International Research Teams Explore Genetic Effects of Chernobyl Radiation

DNA sequencing technology helps explore the effects of radiation from the Chernobyl nuclear disaster on human health.

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In two landmark studies, researchers have used cutting-edge genomic tools to investigate the potential health effects of exposure to ionizing radiation, a known carcinogen, from the 1986 accident at the Chernobyl nuclear power plant in northern Ukraine. One study found no evidence that radiation exposure to parents resulted in new genetic changes being passed from parent to child. The second study documented the genetic changes in the tumors of people who developed thyroid cancer after being exposed as children or fetuses to the radiation released by the accident.

The findings, published around the 35th anniversary of the disaster, are from international teams of investigators led by researchers at the National Cancer Institute (NCI), part of the National Institutes of Health. The studies were published online in Science on April 22.

“Scientific questions about the effects of radiation on human health have been investigated since the atomic bombings of Hiroshima and Nagasaki and have been raised again by Chernobyl and by the nuclear accident that followed the tsunami in Fukushima, Japan,” said Stephen J. Chanock, M.D., director of NCI’s Division of Cancer Epidemiology and Genetics (DCEG). “In recent years, advances in DNA sequencing technology have enabled us to begin to address some of the important questions, in part through comprehensive genomic analyses carried out in well-designed epidemiological studies.”

The Chernobyl accident exposed millions of people in the surrounding region to radioactive contaminants. Studies have provided much of today’s knowledge about cancers caused by radiation exposures from nuclear power plant accidents. The new research builds on this foundation using next-generation DNA sequencing and other genomic characterization tools to analyze biospecimens from people in Ukraine who were affected by the disaster.

The first study investigated the long-standing question of whether radiation exposure results in genetic changes that can be passed from parent to offspring, as has been suggested by some studies in animals. To answer this question, Dr. Chanock and his colleagues analyzed the complete genomes of 130 people born between 1987 and 2002 and their 105 mother-father pairs.

One or both of the parents had been workers who helped clean up from the accident or had been

evacuated because they lived in close proximity to the accident site. Each parent was evaluated for protracted exposure to ionizing radiation, which may have occurred through the consumption of contaminated milk (that is, milk from cows that grazed on pastures that had been contaminated by radioactive fallout). The mothers and fathers experienced a range of radiation doses.

The researchers analyzed the genomes of adult children for an increase in a particular type of inherited genetic change known as de novo mutations. De novo mutations are genetic changes that arise randomly in a person's gametes (sperm and eggs) and can be transmitted to their offspring but are not observed in the parents.

For the range of radiation exposures experienced by the parents in the study, there was no evidence from the whole-genome sequencing data of an increase in the number or types of de novo mutations in their children born between 46 weeks and 15 years after the accident.

The number of de novo mutations observed in these children were highly similar to those of the general population with comparable characteristics. As a result, the findings suggest that the ionizing radiation exposure from the accident had a minimal, if any, impact on the health of the subsequent generation.

"We view these results as very reassuring for people who were living in Fukushima at the time of the accident in 2011," said Dr. Chanock. "The radiation doses in Japan are known to have been lower than those recorded at Chernobyl."

In the second study, researchers used next-generation sequencing to profile the genetic changes in thyroid cancers that developed in 359 people exposed as children or in utero to ionizing radiation from radioactive iodine (I-131) released by the Chernobyl nuclear accident and in 81 unexposed individuals born more than nine months after the accident. Increased risk of thyroid cancer has been one of the most important adverse health effects observed after the accident.

The energy from ionizing radiation breaks the chemical bonds in DNA, resulting in a number of different types of damage. The new study highlights the importance of a particular kind of DNA damage that involves breaks in both DNA strands in the thyroid tumors. The association between DNA double-strand breaks and radiation exposure was stronger for children exposed at younger ages.

Next, the researchers identified the candidate "drivers" of the cancer in each tumor — the key genes in which alterations enabled the cancers to grow and survive. They identified the drivers in more than 95% of the tumors. Nearly all the alterations involved genes in the same signaling pathway, called the mitogen-activated protein kinase (MAPK) pathway, including the genes BRAF, RAS, and RET.

The set of affected genes is similar to what has been reported in previous studies of thyroid cancer. However, the researchers observed a shift in the distribution of the types of mutations in the genes. Specifically, in the Chernobyl study, thyroid cancers that occurred in people exposed to higher radiation doses as children were more likely to result from gene fusions (when both strands

of DNA are broken and then the wrong pieces are joined back together), whereas those in unexposed people or those exposed to low levels of radiation were more likely to result from point mutations (single base-pair changes in a key part of a gene).

The results suggest that DNA double-strand breaks may be an early genetic change following exposure to radiation in the environment that subsequently enables the growth of thyroid cancers. Their findings provide a foundation for further studies of radiation-induced cancers, particularly those that involve differences in risk as a function of both dose and age, the researchers added.

“An exciting aspect of this research was the opportunity to link the genomic characteristics of the tumor with information about the radiation dose — the risk factor that potentially caused the cancer,” said Lindsay M. Morton, Ph.D., deputy chief of the Radiation Epidemiology Branch in DCEG, who led the study.

“The Cancer Genome Atlas set the standard for how to comprehensively profile tumor characteristics,” Dr. Morton continued. “We extended that approach to complete the first large genomic landscape study in which the potential carcinogenic exposure was well-characterized, enabling us to investigate the relationship between specific tumor characteristics and radiation dose.”

She noted that the study was made possible by the creation of the Chernobyl Tissue Bank about two decades ago — long before the technology had been developed to conduct the kind of genomic and molecular studies that are common today.

“These studies represent the first time our group has done molecular studies using the biospecimens that were collected by our colleagues in Ukraine,” Dr. Morton said. “The tissue bank was set up by visionary scientists to collect tumor samples from residents in highly contaminated regions who developed thyroid cancer. These scientists recognized that there would be substantial advances in technology in the future, and the research community is now benefiting from their foresight.”

About the National Cancer Institute (NCI): NCI leads the National Cancer Program and NIH’s efforts to dramatically reduce the prevalence of cancer and improve the lives of cancer patients and their families, through research into prevention and cancer biology, the development of new interventions, and the training and mentoring of new researchers. For more information about cancer, please visit the NCI website at cancer.gov or call NCI’s contact center, the Cancer Information Service, at 1-800-4-CANCER (1-800-422-6237).

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