Genetic analyses of heme oxygenase 1 (HMOX1) in different forms of pancreatitis.

Abstract:
Heme oxygenase 1 (HMOX1) is the rate limiting enzyme in heme degradation and a key regulator of inflammatory processes. In animal models the course of pancreatitis was ameliorated by up-regulation of HMOX1 expression. Additionally, carbon monoxide released during heme breakdown inhibited proliferation of pancreatic stellate cells and might thereby prevent the development of chronic pancreatitis (CP). Transcription of HMOX1 in humans is influenced by a GT-repeat located in the promoter. As such, HMOX1 variants might be of importance in the pathogenesis of pancreatitis. The GT-repeat and SNP rs2071746 were investigated with fluorescence labelled primers and by melting curve analysis in 285 patients with acute pancreatitis, 208 patients with alcoholic CP, 207 patients with idiopathic/hereditary CP, 147 patients with alcoholic liver cirrhosis, and in 289 controls, respectively. GT-repeat analysis was extended to a total of 446 alcoholic CP patients. In addition, we performed DNA sequencing in 145 patients with alcoholic CP, 138 patients with idiopathic/hereditary CP, 147 patients with alcoholic liver cirrhosis, and 151 controls. Exon 3 screening was extended to additional patients and controls. S- and L-alleles of the GT-repeat, genotypes and alleles of SNP rs2071746 and
non-synonymous variants detected by sequencing were found with similar frequencies in all groups. Although functional data implicate a potential influence of HMOX1 variants on the pathogenesis of pancreatitis, we did not find any association. As rare non-synonymous HMOX1 variants were found in patients and controls, it is rather unlikely that they will have functional consequences essential for pancreatitis development.