EVALUATING TISSUE AND PLASMA MIRNAS AS BIOMARKERS OF HIGH-RISK PANCREATIC CYSTS

Presented by:
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Assistant Member
Departments of Cancer Epidemiology and Gastrointestinal Oncology
Objectives

- Describe why early detection research is needed for pancreatic cancer.
- Understand how molecular studies of tissue and blood can improve diagnostic abilities for pre-cancerous lesions of the pancreas.
- Appreciate the importance of a multidisciplinary approach to cancer diagnosis and treatment.
### Leading Causes of Cancer Deaths in the US

<table>
<thead>
<tr>
<th>Estimated Deaths</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>84,590</td>
<td>71,280</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>27,150</td>
<td>40,610</td>
</tr>
<tr>
<td>Prostate</td>
<td>26,730</td>
<td>23,110</td>
</tr>
<tr>
<td>Pancreas</td>
<td>22,300</td>
<td>20,790</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>19,610</td>
<td>14,080</td>
</tr>
<tr>
<td>Leukemia</td>
<td>14,300</td>
<td>10,920</td>
</tr>
<tr>
<td>Esophagus</td>
<td>12,720</td>
<td>10,200</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>12,240</td>
<td>9,310</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>11,450</td>
<td>8,690</td>
</tr>
<tr>
<td>Brain &amp; other nervous system</td>
<td>9,620</td>
<td>7,080</td>
</tr>
<tr>
<td>All sites</td>
<td>318,420</td>
<td>282,500</td>
</tr>
</tbody>
</table>
Pancreatic Cancer is Projected to Become the 2nd Leading Cancer Killer by 2020
The urgent need for early detection and prevention strategies for pancreatic cancer (PC)

- Early, operable tumors are difficult to detect.
  - Anatomic location of the pancreas
  - Symptoms occur LATE in the disease process
  - No existing biomarkers accurately detect disease EARLY
PRIME OPPORTUNITY FOR EARLY DETECTION AND PREVENTION EFFORTS

Precursors to pancreatic cancer
Three pancreatic cancer precursors exist

Pre-cancerous pancreatic cysts

IPMN=intraluductal papillary mucinous neoplasms
MCN=mucinous cystic neoplasms

Distler et al (2014), Biomed Research International
Illustration of the degrees of IPMN dysplasia

From Castellano-Megias (2014), World Journal of Gastrointestinal Oncology
IPMN

- Account for up to 40% of the ~150,000 pancreatic cysts detected incidentally each year.

- Challenging to manage due to the inability to predict:
  - which lesions can be safely monitored,
  - which are likely to progress to invasion, and
  - which may have an associated invasive component.

- Only way to accurately determine severity is surgery & pathologic evaluation.

- Consensus guidelines exist to predict IPMN pathology…
Fukuoka Consensus Guidelines for IPMN management

High risk stigmata or malignancy present?
1. Obstructive jaundice
2. Enhancing solid component within cyst
3. Main pancreatic duct >10 mm in size

Yes
Consider resection if clinical condition permits

No

Worrisome features?
1. Pancreatitis
2. Cyst ≥3 cm
3. Thickened / enhancing cystic walls
4. MPD: 5-9 cm
5. Non-enhancing mural nodules
6. Abrupt change MPD caliper with distal pancreatic atrophy

Yes
Endoscopic Ultrasound

No

Any of these present?
1. Definitive mural nodule
2. Main duct features suspicious for involvement
3. Cytology: suspicious or positive malignancy

Yes

<1 cm
CT / MR in 2-3 years

1-2 cm
CT/MRI yearly x2 year, then lengthen interval if no change

2-3 cm
EUS in 3-6 months, then lengthen interval alternating MRI with EUS as appropriate. Consider surgery in young, fit patient

>3 cm
Consider surveillance alternating MRI with EUS every 3-6 months. Strongly consider surgery in young, fit patients

No
Size of largest cyst

Inconclusive

Guidelines inaccurately predict pathology for 30-70% of cases!

Tanaka et al, Pancreatology (2012)
Long-Term Goal

Develop a noninvasive approach that can rapidly, cost-effectively, and accurately distinguish low-risk IPMNs that can be monitored from high-risk IPMNs that warrant resection.

