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Aberrant methylation of secreted apoptosis-related protein 2 (SARP2) in pure pancreatic juice in diagnosis of pancreatic neoplasms

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Secreted apoptosis-related protein (SARP) families are considered to counteract the oncogenic Wnt signaling pathway and inactivation of this gene may aid cancer development and progression. Recently, the aberrant methylation of SARP2 was detected frequently in pancreatic carcinoma (PCa) tissues, but not in normal pancreatic tissues.

We evaluated the hypermethylation of SARP2 in pure pancreatic juices (PPJ) aspirated endoscopically from patients with PCa, intraductal papillary mucinous neoplasm of the pancreas (IPMN), chronic pancreatitis (CP), and a control group (C) who was consequently free of pancreatic disease by methylation-specific PCR (MSP) and real-time MSP.

The incidence of the aberrant methylation of SARP2 using MSP was 79% (26/33) in the PPJ with PCa, and 85% (17/20) with IPMN. However, it was only 5% (1/19) in the PPJ with CP and 0% (0/10) in the PPJ of C, respectively. The incidences of aberrant methylation of SARP2 in the PPJ with PCa and IPMN were significantly higher than that in the PPJ with CP (p< 0.001, p< 0.001). Melting curve analysis by real-time MSP as shown in Figure revealed that the incidence of aberrant methylation of SARP2 in PPJ was 85% (28/33) with PCa, 82% (9/11) with the malignant group of IPMN, 56% (5/9) with the benign group of IPMN and 26% (5/19) with CP. In this analysis, there were significant differences between PCa and CP (p<0.001), and between the malignant group of IPMN and CP (p<0.005). In the quantitative analysis by real-time MSP with a suitable cut-off value, the incidences of aberrant methylation of SARP2 in the PPJ with PCa, the malignant group of IPMN, the benign group of IPMN and CP were 58 % (19/33), 55% (6/11), 33% (3/9) and 11% (2/19), respectively. The incidence of the aberrant methylation of SARP2 in the PPJ was significantly different between PCa and CP, and between the malignant group of IPMN and CP (p<0.005, p<0.05).

These results suggest that promoter methylation of SARP2 in the PPJ may be a highly sensitive and useful marker for the detection of pancreatic neoplasms, including PCa and the malignant group of IPMN.

Figure  Melting curve analysis of the quantitative MSP products by real-time PCR
Representative case of aberrant methylation of SARP2 in the PPJ sample from patients with PCa revealed a similar melting curve (red curve) and the same melting temperature (83°C), compared with methylation profiles of the human PCa cell line Mia PaCa-2 as a methylated control of SARP2.