Risk Factors and Early Detection Efforts for Pancreatic Cancer

by

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Outline

- Introduction to pancreatic cancer
- Known risk factors
  - Environmental/Lifestyle
  - Genetic
  - Risk assessment
- Research on PC screening and early detection biomarkers
- Resources
INTRODUCTION
Leading Causes of Cancer Deaths in the US

Estimated Deaths

**Male**
- Lung & bronchus: 85,920 (27%)
- Prostate: 26,120 (8%)
- Colon & rectum: 26,020 (8%)
- Pancreas: 21,450 (7%)
- Liver & intrahepatic bile duct: 18,280 (6%)
- Leukemia: 14,130 (4%)
- Esophagus: 12,720 (4%)
- Urinary bladder: 11,820 (4%)
- Non-Hodgkin lymphoma: 11,520 (4%)
- Brain & other nervous system: 9,440 (3%)
- All sites: 314,290 (100%)

**Female**
- Lung & bronchus: 72,160 (26%)
- Breast: 40,450 (14%)
- Colon & rectum: 23,170 (8%)
- Pancreas: 20,330 (7%)
- Ovary: 14,240 (5%)
- Uterine corpus: 10,470 (4%)
- Leukemia: 10,270 (4%)
- Liver & intrahepatic bile duct: 8,890 (3%)
- Non-Hodgkin lymphoma: 8,630 (3%)
- Brain & other nervous system: 6,610 (2%)
- All sites: 281,400 (100%)

*Pancreatic ductal adenocarcinoma (PDAC)*
Pancreatic Cancer is Projected to Become the 2nd Leading Cancer Killer by 2020

Rahib, Can Res 2014
PC poses numerous clinical challenges

- Usually very aggressive.
- Early, operable tumors are difficult to detect.
- Need strategies to identify those ‘at increased risk.’
- Most patients do not respond to standard treatment options.
- Quality of life (QOL) is sub-optimal.
RISK FACTORS AND ASSESSMENT
Modifiable and non-modifiable risk factors

- Average age: 71
- Males
- African American
- Ashkenazi Jewish
- Obesity
- Pancreatitis
- Diabetes
  - chronic & new
  - Infections
- Familial
- Inherited cancer syndrome
# Ranking of individual risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Population Exposed</th>
<th>Relative Risk</th>
<th>Attributable Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco smoking</td>
<td>25-40%</td>
<td>1.5-2.2</td>
<td>PAF 11-32%</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em> infection</td>
<td>25-50%</td>
<td>1.2-1.7</td>
<td>PAF 4-25%</td>
</tr>
<tr>
<td>Non-O blood group</td>
<td>50-60%</td>
<td>1.3-1.4</td>
<td>PAF 13-19%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4-17%</td>
<td>1.4-2.2</td>
<td>PAF 1-16%</td>
</tr>
<tr>
<td>Obesity</td>
<td>20-40%</td>
<td>1.2-1.5</td>
<td>PAF 3-16%</td>
</tr>
<tr>
<td>Reducing adiponectin level</td>
<td>Continuous</td>
<td>1.6*</td>
<td>PIF 11%</td>
</tr>
<tr>
<td>Increasing red or processed meat</td>
<td>Continuous</td>
<td>1.1-1.5*</td>
<td>PIF 2-9%</td>
</tr>
<tr>
<td>Heavy alcohol intake</td>
<td>5-20%</td>
<td>1.1-1.5</td>
<td>PAF &lt;9%</td>
</tr>
<tr>
<td>Family history</td>
<td>5-10%</td>
<td>1.7-1.8</td>
<td>PAF 3-7%</td>
</tr>
<tr>
<td>History of chronic pancreatitis</td>
<td>0-1%</td>
<td>2.7-5.1</td>
<td>PAF &lt;3%</td>
</tr>
<tr>
<td><em>Hepatitis B</em> infection</td>
<td>0-5%</td>
<td>1.2-1.4</td>
<td>PAF &lt;1%</td>
</tr>
<tr>
<td>History of cholecystectomy</td>
<td>4-8%</td>
<td>1.2</td>
<td>PAF &lt;1%</td>
</tr>
<tr>
<td>History of gastrectomy</td>
<td>1-2%</td>
<td>1.5</td>
<td>PAF &lt;1%</td>
</tr>
<tr>
<td>Increasing physical activity</td>
<td>Continuous</td>
<td>0.75*</td>
<td>PIF (5%)</td>
</tr>
<tr>
<td>History of allergy</td>
<td>10-20%</td>
<td>0.7-0.8</td>
<td>PPF (3-7%)</td>
</tr>
<tr>
<td>Increasing fruit or folate intake</td>
<td>Continuous</td>
<td>0.5-1.0*</td>
<td>PIF (&lt;12%)</td>
</tr>
</tbody>
</table>

