Endocrine Abstracts

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Introduction

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy, with a steadily increasing incidence in the last few decades worldwide. Studies revealed the predisposition to PTC by the heterozygous state of rs2910164 within the precursor of microRNA146a. Interestingly, on the same chromosome, 40Kb separate the pre-miR-146a from the pituitary tumor transforming gene (PITG1), a proto-ontogene involved in thyroid carcinomas. A genome-wide study revealed an association of the genomic region encompassing pre-miR-146a and PTG1 gene with systemic lupus erythematosus. In this study, we analyzed, with a case–control design, the genetic association between PTC and pre-miR-146a rs2910164 as well as PTG1 (rs1862391/A and rs2910201/C/T).

Methods

Two hundred and six healthy controls (30–78 of age) and 307 PTC patients (30–74 of age) were enrolled. The diagnosis of PTC was histological at surgery. Thyroid sonography was performed in controls to exclude nodules. SNP genotyping of pre-miR-146a and PTG1 was performed by Sanger sequencing and high resolution melting. Linkage disequilibrium (LD) analysis and statistics were performed with Haploviev 4.2 and GraphPad Prism 5 software.

Results and conclusions

Pre-miR-146a rs2910164 allelic frequencies were not statistically different in patients (C=24.3%) and controls (C=28.6%) and the SNP was not in LD with the investigated PTG1 SNPs. We did not confirm a previously described association of the CG genotype with PTC. However, a significant association between the GG genotype and PTC (GG vs GC+CC odds ratio = 1.38, 95% CI 0.8–2.4) was found. The PTG1 SNPs (rs1862391/A and rs2910201/C/T), in perfect LD, have the same allelic frequency in patients (A=76.7%) and controls (A=76.2%) and are not associated with PTC. In conclusion, the study showed a new evidence of association between pre-miR-146a rs2910164 and PTC while PTG1 did not seem to be involved.

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P1083

Circulating microRNAs may help to differentiate malignant from benign thyroid nodules

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Introduction

MicroRNAs (miRNAs) are small, endogenous, non-coding RNAs that act as negative regulators of gene expression. The miRNA expression is impaired in many types of human cancer including thyroid cancer. The tissue profile of miRNAs has been shown to be useful for differentiating benign from malignant thyroid nodules, however attainment of tissue samples requires an invasive procedure while blood sampling is minimally invasive and easy to obtain. The aim of this study was to evaluate the circulating levels of a series of miRNAs in 46 patients with nodular goiter in order to identify those that might be useful in the differential diagnosis of thyroid nodules.

Methods

Thirteen miRNAs (miR-222, miR-221, miR-146a, miR-146b, miR-21, miR-155, miR-181a miR-181c, miR-7, miR-30d, miR-126, miR-344b, miR-let7g) were extracted from serum, reverse transcribed, subjected to real-time PCR and then analyzed by the ΔΔCt method. 10/13 miRNAs were evaluated post-surgically in a subset of patients undergone thyroidectomy.

Results

41/46 patients performed fine-needle aspiration cytology of the dominant nodule (20 benign, three non-diagnostic, six indeterminate, four suspicious for malignancy and eight malignant) and 24/46 patients underwent total thyroidectomy (14 benign lesions and 14 papillary thyroid cancer (PTC)). MiR-21 and -222 were higher in patients with benign histology compared to malignant. On the contrary miR-374a was significantly higher in patients with suspicious or malignant cytology and with PTC compared to those with benign disease. After thyroidectomy, the majority of miRNAs decreased while a minority of miRNAs increased or remained unchanged. Moreover miR-7 was significantly lower in patients ablated with radioiodine compared to those treated only surgically.

Conclusions

Our data, although preliminary, suggest the utility of circulating miRNAs (miR-374a showing the best diagnostic accuracy) in the differential diagnosis of thyroid nodules and the lower expression of miR-7 in patients ablated suggests its potential use as a tumor marker.

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