Maternal Inheritance Pattern of Hereditary Pancreatitis in Patients With Pancreatic Carcinoma

Hereditary pancreatitis is an autosomal dominant disorder whose phenotype is associated with distinct point mutations in the cationic trypsinogen gene on chromosome 7q35 (1,2). Affected patients have recurrent episodes of pancreatitis that often begin during childhood. Compared with the general population or patients with chronic pancreatitis of common etiologies who have a somewhat increased cancer risk (3), patients with hereditary pancreatitis have a risk of developing pancreatic carcinoma that approaches 40% (4). Because all previously reported cases of pancreatic cancer associated with hereditary pancreatitis were diagnosed in patients who had inherited the disease from their father, the cumulative risk of developing cancer of the pancreas is considered to be even greater (approximately 75%) when hereditary pancreatitis is inherited from the father (4). In this correspondence, we report two kindreds with hereditary pancreatitis, each of which were affected by an R117H mutation of the trypsinogen gene, and in each case the patient with pancreatic cancer had inherited the defective cationic trypsinogen gene from the mother.

When informed consent for genetic testing was obtained, R117H mutations were identified by the characteristic band pattern on ethidium bromide-stained agarose gels after AflIII digestion of leukocyte DNA and confirmed by DNA sequencing as previously reported (1). In family 1 from the U.K. (Fig. 1, A), patient I:2 and her daughter

![Diagram](https://academic.oup.com/jnci/article-abstract/91/8/723/2519451)
II:2 had recurrent pancreatitis and, therefore, were tested for mutations of the trypsinogen gene. When patient II:2 underwent abdominal surgery for complications of hereditary pancreatitis, biopsy specimens were taken from the pancreas and paraffin sections revealed a poorly differentiated adenocarcinoma. In family 2 (Fig. 1, B) from Germany, the index patient III:14 had recurrent episodes of pancreatitis since early infancy. Because his mother, aunt, and brother were all affected by similar symptoms, genetic testing was performed and confirmed hereditary pancreatitis in all five subjects. His grandmother (I:2) and uncle (II:3) had a lifetime history of chronic pancreatitis as well, and the latter died at age 49 years from histologically confirmed, metastatic ductal adenocarcinoma of the pancreas.

Patients with hereditary pancreatitis are, in addition to their life-long morbidity from recurrent pancreatitis, burdened with an excessive risk of developing pancreatic cancer. The data currently available, however, have suggested that the pancreatic cancer risk exclusively involves patients with a paternal inheritance pattern of the disease (4). The statistically significant association of pancreatic cancer with a paternal inheritance pattern of the trypsinogen mutation was so strong that genomic imprinting was suggested as a possible explanation, as previously reported for other inherited types of cancers (5). In view of the kindreds reported in this correspondence, this assumption becomes less likely. Moreover, genetic counseling about the risk of pancreatic cancer now has to include patients with hereditary pancreatitis who have inherited their defective gene from the mother. Until more data become available, the paternal as well as the maternal inheritance of the disease represents a comparable and excessive cumulative risk for the development of cancer of the pancreas.

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**References**


**Notes**

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Medical record information and DNA of affected individuals have been deposited with the German Hereditary Pancreatitis Registry, Leipzig, Germany; the European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer; Liverpool, U.K.; and the Midwest Multicenter Pancreatic Study Group, Pittsburgh, PA.