CCK-B receptor variant as a potential prognostic factor in pancreatic adenocarcinoma.

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Background: Cholecystokinin-B (CCK-B) receptor is often over-expressed in pancreatic ductal adenocarcionoma (PDAC); stimulation of the receptor promotes tumor growth. An intronic mutation (c.811+37C>A) in the CCKBR gene causes retention of intron-4, resulting in a new spliceform, which was previously shown to correlate with higher PDAC risk and a more aggressive phenotype.

Aims: Our aim was to test the effect of the c.811+37C>A mutation on PDAC risk and prognosis in a Hungarian population.

Patients & methods: 122 subjects with PDAC (cases) and 106 subjects with no pancreatic disease (controls) were recruited from the Hungarian National Pancreas Registry. Genomic DNA was isolated from peripheral blood. Intron-4 of the CCKBR gene, including exon-intron boundaries, was amplified and sequenced.

Results: We found the c.811+37C>A intronic mutation in 35 heterozygous and 5 homozygous cases and in 32 heterozygous and 3 homozygous controls (allele frequency 18.4% and 17.9% respectively). One case subject carried a p.R319Q and one control subject a p.R319W missense mutation. Preliminary data on survival analysis showed significanly lower median survical for patients harboring the mutation (121 days vs. 333 days).

Conclusion: In our cohort, the c.811+37C>A intronic mutation was not associated with increased risk for PDAC. However, the mutation was associated with shorter survival, indicating that this genetic variant is a clinically relevant prognostic factor. Supported by TÁMOP and OTKA.