Association of Genetic Polymorphisms with Survival in Pancreatic Ductal Adenocarcinoma Patients

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Context Overall survival (OS) of pancreatic ductal adenocarcinoma (PDAC) patients is only partially explained by clinical and pathological features. Germline genetic variability can contribute to variation in OS of PDAC patients. A genome-wide association study (GWAS) on PDAC OS has been recently performed. Twenty-eight genomic regions showed association with OS with P<10^-5. Objective We sought to confirm the reported associations of single nucleotide polymorphisms (SNPs) with OS of PDAC in the PANcreatic Disease ReseArch (PANDoRA) consortium. Methods We genotyped 41 SNPs tagging the 28 regions emerging from the GWAS on PDAC OS has been recently performed. We tested each SNP for association with OS of the patients. Results We observed statistically significant associations with OS of PDAC patients at three regions, located in the CTNNA2 gene on chromosome 2 (rs1567532; HR=1.58, 95% CI: 1.24-2.01; P=2.4x10^-4), in the ASTN2 gene on chromosome 9 (rs10818020; HR=0.74, 95% CI: 0.61-0.91, P=4x10^-3), and in the SMAP2 gene on chromosome 1 (rs16827275; HR=1.61, 95% CI: 1.00-2.60; P=0.049). Among three SNPs reported by the previous GWAS to be associated with OS with P<10^-6, we observed a weak association at rs16861827 on chromosome 1 (HR=1.69, 95% CI: 1.02-2.80; P=0.043), but did not confirm the other two. All associations were observed with a recessive model. Conclusion These findings add to the evidence that germline genetic polymorphisms affect OS of PDAC patients. If confirmed in further studies, these variants may have the potential to impact treatment decisions and design of clinical trials.