Low-risk/Benign          High-risk/Malignant
Low-grade                High-grade
Moderate-grade           Invasive

Surveillance             Resection

Radiomic features → Gene expression
Clinical data/radiologic features

Aerts, Nat Comm 2014
Exploring Novel Hypotheses Related to ‘Non-coding RNA’

‘Non-protein-coding’ RNA
MicroRNAs (miRNAs) as attractive candidate biomarkers of early pancreatic malignancy

- regulate cancer-related pathways
  - Each miRNA can regulate 1000’s of genes.
- remarkably stable in tissue and biofluids
- dysregulated in PC vs. normal pancreas tissue
- a few candidate miRNAs differentiated between IPMNs and normal pancreas tissue (Habbe et al, 2009)

Objective

To retrospectively investigate 100’s of miRNAs using surgically-resected, pathologically-confirmed IPMN tissue and discover a miRNA signature that accurately differentiates:

- Low-risk IPMNs
- High-risk IPMNs
- Low-grade (A)
- Moderate-grade (B)
- High-grade (C)
- Invasive (D)

Surveillance → Low-risk IPMNs → Resection

Surveillance → High-risk IPMNs → Resection

Surveillance → Low-grade (A) Moderate-grade (B) → Resection

Surveillance → High-grade (C) Invasive (D) → Resection
RESEARCH ARTICLE

A Genome-Wide Investigation of MicroRNA Expression Identifies Biologically-Meaningful MicroRNAs That Distinguish between High-Risk and Low-Risk Intraductal Papillary Mucinous Neoplasms of the Pancreas

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Abstract

Background

Intraductal papillary mucinous neoplasms (IPMNs) are pancreatic ductal adenocarcinoma (PDAC) precursors. Differentiating between high-risk IPMNs that warrant surgical resection and low-risk IPMNs that can be monitored is a significant clinical problem, and we sought to discover a panel of mi(cro)RNAs that accurately classify IPMN risk status.
Evaluate the most deregulated miRNAs in an independent set of 21 IPMNs (13 high-risk, 8 low-risk) and assess correlations between miRNA expression and clinical characteristics.

Discovery (Aim 1)

Identify miRNAs significantly deregulated between 19 high-risk and 9 low-risk IPMN cases using archived tissue.

Validation (Aims 2 & 3)

Evaluate the most deregulated miRNAs in an independent set of 21 IPMNs (13 high-risk, 8 low-risk) and assess correlations between miRNA expression and clinical characteristics.

Follow-up (Aim 4)

Predict genes and pathways controlled by the most deregulated miRNAs. (bioinformatics and microarray analysis)
Methods

Identified Moffitt patients who underwent pancreatic resection for IPMNs between 1999 & 2011; selected and retrieved FFPE blocks.

Diagnosis and grade pathologically confirmed; regions selected; sectioning.

Laser capture microdissection (LCM) & RNA isolation.

miRNA expression analysis with Taqman Low Density Arrays (TLDA); 378 miRNAs + 6 controls.

Statistical Analysis (normalization, comparative CT method, non-parametric tests).

Aga Kasprzak

Susan McCarthy

Ann Chen

Kate Fisher

Mokenge Malafa

Vonetta Williams

Kavita Ghia

Michelle Fournier

Domenico Coppola

Lidia Espinosa
Heatmap (N=28) for the 25 most de-regulated miRNAs ($P<0.05$)
Candidate miRNAs *down-regulated* in high-risk (n=19) vs low-risk (n=9) IPMN tissue

<table>
<thead>
<tr>
<th>miRNA</th>
<th>P-value</th>
<th>Median Fold change</th>
<th>Mean Fold change</th>
<th>Experimentally validated gene target(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-100</td>
<td>$1.6 \times 10^{-3}$</td>
<td>5.9</td>
<td>4.9</td>
<td>ATM, FGFR3, IGF1R, MMP13, mTOR, PLK1, RPTOR</td>
</tr>
<tr>
<td>miR-99b</td>
<td>$2.7 \times 10^{-3}$</td>
<td>4.7</td>
<td>3.7</td>
<td>RAV2R2</td>
</tr>
<tr>
<td>miR-99a</td>
<td>$2.7 \times 10^{-3}$</td>
<td>4.8</td>
<td>4.7</td>
<td>AGO2, COX2, FGFR3, IGF1R, MEF2D, mTOR, RAVER2, RPTOR, SERPINE1, SKI, TRIB1</td>
</tr>
<tr>
<td>miR-342–3p</td>
<td>$3.7 \times 10^{-3}$</td>
<td>4.8</td>
<td>3.3</td>
<td>BMP7, DNMT1, GEMIN4</td>
</tr>
<tr>
<td>miR-126</td>
<td>$3.7 \times 10^{-3}$</td>
<td>3.1</td>
<td>6.7</td>
<td>ADAM9, CCNE2, CRH, CRK, CRKL, DNMT1, EGFL7, KRAS, HOXA9, IRS1, PGF, PIK3R2, PLK2, PTPN7, RGS3, SLC45A3, SOX2, SPRED1, TOM1, TWF2, VCAM1, VEGFA</td>
</tr>
<tr>
<td>miR-130a</td>
<td>$5.9 \times 10^{-3}$</td>
<td>4.7</td>
<td>5.0</td>
<td>APP, ATG2B, ATXN1, CSF1, Dicer1, ESR1, HOXA10, HOXA5, KLF4, MAFB, MEOX2, PARG, RUNX3, TAC1, TP53INP1</td>
</tr>
</tbody>
</table>

