
Screening programs are recommended for individuals at risk (IAR) from families with familial pancreatic cancer (FPC). However, reliable imaging methods or biomarkers for early diagnosis of pancreatic ductal adenocarcinoma (PC) or its precursor lesions are still lacking. The ability of circulating microRNAs (miRNAs) to discriminate multifocal high-grade precursor lesions or PC from normal was examined. The presence of miRNA-21, -155, -196a, -196b and -210 was analyzed in the serum of transgenic KPC mice to test their ability to distinguish mice with different grades of pancreatic intraepithelial neoplasia (mPanIN1-3) or PC from control mice. Serum levels of miR-196a and -196b were significantly higher in mice with PanIN2/3 lesions (n = 10) or PC (n = 8) as compared to control mice (n = 10) or mice with PanIN1 lesions (n = 10; P = .01). In humans, miR-196a and -196b were also diagnostic. Patients with PC, sporadic (n = 9) or hereditary (n = 10), and IAR with multifocal PanIN2/3 lesions (n = 5) had significantly higher serum levels than patients with neuroendocrine pancreatic tumors (n = 10) or chronic pancreatitis (n = 10), IAR with PanIN1 or no PanIN lesions (n = 5), and healthy controls (n = 10). The combination of both miR-196a
and -196b reached a sensitivity of 1 and specificity of 0.9 (area under the curve = 0.99) to diagnose PC or high-grade PanIN lesions. In addition, preoperative elevated serum levels of miR-196a and -196b in patients with PC or multifocal PanIN2/3 lesions dropped to normal after potential curative resection. The combination of miR-196a and -196b may be a promising biomarker test for the screening of IAR for FPC.