

Researchers discover atomic bomb effect results in adult-onset thyroid cancer

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Radiation from the atomic bomb blasts in Hiroshima and Nagasaki, Japan, in 1945, likely rearranged chromosomes in some survivors who later developed papillary thyroid cancer as adults, according to Japanese researchers.

In the September 1, 2008, issue of *Cancer Research*, a journal of the American Association for Cancer Research, the scientists report that subjects who lived close to the blast sites, were comparably young at the time, and developed the cancer quickly once they reached adulthood, were likely to have a chromosomal rearrangement known as RET/PTC that is not very frequent in adults who develop the disease.

"Recent in vitro and in vivo studies suggest that a single genetic event in the MAP kinase-signaling pathway may be sufficient for thyroid cell transformation and tumor development," said the study's lead author, Kiyohiro Hamatani, Ph.D., laboratory chief, Department of Radiobiology and Molecular Epidemiology at the Radiation Effects Research Foundation (RERF) in Hiroshima.

"Thyroid cancer is associated with exposure to external or internal ionizing radiation. Elucidation of mechanisms of radiation-induced cancer in humans, especially early steps and pathways, has potential implications for epidemiological risk analyses, early clinical diagnosis, and chemopreventive interventions," Hamatani said.

He adds that there are several irradiated populations worldwide that have

been shown to have an increase in thyroid cancer, and that children exposed to radioactive fallout from the 1986 Chernobyl nuclear power plant accident who develop papillary thyroid cancer have also been found to have RET/PTC rearrangements, although they are slightly different.

This study is part of the foundation's long running follow-up research on 120,000 atomic bomb survivors. During 1958 to 1998, the study found about 470 thyroid cancer cases of which the estimated number of excess cases attributable to radiation is 63. About 90 percent of thyroid cancer among the survivors is of the papillary type.

Hamatani and colleagues from across Japan made a comparison between adult-onset papillary thyroid cancers with RET/PTC rearrangements and those with a BRAF mutation. More than 70 percent of adult onset papillary thyroid cancer in non-exposed patients is associated with mutations in the BRAF gene.

The researchers looked at the genetic profile of cancer patients in the RERF's follow-up study--50 patients who were exposed to atomic bomb radiation and 21 patients who were not. Three factors were found to be independently associated with the development of adult-onset papillary thyroid cancer with RET/PTC rearrangements. They were greater radiation dose, shorter time elapsed since radiation exposure, and younger age at the time of the bombings, Hamatani says.

"That means that a younger person living close to the bombing site would be more likely to have adult onset thyroid cancer having RET/PTC rearrangements," he said. "This is the first time this has been shown."

The findings also suggest that in childhood papillary thyroid cancer RET/PTC rearrangements may be much less clearly associated with

radiation exposure, compared with adult-onset cancer, because RET/PTC rearrangements are frequent in childhood papillary thyroid cancer patients regardless of history of radiation exposure.

The researchers do not know exactly how radiation is involved in the occurrence of RET/PTC rearrangements. "It could be either by direct DNA damage or by other pathways such as a result of radiation-induced genomic instability," Hamatani said.

Source: American Association for Cancer Research

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