A Non-Invasive Diagnostic combining a miRNA Signature with Radiological Features for Early Detection of Malignancy in IPMN

Intraductal papillary mucinous neoplasms (IPMN) are pancreatic cancer precursors discovered (often incidentally) through CT scans or MRI imaging, and in the absence of timely medical intervention (surgical resection), can quickly transform into pancreatic cancer with a 5-year survival of just 6%. However, it is extremely difficult to differentiate malignant IPMN from benign ones this early in the disease process. The standard clinical guidelines routinely used for this purpose rely on radiologic features (called High Risk Stigmata, HRS) and lack accuracy. As a result some patients are inaccurately considered malignant based on HRS, and vice versa. This technology combines 5 miRNAs detected in the plasma with HRS to more accurately determine malignancy of IPMNs at an early stage to improve clinical outcomes with an AUC=0.95.

COMMERCIAL OPPORTUNITY

- Currently, precancerous IPMN are nearly half of the 150k pancreatic cysts discovered incidentally in CT or MRI scan-based studies each year. However, clinical management of these cysts is difficult due to the difficulty in accurately predicting malignancy in a timely manner. Current guidelines use a radiologic presentation called HRS as indicators of malignancy, and candidates for surgical resection. However, these criteria are not accurate and can result in resection of benign patients who display HRS, or no surgical invention for malignant patients who appear benign due to the absence of HRS.
- The addition of five miRNAs from blood plasma to the physician algorithm might work well as HRS is the preferred current non-invasive method of determining which cysts are malignant or benign. However, in a study of 38 patients it was shown that the sensitivity and specificity of HRS were 83% and 85%, respectively. In this example 3/20 benign IPMNs had HRS and 3/18 malignant IPMNs did not have HRS. Combining the miRNA signature with HRS results in a sensitivity and specificity of 0.94 and 0.90.
- miRNAs represent ideal candidates for overcoming limitations of single blood-based biomarkers because they can reflect physiological and pathological conditions and act as extracellular messengers of biological signals derived from the cross talk between the tumor and its microenvironment.

TECHNOLOGY

The technology uses a combination of five miRNAs (miR-200a-3p, miR-1185-5p, miR-33a-5p, miR-574-4p, and miR-664b) and HRS radiological features including main duct involvement >10mm, obstructive jaundice with a cystic lesion in pancreatic head, or an enhanced solid component or nodule within the cyst. Blood plasma samples were taken from 42 surgically-resected and pathologically confirmed IPMN patients pre-operatively, and this cryopreserved plasma was thawed and analyzed for the presence of the 5 miRNA signature using an miRNA assay called miRNA Expression Assay Codeset (Nanotechnologies). This miRNA signature and HRS were better at predicting malignancy than standard HRS alone (AUC= 0.95 (95% CI= 0.88-1.00), Sensitivity/ True Positive Rate = 0.94, Specificity/ True Negative Rate = 0.90, PPV (True positives as a proportion of all positives) = 0.89, NPV (True negatives as a proportion of all negatives) = 0.95).

PUBLICATION/PATENT

- A provisional patent has been filed in 2017 for Dr. Permuth.
- Publication by Permuth et al. in Oncotarget, 2016, Vol. 7, (No. 52), pp: 85785-85797

CONTACT

Haskell Adler PhD MBA CLP
Senior Licensing Manager
Haskell.Adler@Moffitt.org
(813) 745-6596

LICENSING OPPORTUNITY

MOFFITT CANCER CENTER

17MA001.2018.03