PepT1 oligopeptide transporter (SLC15A1) gene polymorphism in inflammatory bowel disease.

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Abstract: Human polymorphisms affecting gut epithelial barrier and interactions with bacteria predispose to the inflammatory bowel diseases (IBD) Crohn's disease (CD) and ulcerative colitis (UC). The intestinal transporter PepT1, encoded by the SLC15A1 gene, mediates intracellular uptake of bacterial products that can induce inflammation and NF-kappaB activation upon binding to NOD2, a protein often mutated in CD. Hence, we tested SLC15A1 polymorphisms for association with IBD.

Twelve SLC15A1 single nucleotide polymorphisms (SNPs) were genotyped in 1783 individuals from 2 cohorts of Swedish and Finnish IBD patients and controls. An in vitro system was set up to evaluate the potential impact of SLC15A1 polymorphism on PepT1 transporter function by quantification of NOD2-mediated activation of NF-kappaB.

The common allele (C) of a coding polymorphism (rs2297322, Ser117Asn) was associated with CD susceptibility both in Sweden and in Finland, but with genetic effects in opposite directions (risk and protection, respectively). The best evidence of association was found in both populations when the analysis was performed on individuals not carrying NOD2 common risk alleles (Sweden allelic P = 0.0007, OR 1.97, 95% confidence interval [CI] 1.34-2.92; Finland genotype P = 0.0013, OR 0.63, 95% CI 0.44-0.90). The PepT1 variant encoded by the C allele (PepT1-Ser117) was associated with reduced signaling downstream of NOD2 (P

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