Gene-Wide Association Study on the TERT Locus and PDAC Susceptibility. Results from the PANDoRA Consortium

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Context SNPs in the telomerase reverse transcriptase (TERT) locus were reported to be associated with pancreatic cancer risk in a genome-wide association study (GWAS). TERT is essential for maintaining telomere ends. Its over-expression in normal cells can lead to prolonged cell lifespan and transformation. While telomerase activity cannot be detected in most normal tissues, it is seen in approximately 90% of human cancers. Objective We attempted to replicate and expand the association with the locus in a series of PDAC and healthy controls of European ancestry within the PANcreatic Disease ReseArch (PANDoRA) consortium. Methods We genotyped 13 SNPs in 1,034 PDAC cases and 2,443 controls from the PANDoRA consortium. We tested each SNP for association with PDAC risk and also with survival of the patients. Results We replicated the association reported in the GWAS with rs401681 (OR=1.53; 95%CI 1.22-1.92; P=0.0002) and found a novel association between rs2736098 and decreased PDAC risk (OR=0.75; 95%CI: 0.63-0.88; P=0.001). Another polymorphism (rs4246742) was associated with worse survival (HR=1.75, 95%CI: 1.15-2.67; P=0.009). Conclusion We report here two novel findings: an association with risk (rs2736098) and one with survival of the patients (rs4246742). These results further contribute to our understanding in the genetic etiology of pancreatic cancer and suggest a new marker for disease prognosis.