Maisonneuve and Lowenfels, *IJE* 2015
Sporadic vs. Familial vs. Inherited PC

Risk increases with # of affected first degree relatives (FDR):
2-4.6x (1 FDR),
3-6.4x (2 FDR),
32-57x (3 FDR)

90%

(Average lifetime risk = 1 in 67 (1.5%))

## Inherited Predisposition to PC

<table>
<thead>
<tr>
<th>Inherited Syndrome</th>
<th>Gene(s)</th>
<th>Risk by age 70-75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary Breast and Ovarian Cancer</td>
<td>BRCA2, BRCA1, PALB2</td>
<td>4.5-8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.6%</td>
</tr>
<tr>
<td>Peutz-Jeghers</td>
<td>STK11/LKB1</td>
<td>36%</td>
</tr>
<tr>
<td>Familial atypical multiple-mole melanoma (FAMMM)</td>
<td>p16/CDKN2A</td>
<td>13-17%</td>
</tr>
<tr>
<td>Hereditary non-polyposis colorectal cancer</td>
<td>MSH2, MLH1, MSH6, PMS1, PMS2</td>
<td>3.7%</td>
</tr>
<tr>
<td>Familial adenomatous polyposis</td>
<td>APC</td>
<td>1.7%</td>
</tr>
<tr>
<td>Ataxia telangiectasia</td>
<td>ATM</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Li Fraumeni</td>
<td>TP53</td>
<td>&lt;5</td>
</tr>
<tr>
<td><strong>Syndromes with chronic inflammation of the pancreas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary pancreatitis</td>
<td>PRSS1, SPINK1</td>
<td>25-54%</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>CFTR</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Tidbits about BRCA2 carriers and PC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-6x increased PC risk (vs. non-carriers)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>~10% of BRCA2+ families have &gt;1 relative with PC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA2 mutations are identified in 4-17% of families with familial PC, and are the most common alteration in this condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence of BRCA2 mutations in patients with sporadic PC is 4-7% vs. 0.2% in general population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA2 mutations (6174delT) are associated with 10-20% of unselected, sporadic PC in Ashkenazi Jews</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with BRCA2+ PC are younger than counterparts with sporadic PC (63 vs 70 years old)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The survival rate in patients with familial PC tends to be better than those with sporadic PC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Rare and common genetic variants contribute to PC susceptibility

What is *my* risk to develop PC?
**Risk assessment is provided during genetic counseling (www.nsgc.org)**

<table>
<thead>
<tr>
<th>PancPro</th>
<th>Absolute risk model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provides probability of:</td>
<td>Provides probability of:</td>
</tr>
<tr>
<td>- carrying a concerning mutation in a PC</td>
<td>- developing PC</td>
</tr>
<tr>
<td>susceptibility gene</td>
<td></td>
</tr>
<tr>
<td>- developing PC</td>
<td></td>
</tr>
<tr>
<td>Takes into account:</td>
<td>Takes into account:</td>
</tr>
<tr>
<td>- cancer history for counselee and family</td>
<td>- Established risk factors (age, sex, ethnicity, smoking</td>
</tr>
<tr>
<td>members, age(s) at diagnosis, and current</td>
<td>history, diabetes, alcohol use, family history, body mass</td>
</tr>
<tr>
<td>age/age at last follow-up</td>
<td>index, common genetic variants)</td>
</tr>
</tbody>
</table>

Wang, JCO, 2007  
Klein, PLoS One, 2013
What can I do about my risk? 

Is it possible to prevent PC cancer or detect it really early?
PRIME OPPORTUNITY FOR EARLY DETECTION AND PREVENTION EFFORTS

Precursors to pancreatic cancer
Three pancreatic cancer precursors exist

Pre-cancerous pancreatic cysts

IPMN=intrductal papillary mucinous neoplasms
MCN=mucinous cystic neoplasms

Distler et al (2014), *Biomed Research International*
IPMNs

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

- **Detected in high-risk cohorts.**
  - Found more often in familial than sporadic cases.

- **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.
Need better strategies to identify ‘concerning’ IPMNs

- Only *accurate* way to determine severity
  - surgery & pathologic evaluation

- Consensus guidelines exist to predict IPMN severity

- based on standard clinical and radiologic features.

