ASSOCIATION BETWEEN THR21MET AND SER89ASN POLYMORPHISMS OF THE UROTENSIN II GENE AND DIABETIC RETINOPATHY
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Purpose: To evaluate possible role of the U-II gene (UTS2) polymorphisms (Thr21Met and Ser89Asn) in the genetic susceptibility to diabetic retinopathy (DR) in a Turkish population

Methods: Total number of 280 patients with DR (nonproliferative DR 170 and proliferative DR 110), 291 nondiabetic healthy controls, and 133 diabetic controls (without DR) were included to this study. The detection of UTS2 gene polymorphisms was achieved with PCRRFLP technique. The Discovery Studio 2.1 programme was used for molecular modeling analysis.

Results: Thr21Met (T21M) and Ser89Asn (S89N) polymorphisms of the UTS2 gene were markedly associated with the risk of developing diabetes and DR. M21M genotype frequencies were markedly high in PDR (8.9% in diabetic control vs. 54.6% in PDR, P=0.0092) group. Marked increases in 21M allele frequency (52.7% in diabetic control vs. 76.4% in PDR, P<0.0001) frequency in PDR group were detected. However, there were no marked changes in genotype and allele frequencies for T21M in NPDR group. There were significant decreases in the S89N genotype (23.9% in diabetic control vs. 13.5%) and 89N allele frequencies (11.9% in diabetic control vs. 6.8%) in NPDR group. However, S89S genotype (76.1% in diabetic control vs. 86.4%) and 89S allele frequencies (88.1% in diabetic control vs. 93.2%) were high in NPDR group. Three haplotypes (MN, MS and TS) were markedly associated with NPDR patients (P<0.001), but only MN (P<0.001) and TS haplotypes (P=0.018) were associated in PDR group. Molecular modeling analysis showed that these two polymorphisms changed the 3D structure of UTS2, and provided interactions with neighboring residues.

Conclusion: The marked associations between Thr21Met and Ser89Asn polymorphisms in the UTS2 gene and DR strongly suggest that these SNPs may be an important a risk factor for the development of DR in Caucasians, and could be candidate markers for earlier diagnosis and targets for DR therapy.