TPO GENETIC VARIANTS AND RISK OF DIFFERENTIATED THYROID CARCINOMA (DTC)

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Thyroid cancer risk involves the interaction of genetic and environmental factors. The thyroperoxidase (TPO) has a key role in the iodine metabolism, being essential for the thyroid function. Mutations in the *TPO* gene are common in congenital hypothyroidism, and there are also signs of the implication of *TPO* in thyroid cancer. We performed a case-control association study of single nucleotide polymorphisms (SNPs) in *TPO* (i.e. rs2048722, rs732609 rs1042589), and differentiated thyroid carcinoma (DTC) in 1190 cases and 1290 controls. Multivariate logistic regression analyses were performed separately for each SNP. From the three studied polymorphisms significant associations were detected between DTC and rs2048722 (OR=0.79, 95% CI=0.63-1.00, *P*=0.045) and rs732609 (OR=0.72, 95% CI=0.55-0.94, *P*=0.016). The corresponding associations for the subgroup of the papillary thyroid carcinoma were similar to those for all DTC. No association was detected for the third *TPO* polymorphism. Interestingly, rs732609 encodes for a Threonine to Proline missense change in position 725 within *TPO*, that resides near the complement control protein (CCP)-like gene module (aa 741-795), but the functional significance of this change is unknown. Since the proline residue is conserved in most of the vertebrates, it could be hypothesized that the change affects the conformation of the protein, conferring a reduced flexibility to the carbamidic bond (given its cyclic structure). Thus, present results point to *TPO* as a gene involved in the risk of DTC, and could be of relevance for future studies to understand the role of *TPO* in thyroid tumorigenesis.