

POSTER PRESENTATION

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High-density microarray expression profiling in conventional papillary thyroid carcinomas with versus without a BRAF mutation

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Background

Whereas 40 % to 70 % of papillary thyroid carcinomas (PTCs) are characterized by a BRAF mutation (BRAF^{mut}), unified biomarkers for the genetically heterogeneous group of BRAF wild type (BRAF^{wt}) PTCs are not established yet [1,2]. Using state-of-the-art technology we compared RNA expression profiles between conventional BRAF^{wt} and BRAF^{mut} PTCs.

Materials and methods

Affymetrix HuGene 1.0 ST microarrays were used to generate whole transcript expression profiles in 11 BRAF^{wt} and 14 BRAF^{mut} PTCs. A p-value with a false discovery rate (FDR) ≤ 0.05 and a fold change > 2 were used as a threshold of significance for differential expression. Spearman's correlation as a similarity matrix was utilized for unsupervised two dimensional hierarchical clustering. The BRAF mutational status was surveyed by direct sequencing the hotspot region of BRAF exon 15.

Results

Hundred eighty transcripts from annotated genes were significantly differentially expressed between BRAF^{wt} and BRAF^{mut} PTCs and unsupervised cluster analysis was able to separate both groups. The most significantly upregulated genes in BRAF^{mut} compared to BRAF^{wt} PTCs include transmembrane 7 superfamily member 4 (TM7SF4, located on 8q23), glutaminase 2 (GLS2; 12q13), ladinin 1 (LAD1; 1q25.1-q32.3), TBC1 domain family, member 2 (TBC1D2; 9q22.33), chromosome

19 open reading frame 33 (C19orf33; 19q13.2), keratin 19 (KRT19; 17q21.2), and poliovirus receptor-related 4 (PVRL4; 1q22-q23.2). The most downregulated genes in BRAF^{mut} PTCs include inositol 1,4,5-triphosphate receptor, type 1 (ITPR1; 3p26-p25), leucine rich repeat and Ig domain containing 2 (LINGO2; 9p21.2-p21.1), solute carrier family 26, member 4 (SLC26A4; 7q31), deiodinase, iodothyronine, type I (DIO1; 1p33-p32), and hepatic leukemia factor (HLF; 17q22). Among differentially expressed microRNAs, mir492 was highly upregulated in BRAF^{mut} PTCs.

Conclusions

This study provides a detailed overview of differentially expressed genes between BRAF^{wt} vs. BRAF^{mut} conventional PTCs using whole transcript, high-density microarrays. Valuable candidate genes shall be assessed further to identify molecular pathways and molecular biomarkers which distinguish BRAF^{wt} from BRAF^{mut} PTCs.

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