Association of the rs1883832 variant of CD40 with NSCLC risk and overall survival

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Background: During the last few years a growing number of studies has attempted to shed light on the role of CD40 (Tumor Necrosis Factor Receptor Superfamily Member 5) in non-small-cell lung cancer (NSCLC), which remains the leading cause of cancer-related deaths worldwide. The aim of the current study was to investigate the clinical relevance of CD40 functional single nucleotide polymorphism (SNP) rs1883832 (-1G/T) with susceptibility to NSCLC, the clinicopathological parameters, relapse and survival rates of NSCLC patients, as well as with the protein expression of CD40.

Methods: CD40 SNP rs1883832 was genotyped in 268 randomly selected NSCLC patients and 279 age- and gender-matched healthy donors. Patients were under observation during a five-year period. Immunohistochemical analysis for CD40 was performed on 106 NSCLC tumor tissue samples. All the participants were Greeks with Caucasian origin.

Results: Genotype frequencies of rs1883832 (GC, CT, and TT) were significantly different between healthy controls and patients. CC homozygotes had higher risk for NSCLC compared to T allele carriers in univariate (P < 0.001), as well as in multivariate analysis (P = 0.006). In addition, rs1883832 was related to overall survival. More specifically, CT heterozygotes had worse clinical outcome after two-, three- and five-year observation compared to TT and CC homozygotes (P = 0.015, P = 0.005 and P = 0.017, respectively). Stratifying according to histological subtype, this association was observed only in patients with adenocarcinomas (P = 0.028) and not in patients with squamous- and large-cell carcinomas. Furthermore, taking into consideration disease stage, worse survival for CT heterozygotes was observed in stage II patients and not in patients of other stages (P = 0.016). Moreover, the variant had also strong association with brain metastases, with T allele carriers developing more often metastatic disease in CNS (P = 0.018). Interestingly, rs1883832 was related to CD40 protein expression in malignant cells (P < 0.001) as well as in stromal cells (P = 0.004).

Conclusions: The present findings suggest that investigated SNP rs1883832 may be a useful and independent biomarker in NSCLC. However, more studies are needed in order to further demonstrate their role in NSCLC.

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