The Influence of Polymorphisms in TumorSuppressor Genes in Thyroid Carcinomas

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Introduction:
Thyroid carcinomas are the most often endocrine malignancy and their incidence is still growing. But the genetic predisposition to the development of thyroid cancer is still unknown. Besides mutations in the specific oncop genes, the genetic predisposition to the thyroid cancer could be influenced by risk variants in tumor suppressor genes encoding key proteins in regulation of cell cycle and cell surviving.

CDKN1B (12p13.1-p12)
- Encoding cyclin-dependent kinase inhibitor 1B (p27, Kip1)
- Localized in the cell nucleus
- Controls cell proliferation, differentiation and division

TP53 (17p13.1)
- Encoding protein p53
- Localized in the cell nucleus
- Regulation of cell division and proliferation
- „The guardian of the genome“

Aim of the study:
To determine the influence of polymorphisms Val109Gly (T/G) in the gene CDKN1B encoding protein p27/Kip1 and Arg72Pro (C/G) in the gene TP53 encoding protein p53 on the development of the thyroid cancer.

Our cohorts:
- 345 patients with sporadic medullary thyroid carcinoma (MTC)
- 269 patients with papillary thyroid carcinoma (PTC)
- 374 healthy controls

Methods:
- DNA isolation from peripheral leukocytes or from thyroid cancer tissues - QIAamp DNA Blood Kit or Trizol
- Detection of polymorphisms Val109Gly (T/G) in the gene CDKN1B and Arg72Pro (C/G) in the gene TP53 - TaqMan specific assays; Real Time PCR (Light Cycler 480, Roche)
- Statistical evaluation - NCSS 2004 programme (Statistical Solutions, Saugus, MA, USA) and Chi-square test

Conclusion:
Although total distributions of alleles of each gene were not statistically different in patients compared to controls, the remarkable risk is in combination of specific alleles of these genes. G allele in TP53 in combination with T allele in CDKN1B is more often in patients with PTC than in controls (84.4 % vs. 74.7 %, OR=1.82; CI95% (1.23-2.70); p=0.003) and specifically the TT genotype in CDKN1B is the most risk in comparison with controls (70.8 % vs. 56.6 %, OR=1.86; CI95% (1.18-2.94); p=0.01). In MTC patients, C allele in TP53 with GG genotype in CDKN1B is more frequent compared to controls (6.2 % vs. 2.9 %, OR=2.2; CI95% (1.19-4.08); p=0.016). It seems that genetic variants of tumor suppressor genes and mainly their cumulative risk effect play a role in the development of PTC and MTC.

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