

A Non-Invasive Diagnostic Combining a miRNA Signature with Radiologic Features to Identify Malignant Pancreatic Cysts



Intraductal papillary mucinous neoplasms (IPMN) are pancreatic cancer precursors typically discovered incidentally by CT or MRI scans performed for reasons unrelated to the pancreas. In the absence of timely medical intervention (surgical resection), some IPMNs can quickly transform into pancreatic cancer which has a 5-year survival of just 9%. Clinically, it is extremely challenging to differentiate 'malignant' IPMNs that should be surgically removed from 'benign' IPMNs that can undergo surveillance. Consensus guidelines routinely rely on radiologic features to predict malignant potential, but these guidelines lack accuracy and result in over- and under-treatment. This technology leverages 5 miRNAs detected in plasma to provide more accurate risk stratification.

COMMERCIAL OPPORTUNITY

- Precancerous IPMNs account for nearly half of the 150,000 pancreatic cysts discovered incidentally on CT or MRI scans each year. However, clinical management of these cysts is challenging due to the difficulty in accurately predicting malignancy in a timely manner. Current guidelines use radiologic characteristics classified as high-risk stigmata (HRS) and worrisome features (WF) to identify appropriate candidates for surgical resection. However, these criteria lack accuracy in predicting final pathology and can result in resection of benign disease (over-treatment) or no surgical intervention for malignant disease (under-treatment).
- There is an unmet need to develop a readily-available, cost-effective, and accurate blood-based biomarker test that can act as a diagnostic adjunct to radiologic characteristics and help improve diagnostic performance, especially for individuals who only present with WF.
- miRNAs represent ideal candidates for overcoming limitations of single blood-based biomarkers because they reflect physiological and pathological conditions and act as extracellular messengers of biological signals derived from the cross talk between the tumor and its microenvironment.
- The addition of five miRNAs obtained pre-operatively from blood plasma increases diagnostic performance and can aid with medical decision-making, especially when combined with a new set of quantitative 'radiomic' features hidden to the radiologist's eyes .

TECHNOLOGY

The technology includes a panel of five miRNAs (miR-200a-3p, miR-1185-5p, miR-33a-5p, miR-574-4p, and miR-664b) discovered using the miRNA Expression Assay Codeset (Nanosttring, Inc). This diagnostic would be incorporated as part of an algorithm that also considers presence of HRS (main duct involvement >10mm, obstructive jaundice with a cyst in pancreatic head, or an enhanced solid component or nodule within the cyst), WF (main duct dilation 5-9 mm, cyst size > 3 cm, thickened enhanced walls, non-enhanced mural nodules), and 14 radiomic features.

This miRNA signature and HRS were better at predicting malignancy than HRS alone (AUC= 0.95 (95% CI= 0.88-1.00), Sensitivity/True Positive Rate = 0.94, Specificity /True Negative Rate = 0.90, Positive predictive value (True positives as a proportion of all positives) = 0.89, Negative Predictive Value (True negatives as a proportion of all negatives) = 0.95). The miRNA signature and WF were also better at predicting malignancy than WF alone, especially when combined with radiomic features (AUC=0.93).

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

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