# 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.

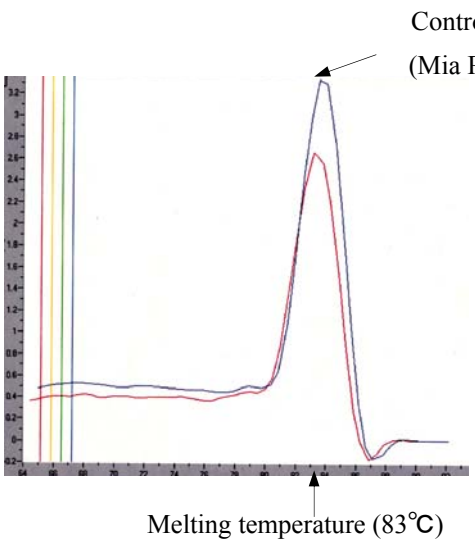


**Figure Melting curve analysis of the quantitative MSP products by real-time PCR**

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℃), compared with methylation profiles of the human PCa celll line Mia PaCa-2 as a methylated control of *SARP2*.