A multi-center Study of a MicroRNA-based Assay for the Diagnosis of Pancreatic Ductal Adenocarcinoma in Fine Needle Aspirates


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INFORMATION

The miRInform™ Pancreas LDT, interrogating expression of miR-130b, -135b, -148a, -196a, -375, -96 and -24, was developed and validated in accordance with CLIA and CAP regulations using 95 FFPE and 186 FNA pancreatic specimens, respectively. In conjunction with FNA cytology, the miRInform™ Pancreas LDT allows diagnosis of PDAC with 92.5% accuracy, as compared to 80.6% for FNA cytology alone.

The miRInform™ Pancreas LDT enables resolution of "Indeterminate" cytology with an accuracy of 78.2%.

INTRODUCTION

Differential diagnosis between chronic pancreatitis (CP) and pancreatic ductal adenocarcinoma (PDAC) in patients with solid pancreatic masses often represents a clinical dilemma. Cystoscopic ultrasonographic guided fine needle aspiration (EUS-FNA) is the most commonly used procedure for diagnosis in high volume tertiary medical centers. EUS FNA has a reported sensitivity (Sen), specificity (Spe) and positive predictive value (PPV) approaching 100%. However, its negative predictive value (NPV) can be as low as 70%, resulting in up to 30% false negative results. This can stem from such confounding factors as co-existing benign pathology, ambiguous benign conditions and pancreatic cancer.

Mature microRNAs (miRNAs) are small 19-23 nt regulatory RNAs that control gene expression at the post-transcriptional level and whose dysregulation has been linked to many human cancers, including pancreatic cancer. We previously identified a miRNA model consisting of miR-19a and miR-217 that distinguishes from chronic pancreatitis and pancreatic cancer. We further established the excellent performance of this model in accordance with CLIA and College of American Pathologists (CAP) guidelines using a blinded set of FFPE specimens, with the sensitivity and specificity of approximately 95%.

Performance evaluation of this laboratory developed test (LDT) in resected pancreatic specimens was a key step to ensure success of the test. The final pathology is not always available and/or more difficult to obtain. The development of the final miRInform™ Pancreas LDT classified specimens as PDAC (scores >0.5) and Benign (scores <0.5).

MATERIALS AND METHODS

FFPE specimens were collected according to a protocol approved by the ethics committee of the Ruhr-University Bochum (permission no. 2534-09 and 2392-04). Three to five 12µm FFPE tissue slices were extracted using the NuGEN BioMinute kit. The tissue slices were extracted using the NuGEN BioMinute kit. 7 miRNA model was extracted with a modified mirVana PARIS kit (Asuragen) and transcribed into cDNA using the NuGEN BioMinute kit. RT-qPCR was performed using the TaqMan® RT-qPCR 7900 system.

The development of the final miRInform™ Pancreas LDT classified specimens as PDAC (scores >0.5) and Benign (scores <0.5).

Validity

The development of the final model in accordance with CLIA and CAP guidelines using a blinded set of FFPE specimens, with the sensitivity and specificity of approximately 95%.

miRInform™ Pancreas LDT classified specimens as PDAC (scores >0.5) and Benign (scores <0.5).

CONCLUSIONS

Using 95 FFPE pancreatic specimens and 186 FNA specimens preserved in RNAstabilisation, we developed and validated a seven miRNA model comprised of miR-130b, -135b, -148a, -196a, -375, -96 and -24 intended to aid in obtaining a differential diagnosis between PDAC and benign pancreatic diseases. This test, the miRInform™ Pancreas LDT, was validated the Asuragen CLIA Laboratory in accordance with CLIA and CAP regulations. When used in conjunction with conventional FNA cytology, this test allows diagnosis of PDAC with 92.5% accuracy, as compared to 80.6% for FNA alone. It also enables resolution of indeterminate FNA cytology specimens, including Acetate, Suspicious, and Non-diagnostic, with an overall accuracy of 78.2%.

REFERENCES