- inaccurate for at least 30-70% of cases!
### ‘Screening’ for Pancreatic Cancer

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Visualization and Accuracy</th>
<th>Radiation Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic ultrasound (EUS) +/- Fine needle aspiration (FNA)</td>
<td>Can detect lesions &lt;1 cm; FNA allows cytological sampling, but is invasive; operator dependent</td>
<td></td>
</tr>
<tr>
<td>MRI-MRCP</td>
<td>Best visualization of cyst communication with main pancreatic duct</td>
<td></td>
</tr>
<tr>
<td>Computed Tomography (CT)</td>
<td>Can visualize large lesions; accurate in depicting vascular invasion and metastases; radiation exposure</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:**
- MRI-MRCP = Magnetic Resonance Imaging (MRI)-Magnetic resonance cholangiopancreatography (MRCP)
Comparison of selected screening strategy recommendations

<table>
<thead>
<tr>
<th>Cancer Syndromes</th>
<th>International Cancer of the Pancreas Screening (CAPS) Consortium</th>
<th>American College of Gastroenterology (ACG)</th>
<th>National Comprehensive Cancer Network® (NCCN®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History</td>
<td>• ≥ 3 close relatives (at least 1 first degree) with PDAC</td>
<td>• Start age 50, Q1-Y, EUS or MRI or MRCP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ≥ 2 first degree relatives with PDAC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Start age 50, Q1-2Y EUS or MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA</td>
<td>• ≥ 1 first degree relative with PDAC</td>
<td>• ≥ 1 FDR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ≥ 2 close relatives with PDAC</td>
<td>Start age 50, Q1-2Y EUS or MRI</td>
<td></td>
</tr>
<tr>
<td>Lynch</td>
<td>• ≥ 1 first degree relative with PDAC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Start age 50, Q1-2Y EUS or MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peutz-Jegher</td>
<td>• All patients</td>
<td>• All patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Start younger, Q1-2Y EUS or MRI</td>
<td>• Start age 30, Q1-2Y EUS or MRCP</td>
<td></td>
</tr>
<tr>
<td>Li Fraumeni</td>
<td>• All patients</td>
<td></td>
<td>All patients</td>
</tr>
<tr>
<td></td>
<td>• Start age 30-35, Q1-2Y EUS or MRCP</td>
<td>• Annual whole body MRI</td>
<td></td>
</tr>
<tr>
<td>FAMMM</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Nearly all studies reported precursor lesions (mostly IPMNs).
Tests are complementary rather than interchangeable.
Prevalence of lesions increased with age.
CT, MRI, and EUS detected abnormalities in 11%, 33.3%, and 42.6% of individuals, respectively (Canto, 2012)
Prevalence of pancreatic cysts in the general population approximates 20-23%.
Candidates for screening:
- FDR of patient with PC from a familial PC kindred with ≥2 affected FDRs; patients with PJS; p16, BRCA2, and HNPCC mutation carriers with ≥1 affected FDR

No consensus on age to initiate screening or stop surveillance

Initial screening should include EUS and/or MRI/MRCP
- accessible, low morbidity, good concordance for lesion size, number, & location; EUS better for detecting small solid lesions; MRI sensitive for small cysts

Need long-term multicenter studies
EARLY DETECTION
BIOMARKERS FOR PC

Research in Progress at Moffitt Cancer Center
Painting a Radiogenomic Portrait of Early Pancreatic Cancer

- Develop a clinical decision-making tool that has added diagnostic value in predicting IPMN pathology beyond that provided by standard radiologic and clinical characteristics.
  - non-invasive
  - cost-effective
  - reliable
  - objective
  - can easily be integrated clinically

Low-risk IPMN (low- or moderate grade) Surveillance

High-risk IPMN (high-grade or invasive) Surgery

Funding Decision Pending: NCI (PI: J. Permuth)
MicroRNAs (miRNAs) as attractive candidate biomarkers of early pancreatic malignancy

- regulate cancer-related pathways.
  - Each miRNA regulates 100’s-1000’s of genes.
- remarkably stable in tissue and biofluids.
- dysregulated in PC vs. normal pancreas tissue.
- differentiate between IPMN grade and/or normal pancreas tissue\(^1,2,3,4,5\).

