Editorial

Excitements in Radiobiology

I profoundly welcome the senior scientists as well as young researchers participating in the 5th Asian Congress for Radiation Research from India and abroad. The main theme of the Congress is to promote radiation research and technology for society by providing an active forum for the exchange of ideas, sharing of recent research progress, and opening new opportunities for collaborations. I strongly believe that the scientific presentations, debates and discussions on various topics related to health and environment would produce fruitful outcomes setting the future direction to establish Congress as a milestone event in the history of almost two decades journey of the Asian Association of Radiation Research (AARR). Let me recall that AARR was founded in Japan mainly by the efforts of some committed radiation scientists led by the late Prof T. Ohnishi of Nara Medical School, Japan, and its 1st Congress was held in Hiroshima in 2005 under his Presidentship. The subsequent Congresses held at Seoul, S. Korea (2009), Beijing, P. R. China (2013), and Astana, Kazakhstan (2017) have made their benchmarks to promote radiation research in Asian Countries and world. The organization of the 5th ACRR was scheduled in 2021 but we were compelled to postpone it due to the COVID-19 pandemic that threatened the health and safety of people across the globe. Notably, during this period, the radiation research community (researchers and clinicians) worldwide contributed immensely to protect and save human lives by advancing knowledge and suggesting low-dose radiation as a new measure to treat pneumonia in the lung. Fortunately, intense efforts by scientists, technologists, and medicine industry took the challenge and worked harder to develop vaccines/drugs in record time and saved humankind from the danger of infection and loss of life. Radiobiology research is expected to yield results in situations of nuclear accidents, terrorist misusing radioactive substances, war situations damaging nuclear installations threatening leakage of radioactive elements in the environment, diagnostic and imaging applications of low linear energy transfer (LET) radiation such as X-rays and gamma rays and industrial applications of radioisotopes. Without a doubt, concerted efforts, and collaborative research among scientists including Asian countries to generate new knowledge and develop proper expertise to protect the population from risks of radiation exposure to health-related and environmental problems would be utterly important. AARR can play a significant role to communicate authentic science-based awareness and reassure public for robust preparedness plans to tackle the radiation exposures threatening human health and contaminating the environment, for example, water, air, and soil.

I now turn to a brief account of history, progress, and excitement in the field of radiobiological research applied to health and medicine, where senior scientists and young researchers from the world over, especially from Asian countries need to play a very constructive role. The application of radiation and radiation technologies would contribute significantly to the growing demand for food security, agriculture, and health/hygiene in Asian countries sharing almost 50% world population, and in this context, the involvement of radiation researchers would be enormous. Needless to say, with the ever-increasing use and applications of radiation technologies in the public domain, research programs in radiation biology both at high- and low-dose levels are highly warranted to further develop nuclear technologies and radiation devices for nuclear energy, industry, nuclear medicine, cancer radiotherapy, and other innovative applications.

Basically, radiation biology concerns studies on the biological effects of ionizing radiation to understand the mechanisms underlying the radiation effects and to determine the safety standards in various applications of nuclear and radiation technologies. The fortuitous discoveries of X-ray and radioactivity at the end of the 19th century brought revolutions in the world, and both scientists and public were unusually excited over possible new applications. In fact, the hype was such that these discoveries were perceived as panacea for all problems in science and society. Evidently, radiation biology is a relatively young branch of science. However, it has widely spanned from basic research to numerous applications in health, industry, environment, food science, agriculture, biotechnology, space research, and allied areas. Unfortunately, within years of these discoveries, a few adverse effects were inflicted on the health of research scientists and serious questions arose for estimating the risks to health due to the harmful effects of radiation. At the beginning of the 20th century, research on the structure of the atom was at the forefront and it became known that nuclear radiation such as alpha, beta, and gamma rays originated from the nucleus of radioactive atoms, and each kind of radiation possessed different penetrating power in living tissues and nonliving materials. The questions on the safety of humans became an urgent new issue to be addressed by the scientific community. To begin with, it sounded like a big challenge to understand how ionizing radiations act on biological systems, particularly on living cells, tissues, and organs including the human body. Intensive research was started to investigate the effects of ionizing radiations such as X-rays and gamma rays on mammalian cells, tissues, organs, plants, and microbial systems and a wealth of new information became available. Realizing the need for establishing a reliable scientific body for setting the standards of safety, radiation and medical scientists decided to form an international scientific body in 1928 to determine the standards of safety after exposure to ionizing radiation from various sources and the International Commission on Radiological Protection (ICRP) was formed.

