animal Experimentation

Department of Radiation Biology (Prof S. Matsuura): The Department identified the Nimergen breakage syndrome gene, NBS1, by positional cloning and made a knockout mouse.

Department of Experimental Oncology (Prof. K. Kamiya): Projects are as follows: 1) Research on molecular mechanisms of radiation-induced mutations and genetics instability; 2) Genetic analysis of radiation-induced mouse hepatomas; 3) Genetic analysis of the mammary carcinoma suppressor gene(s) in genetically resistant Copenhagen rats.

Department of Cellular Biology (Prof H. Watanabe): One focus in the Department is on endogenous and environmental factors influencing experimental carcinogenesis in gastrointestinal organs, and the possibility of new-differentiation of gastrointestinal tissue and other organs transplanted into ectopic sites and also studying cell injury and recovery after irradiation, cell proliferation and abnormal differentiation in tissue damage sites with particular emphasis on mechanisms of tumorigenesis.

Department of Developmental Biology (Prof H. Honda): The department focus on analysis of biological functions of genes and generation of models for human diseases by creating transgenic and knockout mice. In addition, application of ES (embryonic stem) cells for regenerative medicine is being studied.

Education

For the Medical School and Dental School we are taking responsibility for teaching of basic biology, statistics, physics related to the medical and dental sciences, fundamental research training and training in hematology and surgical oncology for clinical students. For the Graduate School of Biomedical Sciences we have research programs leading to doctoral degrees. As the admission requirements, candidates must have graduated from a university with a six year course or have completed a preceding Master's course at the graduate school. Special selection systems are also implemented for foreign students and university graduates.

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