\(^1\) Habbe 2009; \(^2\) Park 2011; \(^3\) Matthaei 2012;
\(^4\) Lubezky 2013; \(^5\) Permuth-Wey 2015

Plasma MicroRNAs as Novel Biomarkers for Patients with Intraductal Papillary Mucinous Neoplasms of the Pancreas
Jennifer Pemthit-Wey, Dung-Tsa Chen, William J. Fulp, Sean J. Yoder, Yonghong Zhang, Christine Georgeades, Kazin Husain, Barbara Ann Centeno, Anthony M. Megliocci, Domenico Coppola, and McKenge Malafa

Abstract
Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers worldwide, partly because methods are lacking to detect disease at an early, operable stage. Noninvasive 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 miRNAs in the progression of IPMN 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 histologically confirmed IPMN and healthy controls and discover plasma miRNAs that distinguish between IPMN patients and controls and between “malignant” and “benign” IPMNs. Using microarray technology to evaluate 800 miRNAs, we showed that a 10-miRNA signature distinguished 42 IPMN cases from 24 controls (area underneath the curve [AUC] = 74.4; 95% confidence interval (CI): 62.3–86.5, P = 0.002). 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 = 73.2; 95% CI, 57.6–88.9, P = 0.005), 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 8(9): 826–34. ©2015 AACR.

Introduction
Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer deaths in the United States, with a 5-year survival rate of only 6% (1). Approximately 85% of cases present with metastases, which can be partly explained by a lack of accurate methods to detect disease at an early, operable stage (1). The detection and treatment of noninvasive precursor lesions may offer the greatest hope in reducing morbidity and mortality. None of the noninvasive PDAC precursor lesions (precursors) exist pancreatic intraepithelial neoplasia (PanIN), mucinous cystic neoplasm (MCN), and intraductal papillary mucinous neoplasml (IPMN) are microscopic cysts accounting for over half of the approximately 150,000 asymptomatic pancreatic cysts detected incidentally in the general population each year by imaging (4). Once detected, endoscopic ultrasound (EUS)-guided fine needle aspirations are often performed to assess the degree of dysplasia, but imaging features and biomarkers obtained from such invasive procedures do not reliably predict disease severity prospectively (3). Noninvasive approaches are needed to aid in IPMN management and prevent progression to malignancy.

miRNAs are biomarkers that regulate one-third of all protein-coding genes and promote carcinogenesis by regulating tumor suppression and oncogene or silencing these functions themselves (5). miRNAs are excellent candidate biomarkers of early disease because of their tissue-specific expression patterns (5), their remarkable stability in tissue (6) and Nucleus (7) due to their small size and protection from endogenous RNase activity, and their ability to regulate hundreds of genes and biologic pathways (5). Recent studies for our group (6) and others (9–11) have evaluated genome-wide miRNA expression in IPMN tissue, and provide data to suggest that key miRNAs may reliably differentiate low-risk/benign IPMNs (i.e., low- and moderate-grade) that can...
Radiomics

- High-throughput extraction of quantitative features (from standard-of-care images) into mineable data.

Image acquisition and reconstruction

- Contrast Issues
- Slice thickness
- Scanner setting

Segment

Feature extraction

- Semi-Automatic
- Texture Features (smooth, coarse, regularity)
- Non-texture (shape/size/volume)
- Prediction of clinical parameters

Analyze

Slide courtesy of Yoganand Balagurunathan, PhD
Combining radiomic features with a miRNA classifier may improve prediction of malignant pathology for pancreatic intraductal papillary mucinous neoplasms

Jennifer B. Permuth1,2, Jung Cho3, Yoganand Balarunathan3, Jongphil Kim3, Dung-Tsa Chen4, Lu Chen3, Sonia Orcutt5, Matthew P. Doepker6, Kenneth Gage3, Geoffrey Zhang6,6, Kuitim Latif6,6, Sarah Hoffe6,6, Kun Jiang3, Domenico Coppola7, Barbara A. Centeno8, Anthony Magliocco9, Qian Li6,6, Jose Trevino6, Nipun Merchant10, Robert Gillies1 and Mokenge Malafa1 on behalf of the Florida Pancreas Collaborative

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Keywords: radiomics, miRNA, risk stratification, pre-malignant lesions, pancreas