Radiobiology discovered that ionizing radiation at high doses killed the living cells and rapidly dividing cells were relatively more sensitive to radiation than slow-dividing or nondividing cells. This finding generated a big hope that radiation could be used to kill cancer cells preferentially because they divide rather rapidly. Further research revealed that radiation exposure affects the cell cycle and cells in G2/M and S phases exhibited greater sensitivity to radiation. Taking the clue from normal cell repair ability, radiotherapy employed the protocol of fractionation of total radiation dose over several weeks to reduce the normal cell toxicity. Physicians were quick to foresee a big opportunity to destroy cancer cells by ionizing radiation. They began using radiation to treat cancer patients and a new discipline called radiotherapy came into existence in hospitals using high doses of ionizing radiation to treat cancer patients. As expected, radiation exposure to tumor resulted in its shrinking. On the other hand, low doses of X-rays were used to image the inside of the human body such as teeth, broken bones, and lungs. The use of X radiation in diagnosis became highly popular in medical practice and it became a buzzword among the general public. In fact, the application of radiation to treat cancer patients proved a boon, and life of many patients suffering from cancer was saved.

Research on cellular radiobiology showed that radiation was toxic to both normal and cancer cells but irradiated cells have the capacity to repair the damage caused by radiation exposure. Studies on cellular response to ionizing radiation discovered "oxygen effect." Cells showed greater sensitivity to radiation in oxygenated conditions than in the nonoxygenated environment. Further research showed that radiation generated a variety of free radicals with unpaired electrons. The role of free radicals in the mechanisms of cancer induction and radiation damage was widely investigated. Radiation chemical studies on aqueous systems showed that water undergoes radiolysis, and several water radicals were formed in irradiated water, radiation generates reactive oxygen species (ROS) [e.g., superoxide radicals (O_2-), hydrogen peroxide and hydroxyl radicals], which initiated a plethora of chemical peroxidative processes in molecules. Consequently, the effects of radiation on biomolecules (namely, DNA, proteins, lipids, and carbohydrates) generate free radicals and cause damage by indirect effects through water radicals produced. It became known that exposure of cells to γ-radiation produced many deleterious effects such as cell-cycle arrest, induction of apoptosis, and eventually cell death. The role of ROS in cellular redox status is a rapidly growing area of research relevant to radiotherapy. In addition, free-radical-mediated mechanisms played important role in developing radioprotectors. Several herbal compounds of plant origin have exhibited radiosensitization and radioprotection properties. These lines of research made significant advancements in the knowledge on modification of radiation damage (radiation modifiers) and continue to be an active area of research at this point in time.

Research progress in radiobiology and radiotherapy showed that ionizing radiation produces differential effects on normal and cancer cells. At high doses, radiation kills cancer cells or slows their growth by damaging their DNA. However, while treating cancer patients, physicians found that radiation adversely affected the nearby healthy cells and may give rise to secondary cancer. Radiation damage to healthy cells caused side effects compelling sometimes the discontinuation of treatment. These observations in clinic led to the search of compounds that can sensitize tumor cells (radiosensitizers), thereby lowering the radiation dose to kill cancer cells and reduce the dose exposure to normal cells (radioprotectors). Clinical physicians found that, if radiation fails to kill all cancer cells, they regrow in the future (relapse). Studies on radiation effects have been expanded widely and invaluable information has been obtained on radiation-induced tumor cell death and signaling pathways involved in sensitivity, resistance, and further molecular sensors that modify the tumor response to radiation. Experiments have shown that high-energy photons, X-rays, and gamma rays, are the most common external radiation treatment but protons and high-LET radiation provide radiobiological advantages compared with the photons. Radiobiology research demonstrated that, for the same radiation dose, magnitude of cell/tissue damage depended on the type of radiation. Radiations can be delivered by a machine outside the body (external beam radiation therapy) or irradiated through the radioactive material placed in the body near to cancer cells/tissue (internal radiation therapy, called brachytherapy). On the other hand, systemic radiation therapy uses radioactive substances, such as radioactive iodine, that travel through the blood to kill thyroid cancer cells. In recent years, remarkable progress has been made toward the understanding of proposed hallmarks of cancer, and its care/treatment modalities. Recently, there have been a major paradigm shift in radiation biology and significant progress has been made to understand the biological and molecular determinants of cellular responses to radiation. New knowledge has been gained that cells irradiated by radiation transfer radiation signal to nonirradiated cells called the bystander effect. Moreover, apart from DNA damage, the damage to membrane and/or cytoplasm also induces DNA damage producing mutation and causing diseases including cancer. Implications of these radiation damage processes are being actively investigated.

