Association of VEGFA Variants with Altered VEGF Secretion and Type 2 Diabetes - A Case Control Study

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Background. Vascular endothelial growth factor (VEGF) contributes to type 2 diabetes (T2DM) pathogenesis, and genetic variations in *VEGFA* gene were suggested to influence VEGF secretion and T2DM pathogenesis. This study examined the potential association of specific *VEGFA* variants with altered VEGF levels, and with T2DM.

Subjects and Methods. A retrospective case-control study, performed on 815 T2DM patients, and 805 healthy controls. VEGF levels were measured by ELISA, genotyping of *VEGFA* variants was done by allelic exclusion method (real-time PCR).

Results. MAF of rs1570360, rs2010963, rs25648, rs833068, rs3025036, and rs3025039 were significantly different between T2DM cases and controls. Increased T2DM risk was associated with rs699947, rs1570360, and rs3025020, while reduced T2DM risk was seen with rs1547651, rs2010963, rs25648, rs3025036, and rs3025039 genotypes, thus assigning T2DM susceptibility and protection, respectively. Reduced VEGF levels were associated with rs833061, rs2010963, and rs3025039 heterozygosity and rs3025036 major allele homozygosity in T2DM cases, while increased VEGF levels were seen in rs833070 homozygous major allele genotype. Both rs699947 and rs1570360 positively, while rs2010963 and rs3025036 negatively correlated with fasting glucose. In addition, rs699947 positively correlated with LDL-cholesterol, and rs3025039 positively correlated with diabetes duration, but negatively with HbA1c and triglycerides. Haploview analysis identified Block 1 containing 8 loci, and Block 2 with the remaining 3 loci. Haplotypes ACTGCCGG and AACGGCGA (Block 1) were negatively associated with T2DM, while haplotype CCC was positively and haplotype CGC (Block 2) were negatively associated with T2DM.

Conclusion. This study confirms the contribution of altered VEGF secretion, resulting from genetic variation in VEGFA gene into T2DM pathogenesis, hence supporting role for *VEGFA* as T2DM candidate locus.