1 Wilcoxon rank-sum test.
2 All fold-changes represent *decreased* expression in the high-risk group (all high-grade IPMNs) versus the low-risk group (all low-grade IPMNs).
Box plots of candidate miRNA expression

Discovery

Validation

(N=9) (N=19) (N=8) (N=13)
Three candidate miRNAs discriminated high-risk from low-risk IPMNs

The 3-miR signature performed better than most clinical factors.
Correlations between clinical factors and miRNA expression

- Most factors were not correlated with miRNA expression level.
- Low miR-99b expression was associated with main duct involvement ($P=.021$).
  - Marker of histologic progression not observed pre-operatively for 6 high-grade cases.
- Serum albumin levels were positively correlated with miR-99a ($r=0.52$, $P=.004$) expression.
  - High serum albumin has been associated with longer survival in PC patients (and with low-risk IPMN status in our study).
Biological plausibility enhanced by:

**Bioinformatics analysis**

- Identified validated miRNA targets and pathways with relevance to pancreatic carcinogenesis.
  - *mTOR, PPARG, SOX2, VEGF-A, IRS1, B-catenin, PLK1*
  - histone deacetylase, calcium/calmodulin-dependent kinases, hypoxia inducible factor regulation, growth factor signaling

**Integration of TCC gene expression data**

- Several targets upregulated in invasive (n=17) vs non-invasive (n=6) IPMNs
  - *DNMT1* (target of miR-342-3p), 1.2x, P=0.032
  - *ATG2B* (target of miR-130a), 1.4x, P=0.046
  - *MEOX2* (target of miR-130a), 2.3x, P=0.046
  - *IRS1* (target of miR-126), 1.9x, P=0.054
Studies of genome-wide miRNA expression in IPMN tissue

<table>
<thead>
<tr>
<th></th>
<th>Matthaei</th>
<th>Lubezky</th>
<th>Permuth-Wey</th>
</tr>
</thead>
<tbody>
<tr>
<td>N IPMNs discovery</td>
<td>22</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>Platform (N miRs)</td>
<td>TLDA (750)</td>
<td>Gene Chip miR Array (850)</td>
<td>TLDA (378)</td>
</tr>
<tr>
<td>N IPMNs validation</td>
<td>23</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>Platform (N miRs)</td>
<td>qRT-PCR (26)</td>
<td>qRT-PCR (4)</td>
<td>qRT-PCR (6)</td>
</tr>
<tr>
<td>Most dereg. miRNAs</td>
<td>miR-24, 30a, 18a, 92a, 342-3p, 99b, 106b, 142-3p, 523-3p</td>
<td>miR-217, 21, 708, 155</td>
<td>miR-100, 99a, 342-3p, 99b, 126, 130a</td>
</tr>
</tbody>
</table>
Conclusions

Our study:

- highlights novel miRNAs that may aid in predicting the severity of an IPMN.
- provides insights into miRNA-mediated progression to pancreatic malignancy.
- supports developing a noninvasive miRNA-based test to aid in pre-operative clinical decision making.

Permuth-Wey et al, *PLOS ONE* 2015
Genomic Research Advances Pancreatic Cancer’s Early Detection and Treatment

By Vicki Brower

Individualizing treatment according to a patient’s genomic mutations is imperative, which means using whole-genome sequencing to diagnose. An earlier study by the same group examined only the exomes, or the protein-coding genes, of the same 100 patients. That study revealed genomic complexity but was insufficient to guide treatment, Biankin said.