Let me return to the often-asked question of how much radiation is safe for researchers, nuclear workers, radiologists, and general public. Radiation researchers mainly derive information from radiation effects on cells, tissues, and animal models at high doses. In 1940–1950s, Herman Joseph Muller from Germany conducted experiments on high-dose radiation effects on *Drosophila* and showed that X-radiation causes a mutation in genes which follows linear relation to dose that is an indicator of DNA damage. He extrapolated his results from dose effects versus radiation dose effects (>1 Gy) on flies, as the model for radiation damage and proposed that radiation, however small, is unsafe. He was honored with Nobel Prize in physiology or medicine in 1946 and ICRP accepted the popularly called linear no-threshold (LNT) principle for radioprotection. Afterward, many objections have been raised against the LNT model, but controversy continues and ICRP regulates radioprotection based on the LNT model. Radiobiology is faced with the challenges to investigate low-dose radiation effects below 100 mSv (average environmental dose ~2.4 mSv) on biological systems (Gy or Sv is the unit of radiation dose which is interchangeable for X-rays and gamma rays). Research on human population studies from Atomic Bomb dropping on Hiroshima and Nagasaki, Japan in 1945 has been subject to intense studies that provided valuable data that high dose of radiation exposure (>4 Gy) killed the victims but those living at the distance from the epicenter and received nonlethal doses developed cancer in advanced age. The analysis of research results suggests that those exposed to lower doses (<500 mGy) in the younger age or reproductive age do not seem to transmit the radiation genetic alterations to the progenies. The experiences gained from Chernobyl (1986) and Fukushima (2011) nuclear accidents have provided research results to take new lessons for determining human safety procedures and have necessitated new guidelines for emergency measures such as the evacuation of large number of people from the risk zone to safer locations. Research and analysis are actively in progress by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) at these locations.

Finally, I earnestly appeal to experts as well as young investigators to accept the challenges in radiobiology research and find answers to the unaddressed questions such as radiation-induced gene responses at high and low doses, phenomenon of genetic instability, and radioresistance of cancer stem cells to effectively treat cancer patients in radiotherapy. It is important that talented and enthusiastic researchers actively engage themselves in radiobiological research and devise methods to efficiently kill tumor cells. It would be crucial to examine the validity of the LNT model for radioprotection by intense research on the growing low-dose radiobiology. In view of the rapidly increasing applications of radiation technologies in diagnostic, cancer therapeutic applications, nuclear medicine and imaging technologies, nuclear power, space exploration programs, the scope and relevance of radiobiology research are vast and enormous new knowledge related to human health and environment is in store for the future. In this regard, I admire the participation of scientists in the Congress covering wider aspects of radiation research across the globe as a perfect example of truly united world scientific community purely guided by the spirit of pursuing science for the service of humanity and society.

K. P. Mishra

Ex-Head, Radiation Biology & Health Sciences Division, Bhabha Atomic Research Center, Mumbai, Maharashtra, India

Address for correspondence: Dr. K. P. Mishra,
E-mail: mishradrkp@gmail.com

Received: 14-10-2022 **Accepted:** 15-10-2022 **Published:** 04-11-2022

Access this article online

Quick Response Code:

Website: www.journalrcr.org

DOI: 10.4103/jrcr.jrcr_76_22

How to cite this article: Mishra KP. Excitements in radiobiology. J Radiat Cancer Res 2022;13:143-5.