DNA Microarray and miRNA Analyses Reinforce the Classification of Follicular Thyroid Tumors

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Résumé en anglais	Context: Focusing on mitochondrial function and thyroid tumorigenesis, we used an integrative approach to identify relevant biomarkers for borderline thyroid lesions. Design: Using cDNA and microRNA (miRNA) microarrays and quantitative RT-PCR analysis (qPCR), we explored samples of various types of thyroid tumors including 25 benign follicular adenomas represented by macrofollicular variants of thyroid adenomas, 38 oncocytic variants of follicular thyroid tumors, 19 papillary thyroid carcinomas, and 10 tumors of uncertain malignant potential, together with 53 normal thyroid tissue samples. Results: Our transcriptomic analysis, which highlighted discrepancies between controls and tumor tissues, as well as between various tumor types, led to the identification of 13 genes, allowing discrimination between the thyroid adenomas, oncocytic variants of follicular thyroid tumors, and papillary thyroid carcinomas, whereas the tumors of uncertain malignant potential were found to overlap these classes. Five of these genes (TP53, HOXA9, RUNX1, MYD88, and CITED1), with a differential expression confirmed by qPCR analysis, are implicated in tumorigenesis, 4 in mitochondrial metabolism (MRPL14, MRPS2, MRPS28, and COX6A1), and 2 in thyroid metabolic pathways (CaMKIINalpha and TPO). The global miRNA analysis revealed 62 differential miRNAs, the expression level for 10 of these being confirmed by qPCR. The differential expression of the miRNAs was in accordance with the modulation of gene expression and the ontologies revealed by our transcriptomic analysis. Conclusions: These findings reinforce the classification of follicular thyroid tumors established by the World Health Organization, and our technique offers a novel molecular approach to refine the classification of thyroid tumors of uncertain malignant potential.
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