With a 5-year survival rate of only 6%, pancreatic cancer is the fourth-highest cause of cancer death but is expected to move to second place by 2030. It is unique among cancers not only because of its complex mutational landscape but also because it is extremely difficult to diagnose in the early stages. Alongside the need for new, effective treatments is an urgent need for early diagnosis and the ability to distinguish between benign conditions and cancer, preferably noninvasively. To meet this need, several recent studies based on microRNAs, or miRNAs, are showing promise for noninvasive tests. “miRNAs are small molecules which function as master regulators and control many cancer-related processes,” said Jennifer Permuth Wey, Ph.D., assistant member of the departments of cancer epidemiology and gastrointestinal oncology at the Moffitt Cancer Center in Tampa, Fla.

Two biomarkers, CA 19-9 (cancer antigen 19-9) and CEA (carcinoembryonic antigen), used to indicate disease progression, lack good specificity and sensitivity, and cannot be used for screening. CA 19-9 is not known to be detected in pancreatic cancer, Permuth Wey said. “We knew that miRNAs could offer potential diagnostic utility, but we didn’t know that we could use them for treatment,” she said.

miRNAs for Early Detection

In the past 5 years, an explosion of miRNA research has occurred, as has much of the work related to pancreatic cancer precursors such as intraductal papillary mucinous neoplasms (IPMNs). More than 1,000 miRNAs are known; some are tumor suppressors, whereas others are oncogenes, Rustgi said. Predictably stable, miRNAs are detectable in blood, plasma, and tumor tissues.

“The advent of miRNA research has opened new avenues to understand mechanisms that may contribute to pancreatic carcinogenesis,” Permuth Wey said. “There’s been a push for miRNA research because they represent excellent candidate biomarkers of early disease,” she said.

miRNAs have tissue-specific expression patterns, can be reliably and reproducibly measured in tissue and biological fluids because of their small size and stability, and can regulate hundreds of cancer-related genes and pathways, she said. Researchers are examining sets of miRNAs found in many settings—including those in peripheral blood, serum, plasma, and tumor tissue—to determine which is most reliable. A general acknowledgment exists that what is found in tissue may not be found in blood or its components, Permuth Wey said.

Permuth Wey and colleagues set out to identify miRNAs that would differ features,” she said.

To find biomarkers for early diagnosis of pancreatic cancer, scientists led by Motohiro Kojima, M.D., Ph.D., of the National Cancer Center Hospital East pathology division in Chiba, Japan, examined miRNA expression in 571 blood samples: 150 from healthy patients, 100 with pancreatic cancer, 98 with biliary-duct cancer, 21 with nonmalignant pancreatic or biliary disorders, and 202 with other cancers (PLoS One, Feb. 25, 2015; doi:10.1371/journal.pone.0118220).

Among 100 pancreatic cancer patients, they found 81 miRNAs for pancreatic cancer and 66 for biliary-duct cancer that had statistically significantly different expression from that of the healthy control group. Between both groups, 55 were common for both cancer types, making it difficult to find only pancreatic cancers. Eight miRNAs achieved sensitivity for pancreatic cancer of 80.3%, specificity of 97.6%, and accuracy of 91.6%, in contrast to CA 19-9 and CEA, which had sensitivities of 65.6% and 40%, specificities of 92.9% and 88.6%, and accuracies of 82.1% and 71.8%, respectively. This panel of miRNAs identified 18 of 21 operable pancreatic cancers and 38 of 48 operable biliary-tract cancers.

miRNAs for Treatment Choice

Using data from the Cancer Genome Atlas, Permuth Wey and colleagues found that patients in whom the levels of a single miRNA were above a certain level had significantly worse survival, Permuth Wey said. “This panel of miRNAs could be highly useful in predicting early stage disease and for treatment decisions,” she said.

Permuth Wey and colleagues said that miRNAs could also be used to identify miRNAs that would differ in expression in response to treatment. They used microarray analysis to identify 15 miRNAs that dropped in expression in response to gemcitabine, the standard chemotherapy treatment used for patients with metastatic pancreatic cancer.

