**FOX1 (rs965513), NKX2-1 (rs944289) and BRAF (V600E) gene mutations and their role in development of papillary thyroid cancer**

Transcription factors play a critical role in tissue homeostasis and development and can also have roles in carcinogenesis. The aim of the study was to perform the genomics analysis of the Forkhead box protein E1 gene (FOXE1) and NK2 homeobox 1 gene (NKX2-1) mutations in patients with Papillary thyroid cancer (PTC) and healthy control group as well as to compare the obtained results with clinical findings.

The study included 112 patients diagnosed with PTC (classical, tall cell and follicular variant) (aged 41-74 years) as well as 124 healthy controls (aged 29-80 years). Mutations of the FOX1 gene (rs965513) and NKX2-1 gene (rs944289) were detected using Real-time polymerase chain reaction method. Diagnosis of PTC was confirmed with cyto/histopathological examination.

The genomics analysis for FOX1 (rs965513) showed that the genotypes “AA,” “AG,” and minor allele “A” were more frequent in patients with PTC than in healthy control group (PTC p(genotype)=0.00071; p(allele)=0.004 vs. PTC p(genotype)=0.23; p(allele)=0.03). A further subsequent analysis of the PTC patients stratified for primary tumor stage (T1-T4), the absence/presence of regional lymph node metastases (N0/N1) as well for distant metastases (M0/M1), showed an association of FOX1 (rs965513) with stages T1-T3 and N1. We could not find an association between the the NKX2-1 gene mutational status (rs944289) and the development of PTC. Additional analysis based on the BRAF mutational status showed strong correlation of FOX1 (rs965513) with BRAFV600E(+) cases (p=0.0001), but not with BRAFV600E(-) cases (p=0.123). For NKX2-1 (rs944289), both subgroups showed no correlation (p=0.04987 for BRAFV600E(+) cases; p=0.0463 for BRAFV600E(-) cases).

The results of our study show that the FOXE1 (rs965513) carry an increased risk for PTC development, particularly allele “A” and the genotypes “AA” and “AG” as well as developing of advanced PTC, which may reflect the course of a more aggressive disease. The NKX2-1 (rs944289) appears to play a non significant role in development of PTC.