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ABSTRACT

Intraductal papillary mucinous neoplasms (IPMNs) are pancreatic cancer precursors incidentally discovered by cross-sectional imaging. Consensus guidelines for IPMN management rely on standard radiologic features to predict pathology, but they lack accuracy. Using a retrospective cohort of 38 surgically-resected, pathologically-confirmed IPMNs (20 benign; 18 malignant) with preoperative computed tomography (CT) images and matched plasma-based 'miRNA genomic classifier (MGC)' data, we determined whether quantitative 'radiomic' CT features (+/- the MGC) can more accurately predict IPMN pathology than standard radiologic features 'high-risk' or 'worrisome' for malignancy. Logistic regression, principal component analyses, and cross-validation were used to examine associations. Sensitivity, specificity, positive and negative predictive value (PPV, NPV) were estimated. The MGC, 'high-risk,' and 'worrisome' radiologic features had area under the receiver operating characteristic curve (AUC) values of 0.83, 0.84, and 0.54, respectively. Fourteen radiomic features differentiated malignant from benign IPMNs (p<0.05) and collectively had an AUC=0.77. Combining radiomic features with the MGC revealed an AUC=0.92 and superior sensitivity (89%), specificity (88%), PPV (88%), and NPV (89%) than other models. Evaluation of uncertainty by 10-fold cross-validation retained an AUC>0.80 (0.87 (95% CI:0.84–0.89)). This proof-of-concept study suggests a noninvasive radiogenomic approach may more accurately predict IPMN pathology than 'worrisome' radiologic features considered in consensus guidelines.
Linc-ing Circulating Long Non-coding RNAs (IncRNAs) to Pancreatic Cancer Precursors: An Exploratory Study

- Long non-coding RNAs (IncRNA): class of noncoding RNAs >200 nucleotides in length without open reading frames.
  - Predominant type of transcribed RNAs.
  - Regulate gene expression and promote carcinogenesis via various mechanisms.
- Emerging data support the role of IncRNAs in PC initiation, progression, and outcomes.
- Evidence supports IncRNA detection in circulation.

Our goal: To be the first to explore the abundance of candidate IncRNAs in archived plasma from patients with IPMNs.

Funding: Departmental Innovation Award (PI: J. Permuth)
Using blood-derived miRNA expression levels and tumor DNA mutations to personalize care for individuals with pancreatic cancer precursors

Goal: Identify a combination of plasma-derived miRNAs and novel somatic mutations that reliably predict IPMN risk status pre-operatively.

Funded by the DeBartolo Personalized Medicine Institute (PI: J. Permuth)
The Florida Pancreas Collaborative (FPC): A Partnership Dedicated to the Early Detection and Prevention of Pancreatic Cancer

Co-PIs:
Jennifer B. Permuth, PhD, MS
Mokenge Malafa, MD
Nipun Merchant, MD
Jose Trevino, MD

Funded by the Florida Academic Cancer Center Alliance (FACCA)
Eligibility

Males and females 18+ who present to the GI Clinic, surgery, or endoscopy at MCC, UF, or SCCC/UM with a clinical suspicion for (or diagnosis of) a pancreatic lesion, mass, or cyst or pancreatitis based on symptoms, imaging, or blood-work (and no prior treatment)

Healthy individuals 18+ without a self-reported personal history of pancreatic disease or related symptoms (companions and high-risk cohort).

Approach to recruit and obtain written informed consent

Kimberly Quinn (MOF)  Amber Bouton (UF)  Dr. Suzanne Lechner (SCCC/UM)
**RESPONSE CARD**


Doctors and researchers at Moffitt, the University of Florida, and the University of Miami are trying to develop better ways to prevent, detect, and treat pancreatic cancer; and we need the help of individuals affected by pancreatic conditions and healthy individuals without pancreatic conditions.

Please check boxes below that apply to your current situation:

- [ ] I am in the process of undergoing an evaluation regarding some findings that involve my pancreas.
- [ ] I have been diagnosed with pancreatic cancer or another condition of the pancreas.
- [ ] I am a companion/friend/family member of an individual who has a pancreatic condition.
- [ ] I am at-risk for pancreatic cancer due to my family history of the disease.
- [ ] Other: ___________________________________________

Please check one of the boxes below to let us know if you are interested in participating in this important study.

- [ ] YES, I am interested in participating in this study and would like more information.
- [ ] MAYBE, I would like to speak with my doctor about this study before deciding.
- [ ] NO, I am not interested in participating in this study and do not wish to be contacted about it.

