A common CCK-B receptor intronic variant does not predict risk for or survival in pancreatic adenocarcinoma

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Introduction: Cholecystokinin-B receptor (CCKBR) is often over-expressed in pancreatic ductal adenocarcinoma; stimulation of the receptor promotes tumor growth. Single nucleotide polymorphism c.811+32C>A in intron 4 of *CCKBR*was previously reported to correlate with higher cancer risk and poorer survival. The variant was suggested to induce retention of intron 4, resulting in a new spliceform with enhanced receptor activity.

Aims: Our objective was to validate the c.811+32C>A variant as an emerging biomarker for pancreatic cancer risk and prognosis.

Patients & methods: We genotyped variant c.811+32C>A in 122 pancreatic adenocarcinoma cases and 106 controls by sequencing and examined its association with cancer risk and patient survival. To test the functional effect of variant c.811+32C>A on pre-mRNA splicing, we constructed minigenes, harboring the *CCKBR* coding sequence and intron 4 with or without the variant. Transcription and splicing of *CCKBR* was evaluated in transiently transfected HEK 293T cells.

Results: We found the intronic variant in 35 heterozygous and 5 homozygous cases and in 32 heterozygous and 3 homozygous controls (allele frequency 18.4% and 17.9%, respectively). Survival analysis showed no significant difference between median survival of patients with the C/C genotype (266 days) and patients with the A/C or A/A genotypes (257 days). *CCKBR* minigenes with or without variant c.811+32C>A exhibited no difference in expression of the intron-retaining splice variant.

Conclusion: These data indicate that variant c.811+32C>A in *CCKBR* does not have a significant impact on pancreatic cancer risk or survival in a Hungarian cohort.