Digital-NGS identifies mutations in pancreatic juice in patients with pancreatic cancer

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Introduction: Genetic analysis of secretin-stimulated pancreatic juice which contains DNA shed from cell linings of the pancreatic ducts may form a test parameter to detect pancreatic ductal neoplasia. Next-generation sequencing (NGS) is widely evaluated as a test to detect mutations in many cancers. However, sequencing errors generated by standard NGS assays limit the ability to identify the mutations at concentrations.

Methods: We employed digital-next-generation sequencing ("digital-NGS") to detect low-abundance mutations in pancreatic juice samples of 115 subjects with either pancreatic ductal adenocarcinoma, intraductal papillary mucinous neoplasms, a familial predisposition to pancreatic cancer undergoing pancreatic screening, or controls without evidence of neoplasia.

Results: Digital-NGS could detect all 28 mutations present at concentration ranging from >0.1 to 1% relative to wild-type DNA. Cases with PDAC and IPMN were more likely and significant to have mutant DNA detected in pancreatic juice than controls. TP53 and/or SMAD4 mutations were commonly detected in juice samples from patients with PDAC and were not detected in controls; mutant TP53/SMAD4 concentrations could distinguish PDAC from IPMN cases and controls. Two of the four patients who developed pancreatic cancer while under surveillance had mutations (TP53 and SMAD4) from their cancer, detected in juice samples collected over one year prior to their pancreatic cancer diagnosis when no suspicious pancreatic lesions were detected by imaging.

Conclusions: The detection in pancreatic juice of mutations are important for the progression of low-grade dysplasia to high-grade dysplasia and invasive pancreatic cancer. Therefore, this may improve the management of patients undergoing pancreatic screening and surveillance.

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