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Titel des Beitrags: Common CFTR haplotypes and susceptibility to chronic pancreatitis and congenital bilateral absence of the vas deferens.

Abstract: CFTR mutations enhance susceptibility for idiopathic chronic pancreatitis (ICP) and congenital bilateral absence of the vas deferens (CBAVD); however, it is unknown why CFTR heterozygotes are at increased disease risk. We recently showed that common CFTR variants are associated with aberrantly spliced transcripts. Here, we genotyped for common CFTR variants and tested for associations in two ICP (ICP-A: 126 patients, 319 controls; ICP-B: 666 patients, 1,181 controls) and a CBAVD population (305 patients, 319 controls). Haplotype H10 (TG11-T7-470V) conferred protection (ICP-A: OR 0.19, P<0.0001; ICP-B: OR 0.78, P = 0.06; CBAVD OR 0.08, P<0.001), whereas haplotype H3 (TG10-T7-470M) increased disease risk (ICP-A: OR 8.34, P = 0.003; ICP-B: OR 1.88, P = 0.007; CBAVD: OR 5.67, P = 0.01). The risk of heterozygous CFTR mutations carriers for ICP (OR 2.44, P<0.001) and CBAVD (OR 14.73, P<0.001) was fully abrogated by the H10/H10 genotype. Similarly, ICP risk of heterozygous p.Asns4Ser SPINK1 mutation carriers (OR 10.34, P<0.001) was compensated by H10/H10. Thus, common CFTR haplotypes modulate ICP and CBAVD susceptibility alone.
and in heterozygous CFTR and p.As634Ser mutation carriers. Determination of these haplotypes helps to stratify carriers into high- and low-risk subjects, providing helpful information for genetic counseling.