“gemcitabine is the gold standard of treatment, and we wanted to identify the molecular mechanisms of its action, and the miRNAs that would be found to be downregulated in response to treatment,” Permuth Wey said. Gemcitabine undergoes deamination, which decreases its toxicity, and expression of a single miRNA was associated with the decrease in gemcitabine toxicity,” she said.
Blood-based studies of miRNAs in patients with PC or IPMNs?

- Studies of miRNA expression in blood of PC patients vs. controls exist.
  - Most detected deregulated miRNAs.
  - But, most cases had locally advanced or metastatic PC.
Evaluating Circulating miRNAs as Biomarkers of High-risk Pancreatic Cysts

Aim 1: To identify miRNAs differentially expressed in archived pre-operative plasma from individuals with IPMNs versus age- and gender-matched individuals without IPMNs.

Aim 2: To identify plasma miRNAs that reliably differentiate between IPMN grades.

Aim 3: To determine whether the plasma miRNA profile in IPMN patients mimics the paired tumor miRNA profile.
Plasma MicroRNAs as Novel Biomarkers for Patients with Intraductal Papillary Mucinous Neoplasms of the Pancreas

Jennifer Permutt-Wey et al.

Abstract

Pancreatic ductal adenocarcinoma (PDAC) is one of the most fatal cancers worldwide, partly because methods are lacking to detect disease at an early, operable stage. Non-invasive PDAC precursors called intraductal papillary mucinous neoplasms (IPMN) exist and strategies are needed to aid in their proper diagnosis and management. Data support the importance of microRNAs in the progression of IPMNs to malignancy, and we hypothesized that miRNAs may be shed from IPMN tissues and detected in blood. Our primary goals were to measure the abundance of miRNAs in archived preoperative plasma from individuals with pathologically confirmed IPMNs and healthy controls and characterize plasma miRNAs that distinguish between IPMN patients and controls and between “malignant” and “benign” IPMNs. Using novel nCounter technology to evaluate 800 miRNAs, we showed that a 30-miRNA signature distinguished 42 IPMN cases from 24 controls (area under the curve (AUC) = 0.86; 95% confidence interval (CI), 0.73–0.99; P = 0.0002). The signature contained novel miRNAs and miRNAs previously implicated in pancreatic carcinogenesis that had 2- to 4-fold higher expression in cases than controls. We also generated a 5-miRNA signature that discriminated between 21 malignant (high-grade dysplasia and invasive carcinoma) and 21 benign (low- and moderate-grade dysplasia) IPMNs (AUC = 0.83; 95% CI, 0.68–0.98; P = 0.05), and showed that paired plasma and tissue samples from patients with IPMNs can have distinct miRNA expression profiles. This study suggests feasibility of using new cost-effective technology to develop a miRNA-based blood test to aid in the preoperative identification of malignant IPMNs that warrant resection while sparing individuals with benign IPMNs the morbidity associated with overtreatment. Cancer Prev Res (Phila) 9(9): 826–34. ©2016 AACR.
Methods

- Plasma retrieval and thawing
- Spike-in oligos added
- Total RNA extraction
- RNA integrity & concentration assessed
- Hemolysis evaluation
- Measure miRNA abundance
Nanostring’s nCounter Human v2 miRNA Expression Assay Codeset

Codeset contains: 800 human miRNAs
- 6 positive controls
- 8 negative controls
- 5 human mRNA housekeeping genes
Data Processing, QC, and Analysis

- Background correction
- Evaluate possible contamination
- Data normalization using spike-ins
- Biological normalization using stable/invariant miRNAs

Development of an IPMN miRNA signature:
Linear models for microarray data (LIMMA) and principal component analysis
Study Population Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>IPMN cases (n=42)</th>
<th>Healthy controls (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)(yrs)</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis/interview</td>
<td>69.0 (10.7)</td>
<td>69.1 (9.6)</td>
</tr>
<tr>
<td>Gender, male: female, n (%)</td>
<td>19:23 (45:55)</td>
<td>12:12 (50:50)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>White, Non-Hispanic</td>
<td>37 (88)</td>
<td>24 (100)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (12)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Family history of pancreatic cancer, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>4 (17)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>No</td>
<td>15 (83)</td>
<td>23 (96)</td>
</tr>
<tr>
<td>Ever Smoker, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>21 (50)</td>
<td>11 (46)</td>
</tr>
<tr>
<td>No</td>
<td>21 (50)</td>
<td>3 (13)</td>
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<tr>
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<td>0 (0)</td>
<td>10 (42)</td>
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<tr>
<td>IPMN Grade, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>Low</td>
<td>4 (9.5)</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>17 (40.5)</td>
<td>-</td>
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<tr>
<td>High</td>
<td>13 (31)</td>
<td>-</td>
</tr>
<tr>
<td>Invasive</td>
<td>8 (19)</td>
<td>-</td>
</tr>
</tbody>
</table>

