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Radiation biomarkers in thyroid cancer

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Childhood thyroid carcinoma incidence is significantly increased after exposure to ionizing radiation. Such an increased thyroid cancer risk in children and adolescents has been observed after the Chernobyl accident in contaminated areas even at moderate or low doses of 150 mGy and below. So far, the molecular mechanisms underlying radiation-induced carcinogenesis in the thyroid gland have not been identified, yet. In order to gain understanding in this field radiation biomarkers that point to deregulated genes and pathways need to be discovered. Several studies on post-Chernobyl thyroid cancers aimed to identify radiation-specific gene expression signatures by using gene expression arrays. We have used an approach in which we integrated a genomic radiation marker that we previously identified by array CGH with mRNA expression data of the genes located in this genomic region. This allowed identifying genes that were altered in both gene and mRNA copy number. Using this approach we found an exclusive association of gain of the chromosome band 7q11.22-11.23 in papillary thyroid carcinomas (PTCs) from patients that were exposed to the Chernobyl radioiodine fallout at very young age. CLIP2, a candidate gene from this chromosomal band was specifically and exclusively overexpressed in the exposed cases at the mRNA and protein level (IHC) in tumours from exposed patients. Systems biology characterisation based on time-series mRNA expression data from cell culture models after specific perturbation of CLIP2 expression are currently carried out in order to identify the CLIP2 interactome and to gain insights into the functional impact of the gene in radiation-associated carcinogenesis of PTCs.

The novel radiation markers provide first important insights into the mechanisms of radiation-related carcinogenesis of young onset PTC and underpin the concept of radiation-specific carcinogenesis. We will deepen this knowledge using new systems approaches and will integrate it with epidemiology in order to improve risk estimation for radiation-induced thyroid cancer.

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