Reply

'Gain of function' PRSS1 mutations are rare in ICP

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We would like briefly to comment on Perri and colleagues' work in several aspects.

First, we are happy that their results support our conclusion that 'gain of function' PRSS1 mutations are rare in ICP.[1]

Second, their detection rate (0%; 0/37) of the most frequent PSTI N34S variant in ICP is not only in sharp contrast with our result (10.3%; 4/39),[1] but also with the 12.6% (11/87),[2] 16.4% (68/415),[3] and 33.3% (6/18),[4] reported in more recently published works.

Third, with respect to the frequency of CFTR mutations/variants in ICP, their results are again in contrast with most of the current available data (see Table 2[1]). This difference may be mainly due to the much lower carrier frequency of CFTR mutations in the Italian population compared with Northern Europeans.[5] In addition, they only analysed the 31 most frequent mutations of the CFTR gene. Thus their results, although interesting, are not strictly comparable to ours.

Nevertheless, Perri and colleagues' work adds to the notion that the detection rate of pancreatitis-associated mutations/variants varies significantly among different studies. We believe this discrepancy could not be solely explained by selection biases and/or small sample sizes, since most of the studies followed roughly the same selection criteria.

The relative contribution of different genetic factors and of genetic factors *vs* environmental factors to the aetiology of ICP may also differ in different populations.

Finally, we agree with them that the search for new predisposing genetic and environmental factors is still far from being complete.

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5 Cystic Fibrosis Mutation Data Base: http://www.genet.sickkids.on.ca/cftr/freqtables.html.