Data represent counts (percentages) unless otherwise indicated. Counts may not add up to the total due to missing values, and percentages may not equal 100 due to rounding.
Results: A 30-miRNA signature discriminates IPMN cases from controls

let-7a-5p, let-7d-5p, let-7f-5p, let-7g-5p, let-7i-5p, miR-107, miR-1260b, miR-126-3p, miR-142-3p, miR-145-5p, miR-146a-5p, miR-148a-3p, miR-15b-5p, miR-181a-5p, miR-191-5p, miR-199a-3p, miR-199b-3p, miR-20a-5p, miR-20b-5p, miR-22-3p, miR-23a-3p, miR-24-3p, miR-26a-5p, miR-27a-3p, miR-29c-3p, miR-335-5p, miR-337-5p, miR-340-5p, miR-423-5p, miR-4454, miR-593-3p, miR-98

Permuth-Wey et al, Cancer Prevention Research 2015
Results: 5 miRNAs differentiated between low-risk and high-risk IPMN cases

miR-200a-3p, miR-1185-5p, miR-33a-5p, miR-574-3p, and miR-663b

AUC=73.2 (95% CI:57.6-88.9)
P=0.005

‘Cell cycle’ and Wnt signaling’ were among top-ranked pathways predicted to be regulated by the 5-miR signature.

Permuth-Wey et al, Cancer Prevention Research, 2015
Plasma miRNA expression levels did not mimic miRNA expression profiles in tumors

- Evaluated matched plasma and tissue from 12 IPMNs.
  - Of 160 miRNA probes evaluated in both specimen types, expression levels of only 3 miRNAs (miR-484, miR-330-5p, miR-574-3p) were significantly positively correlated (P<0.05).

- Possible explanations for this observation:
  - Blood or normal cell contamination.
  - Heterogeneity of the primary tumor.
  - Locoregional inflammation reflecting a response of the host microenvironment to disease.

Permuth-Wey et al (Cancer Prevention Research)
Summary

- Our proof-of-principle study:
  - demonstrates feasibility of evaluating plasma miRNAs using nCounter technology™ for improved prediction of IPMN pathology.

- Underway:
  - Multi-center prospective study
    - clinical, radiologic, & epidemiologic data
    - novel classes of molecular markers
      - circulating long non-coding RNAs
      - circulating tumor DNA (ctDNA) mutations
  - novel imaging features (‘radiomics’)
Partnering to advance early detection and prevention efforts for pancreatic cancer: the Florida Pancreas Collaborative

Jennifer B Permut*1,2, Jose Trevino3, Nipun Merchant4 & Mokenge Malafa2; on behalf of the Florida Pancreas Collaborative

First draft submitted: 22 January 2016; Accepted for publication: 26 January 2016; Published online: 10 February 2016

Team science as a necessity for making advancements in pancreatic cancer research

“Alone we can do so little; together we can do so much.” This quote by Helen Keller embodies the overarching goal of transdisciplinary team science, which is to bring together investigators, community partners and translational collaborators from various disciplines and fields to integrate concepts, theories, methods and approaches from a breadth of expertise to solve real-world clinical problems [1]. Team science is desperately needed to make advances in the battle against pancreatic cancer, the fourth and incidence and death rates, pancreatic cancer is projected to surpass breast, prostate and colorectal cancer and become the second leading cause of cancer deaths by 2020 [1]. Thus, it is critical that researchers and funding agencies invest in transdisciplinary pancreatic cancer research efforts now.

Focusing on early detection & prevention by studying commonly detected pancreatic cancer precursors

Approximately 85% of patients with pancreatic cancer present with advanced

KEYWORDS

• early detection • multi-institutional collaborations • pancreatic cancer

“...the overarching goal of transdisciplinary team science ... is to bring together investigators, community partners and translational collaborators from various disciplines and fields to integrate concepts, theories, methods and approaches from a breadth of expertise to solve real-world clinical problems.”
Thanks to an interdisciplinary team
..and PC survivors and advocates
‘Know it. Fight it. End it. Wage Hope.’