Evaluation of the Avantect Pancreatic Cancer Test for Identifying High-Risk Pancreatic Cysts

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INTRODUCTION

Pancreatic cystic lesions are common incidental findings, but up to half may be precursors of pancreatic cancer. Current diagnostic methods cannot robustly identify cysts that have the highest probability to progress to cancer and require treatment. To address this gap, we evaluated the performance of a non-invasive epigenomic based test employing cell-free DNA, the Avantect Pancreatic Cancer CLIA-CAP test, in a cohort of patients with pancreatic cysts to identify those at higher risk of malignancy.

Avantect is recommended for individuals with high risk for pancreatic cancer such as newly diagnosed with Type 2 Diabetes. The test has been validated in a large case-control study, including patients with pancreatic cystic lesions.

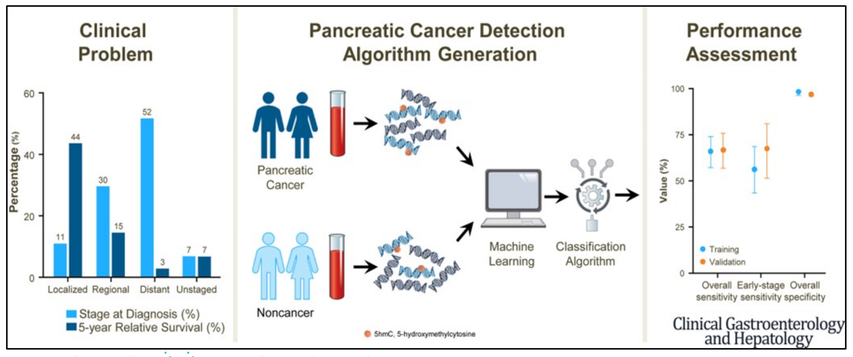
The current pilot study evaluates the ability to detect high-risk patients with pancreatic cystic lesions using the Avantect test.

METHODS

In this study, we investigated the use of Avantect in a cohort of patients with pancreatic cysts. Whole blood was collected from 41 patients with cysts: 17 patients with moderate/high grade dysplasia (HGD) and 24 patients with benign/low grade dysplasia (LGD) cysts. Avantect measures changes in 5-hydroxymethylation (5hmC) in cfDNA, copy number changes and fragment size differences.

In parallel, demographic information, imaging results, surgical reports, and histological findings were collected for analysis and clinical annotation of patients.

AVANTECT TEST VALIDATION SUMMARY



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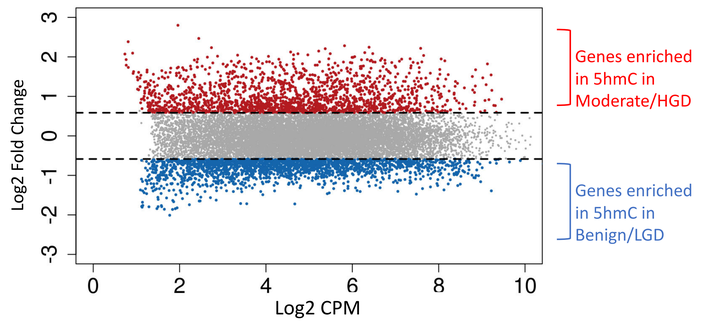
COHORT CHARACTERISTICS

Characteristics	N
Gender at Birth	
Male, n (%)	31.7%
Female, n (%)	68.3%
Mean age (Range)	65.8 (30-82)
Pancreatic Lesion	
Moderate/High Grade Dysplasia (HGD)	17
Benign/Low Grade Dysplasia (LGD)	24
Additional Risk Factors	
Type II diabetes Mellitus	8
Heavy smokers	9
Family history of Pancreatic Cancer	6

DIFFERENTIAL 5hmC LEVELS

Differential 5hmC Occupancy of gene features in Moderate/High Grade Dysplasia compared with Benign/ Low Grade Dysplasia



- Log2 fold-change (FC) of hydroxymethylation levels in gene features are compared as a function of their average log2 counts per millions (CPM) between Moderate/HGD versus Benign/LGD.
- Genes that have significant increase or decrease in 5hmC density (N=3,697), with false discovery rates (FDR) less than 0.05, Moderate/HGD compared to Benign/LGD, are denoted as red and blue scatter dots, respectively. FDR was calculated using Benjamini-Hochberg method.

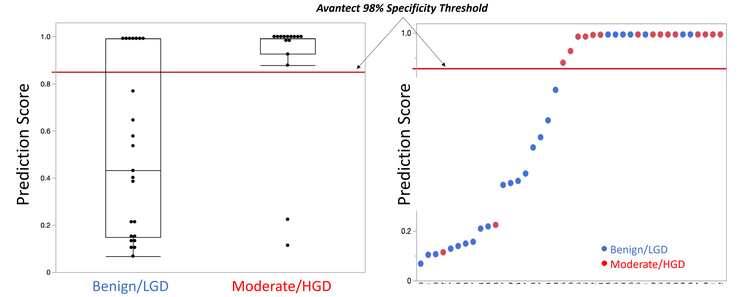
DIFFERENTIAL GENE FEATURES CLASSIFICATION

5hmC Differential analysis enriches specifically for pancreas related Genesets

GSEA Geneset Enriched In Moderate/HGD	GeneRatio	p.adjust
MURARO_PANCREAS_DELTA_CELL	57/1425	1.34E-12
MURARO_PANCREAS_PANCREATIC_POLYPEPTIDE_CELL	32/1425	2E-06
DESCARTES_FETAL_PANCREAS_ENS_NEURONS	33/1425	2E-06
MURARO_PANCREAS_EPSILON_CELL	14/1425	2.4E-05
DESCARTES_FETAL_PANCREAS_ISLET_ENDOCRINE_CELLS	31/1425	2.9E-05
DESCARTES_FETAL_PANCREAS_DUCTAL_CELLS	20/1425	0.00692

GSEA Geneset Enriched In Benign/LGD	GeneRatio	p.adjust
DESCARTES_FETAL_PANCREAS_MYELOID_CELLS	92/1680	3.14E-35
MURARO_PANCREAS_ENDOTHELIAL_CELL	92/1680	1.48E-19
DESCARTES_FETAL_PANCREAS_ERYTHROBLASTS	24/1680	0.00287
DESCARTES_FETAL_PANCREAS_LYMPHOID_CELLS	27/1680	0.00457
DESCARTES_FETAL_PANCREAS_VASCULAR_ENDOTHELIAL_CELLS	13/1680	0.01157

AVANTECT TEST DETECTION



Avantect Prediction Score: distribution across Benign/LGD and Moderate/HGD

Pancreatic Lesions	Number in Pilot Study	Detected by Avantect
Moderate/HGD	17	15 (88%)
Benign/LGD	24	7 (29%)

CONCLUSIONS

- Avantect detection rate was 88% for Moderate/HGD and 29% for Benign/LGD cyts.
- These results show great promise in identifying subjects with Moderate/HGD who benefits from prompt intervention.
- Larger studies have been commenced to enable prospective evaluation of Avantect for the management and surveillance of individuals with pancreatic cysts.