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LETTER

On the role of CFTR, PSSR1 and PST1/SPINK1 in idiopathic chronic pancreatitis

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Marie-Pierre Audrézet and colleagues[1] investigated DNA from 39 unrelated French patients in whom a diagnosis of idiopathic chronic pancreatitis (ICP) had been previously established. They showed that more than 30% of ICP patients carried at least one abnormal allele in one of the three genes (the cystic fibrosis transmembrane conductance regulator (CFTR) gene, the cationic trypsinogen (PRSS1) gene, and the pancreatic secretory inhibitor (PSTI /SPINK1) gene) which have been associated with chronic pancreatitis.

We performed the same mutation analysis on 37 unrelated Italian patients with ICP. The diagnosis of ICP was based on clinical, biochemical and sonographic findings after exclusion of precipitating factors, such as alcohol, gallstones, medication, trauma or metabolic disorders, an age of more than 45 years, and a positive family history of pancreatitis. Mutation screening of the PRSS1 gene was performed by means of the denaturing gradient gel electrophoresis (DGGE) analysis, as described by Chen *et al*.[2] Mutation screening of the PSTI/SPINK1 gene was performed by PCR amplification and sequencing of the entire coding region and the intron/exon junctions, as described by Witt *et al*.[3] The 31 most frequent mutations of the CFTR gene were examined with the widely used genotyping method (OLA kit, Perkin-Elmer). The intron-8 poly(T) variants were analysed according to the method described by Chillon *et al*.[4] All of the 37 patients were screened for both PRSS1 and PSTI/SPINK1 mutations. No patient with ICP was found to carry mutant alleles of the PRSS1 gene (Table 1). One mutant allele of the PSTI/SPINK1 gene (P55S) was found in one patient, a 35-year-old male who was affected by recurrent attacks of acute pancreatitis since age 28 (Table 1). All of the 37 patients but one were screened for the most common mutations of the CFTR gene and the 5T allele. Four mutant alleles of the CFTR gene were found in four patients with ICP (Table 1). None of them suffered from unrecognised CF-related pulmonary symptoms or other atypical CF manifestations, following clinical re-evaluation. The 5T allele was present in five of the 36 (13.9%) patients tested (Table 1). When the relative contribution of each of the three genes was evaluated, we found a carrier rate of mutant alleles of 0, 2.7 and 11.1% for PRSS1, PSTI/SPINK1, and CFTR gene, respectively. These figures are lower than those reported by Audrézet *et al*[1] who found a carrier rate of mutant alleles of 2.6, 10.3, and 20.5% for the three genes, respectively. Moreover, no patients was compound heterozygote and none of those carrying a major CFTR mutation had the 5T allele.

Table 1 Sequence variation identified in the PRSS1, PSTI, and CFTR genes in 37 Italian patients with ICP

			CFTR	
Patient	*PRSS1*	*PSTI*	*Mutant*	*PolyT*
1	–[a]	–	W1282X/N	7T/9T
2	–	–	N187K/N	7T/7T
3	–	–	711+1G/1T	7T/7T
4	–	–	R75Q/N	7T/9T
5	–	–	ND[b]	ND
6	–	–	–	5T/9T
7	–	–	–	5T/7T
8	–	–	–	5T/7T
9	–	–	–	5T/7T
10	–	–	–	5T/7T
11	–	P55S	–	5T/7T
12 to 37	–	–	–	7T/7T or 7T/9T

[a]Indicates two wild alleles. [b]ND, not done due to insufficient DNA samples.

Our findings seem to scale down the relative contribution of CFTR, PRSS1 and PSTI/SPINK1 genes to the aetiology of ICP and clearly show that the search for new predisposing genetic and environmental factors is still far from being complete.

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