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Papillary thyroid carcinoma genetic susceptibility factors in children exposed to radioiodine from Chernobyl fallout

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Background: Statistically significant associations between papillary thyroid cancer (PTC) and specific common single nucleotide polymorphisms (SNP) in MGMT (rs2296675), promotor region of FOXE1 (rs1867277) and ATM (rs1801516) genes were reported in Belarusian children exposed to Iodine-131 (131I) after the Chernobyl nuclear power plant accident. We further pursued genetic determinants associated with individual susceptibility to radiation-related thyroid carcinoma (TC) within the framework of the EPITHYR consortium.
Methods: We investigated the associations between PTC risk and SNPs in candidate DNA repair genes, transcription factors (FOXE1, NKX2-1), growth factor (TGFBI), BRCA1 interacting protein (ZNF350), TSH receptor (TSHR) and RET signalling pathway genes (RET, GFRA1, EPAC) in 343 individuals who were <15 years old at the time of the Chernobyl accident, including 66 histologically verified PTC cases diagnosed between 1992 and 1998, and 277 population-based controls, genotyped using the OncoArray (Illumina). We used an arithmetic mean of 1,000 individual stochastic thyroid doses due to I-131 intake calculated using Monte-Carlo simulation method as radiation dose exposure. We evaluated the associations between 3,510 SNPs and PTC using logistic regression models assuming a log-additive allelic inheritance models and taking into account population stratification, and effects of age, sex and thyroid dose. We accounted for multiple testing by applying the Benjamini & Hochberg correction.
Results: We found some suggestive associations ($P < 0.001$) between PTC risk and polymorphism in the following genes: *POLN* (rs6830513, rs10018786, rs6855461) encoding DNA polymerase type-A family member involved in DNA repair and homologous recombination, and *RECQL* (rs3213212) involved in DNA repair. However, after adjustment for multiple testing, none of these SNPs remained statistically significant. Analyses on other possible pathways, as well as on potential gene-radiation interaction are ongoing.

Primary authors: ZUPUNSKI, L (International Agency for Research on Cancer, Lyon, France); BOUAOUN, L (International Agency for Research on Cancer, Lyon, France); SUGIER, P-E (Paris-Saclay University, Paris-Sud University, UVSQ, Center for Research on Epidemiology and Population Health, INSERM, Villejuif, France); GUIBON, J (Paris-Saclay University, Paris-Sud University, UVSQ, Center for Research on Epidemiology and Population Health, INSERM, Villejuif, France); BOLAND, A (Centre National de Recherche en Génomique Humaine, Evry, France); DELEUZE, J-F (Centre National de Recherche en Génomique Humaine, Evry, France); KESMINIENE, A (International Agency for Research on Cancer, Lyon, France); DROZDOVITCH, V (Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, U.S. DHHS, Bethesda, MD 20892, USA); LESUEUR, F (Inserm, U900, Institute Curie, PSL University, Mines ParisTech, Paris, France); TRUONG , T (Paris-Saclay University, Paris-Sud University, UVSQ, Center for Research on Epidemiology and Population Health, INSERM, Villejuif, France); OSTROUMOVA, E (International Agency for Research on Cancer, Lyon, France)

Presenter: ZUPUNSKI, L (International Agency for Research on Cancer, Lyon, France)

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