SEARCH FOR NOVEL COMMON VARIANTS INFLUENCING DIFFERENTIATED THYROID CANCER

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Thyroid cancer is a common endocrine malignancy with a rapidly increasing global incidence in the recent decades. Differentiated thyroid cancer (DTC), arising from follicular cells, includes the most common histological subtypes, papillary and follicular thyroid cancer, representing 80% and 15% of all thyroid cancers, respectively. Genome-wide association studies (GWASs) have identified robust associations with polymorphisms at 9q22.33 (FOXE1) and 14q13.2 (NKX2-1) and the disease. However, most of the inherited genetic risk factors of DTC remain to be discovered.

To search for new DTC risk variants we performed a GWAS in the high incidence Italian population and followed up the most significant associations in the lower incidence populations from Poland, UK and Spain. After excluding previously identified loci, the strongest association was observed for DIRC3 at 2q35 (P=6.4×10^-10). Additionally promising associations were attained for IMMP2L at 7q31 (P=4.1×10^-6 and P=5.7×10^-6), RARRES1 at 3q25.32 (P=4.6×10^-5) and SNAPC4/CARD9 at 9q34.3 (P=3.5×10^-5).

Our findings provide insights into the genetic and biological basis of inherited genetic susceptibility to DTC. To further improve our knowledge on the disease, new loci, selected on the basis of association signals in our GWAS, will be analyzed.