Chernobyl Thyroid Cancer Research

Vladimir SAENKO,1* Shunichi YAMASHITA1,2,3

1Department of International Health and Radiation Research, Atomic Bomb Disease Institute, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
2Department of Molecular Medicine, Atomic Bomb Disease Institute, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
3Department of Public Health and Environment, Sustainable Development and Health Environment, WHOHQ, Geneva, Switzerland

Thyroid gland is an organ particularly vulnerable to radiation as known from the studies of relationship between thyroid neoplastic disorders and radiation exposure in man. Specifically, papillary thyroid carcinoma (PTC) is a prototypic human malignancy known to develop with an increased rate in the individuals exposed to external or internal radiation, especially if exposure took place at young age.

Since the phenomenon of radiation-induced thyroid cancer has been recognized, extensive efforts have been made to elucidate its distinctive molecular features. Potentially there may be two strategies of approaching to this problem, that are comparative mutational /expression studies in radiation-induced and sporadic PTCs and genomics studies including molecular radiation epidemiology.

A large set of oncogenic events has been identified PTC such as RET/PTC, TRK and AKAP9/BRAF rearrangements, all results of paracentric intrachromosomal inversions, and point mutations of the BRAF gene and RAS family members. A common property of oncogenic proteins, products of these genes, is the ability to activate the MAP kinase signaling pathway. This paradigm apparently holds true for both adult and childhood papillary carcinomas although the prevalence of each oncogene is different between the age groups. The most frequently observed in childhood cancers were RET/PTC rearrangements. By contrast, point mutations of genes implicated in thyroid follicular cells carcinogenesis (RAS, BRAF, Gsx oncogenes and TP53 tumor suppressor) were rather rare. In general, the major molecular distinctions of Chernobyl thyroid cancer appeared to be: 1) a high prevalence of rearrangement-type genetic alterations among which RET/PTC3 (and probably of some other chimeric genes, e.g. rare RET/PTC and AKAP9/BRAF) predominantly occurred in cancers with shorter latency, and 2) the lower frequency of point mutations in thyroid cancer-associated genes as compared to adult cases and PTCs developed after a longer period of latency.

An alternative opportunity to elucidate fundamentals of thyroid cancer development in radiation victims may be the identification of individual genetic characteristics of patients with radiation-associated PTC. In our pilot study, we have profiled a set of SNPs in several genes whose products are involved in the DNA damage pathway, TP53, ATM and MDM2. As a result, several SNPs displaying signs of association with radiation-related or sporadic adult or childhood PTC have been detected. These findings demonstrate that molecular epidemiology studies hold a promise in the problem of detection of the genetic traits potentially contributing to or modifying the susceptibility to radiation-induced thyroid carcinogenesis in humans.

To further elucidate molecular mechanisms and genetics of radiation-induced thyroid carcinogenesis, wide-angled but more profound investigations are needed through international cooperative projects as example by the Chernobyl Tissue Bank (http://www.chernobyltissuebank.com/).

*E-mail: saenko@nagasaki-u.ac.jp