Primary reason(s):

- [ ] I am too busy to participate/do not have time.
- [ ] I am too sick/ill to participate.
- [ ] I don't feel this study is relevant to me.
- [ ] Other (please specify): __________________________________________

For inquiries about FPC, please contact us at:

FPC@moffitt.org

or

813-745-XXXX

(or toll-free at 1-800-XXX-XXXX XXXXX)

Funded by:
The Florida Academic Cancer Center Alliance
http://www.floridacanceralliance.com/

The Florida Pancreas Collaborative (FPC)
A partnership dedicated to the early detection and prevention of pancreatic cancer

“Researchers, doctors, patients, and families united in efforts to prevent, detect, and treat pancreatic cancer”

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INTRODUCTION

- New laboratory technologies are available to allow important advances in the early detection, prevention, and treatment of pancreatic cancer and other conditions affecting the pancreas, including pancreatic cysts and pancreatitis.
- To speed up these research advances, it is important to collect and study biological specimens such as bodily fluids (i.e. blood) donated by individuals with and without pancreatic conditions.
- When combined with information regarding age, gender, presenting symptoms, history of medical conditions, and other factors, knowledge gained from such biospecimens can change the ways doctors diagnose and treat a person’s disease (Figure 1).

WHAT IS THE FLORIDA PANCREAS COLLABORATIVE (FPC) AND WHAT IS ITS PURPOSE?

- The FPC is a partnership between researchers and patients at Moffitt Cancer Center, University of Florida and University of Miami who are committed to:
  - discovering factors that may aid in the prevention, early detection, and/or treatment of pancreatic cancer and other conditions of the pancreas.
  - accelerating the translation of research advances to those affected by or at-risk for pancreatic conditions.

WHO CAN PARTICIPATE?

- You may be able to take part in this study if:
  - you are a male or female 18 years of age or older.
  - you are having an evaluation of your pancreas because of some symptoms, clinical and/or radiologic imaging findings, blood-work, or because you have a family history of pancreatic cancer or related conditions.
  - you do not have a personal history of a pancreatic condition or symptoms, but are interested in contributing to this research.

WHAT ARE THE BENEFITS OF PARTICIPATION?

- There may be no direct benefit to you from participation. However, the information and biospecimens you provide will be useful in learning more about the biology of pancreatic conditions.
- This new knowledge may lead to clinical testing for new ways to help people at increased risk for pancreatic cancer, as well as the discovery of new drugs for treating and preventing pancreatic conditions.

WHAT ARE THE COSTS OF PARTICIPATION?

- You will not need to pay for any procedures performed specifically for this study.
- Tests or procedures obtained as part of routine care will be your responsibility.
- Your participation is entirely voluntary. If you decide not to participate, you will not jeopardize present or future medical care or treatment.
- You may stop participation at any time.

WHAT ABOUT MY PRIVACY?

- Data collected from this study will only be used for research purposes. Results of any tests will not become part of your medical record. Results may be published in a scientific journal, but your identity will not be released.

WILL I KNOW THE RESULTS OF THIS IMPORTANT RESEARCH?

- If clinically useful information arises as a result of this study, we may contact you or a person whom you designate to discuss optional clinical tests or studies.
- We also plan to update you on new developments through a study newsletter.
Who can participate in the Florida Pancreas Collaborative (and how)

- Asymptomatic first or second degree relatives of a family member affected by pancreatic cancer
- Asymptomatic carriers of known PC predisposition mutations
- Individuals with a suspected or diagnosed condition affecting the pancreas.
- Feel free to send in the response form.
- Any q’s, email Dr. Jenny Permuth or Kim Quinn
  jenny.permuth@moffitt.org; kimberly.quinn@moffitt.org
Partnering to advance early detection and prevention efforts for pancreatic cancer: the Florida Pancreas Collaborative

Jennifer B Permutt, Jose Trevino, Nipun Merchant & Mokenge Malafa; on behalf of the Florida Pancreas Collaborative

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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 most common cause of cancer death in the United States. In 2015, an estimated 50,720 people died from pancreatic cancer, and an estimated 56,320 new cases will be diagnosed [2].

Team science is needed to develop new strategies to improve diagnostic accuracy, staging, and treatment of pancreatic cancer. Pancreatic cancer is projected to surpass breast, prostate and colorectal cancer and become the second leading cause of cancer deaths by 2020 [3]. 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 disease at the time of diagnosis. This limited window for therapy places pancreatic cancer at the forefront of the race for a cure. To design effective strategies for early detection and prevention, the role of pancreatic cancer precursors needs to be better understood. Precursors are a broad category for tumors that are not yet cancerous, such as normal cells, hyperplastic cells, dysplastic cells, and in situ cancer. Understanding the molecular mechanisms that drive early stages of pancreatic cancer tumorigenesis may enable earlier detection and improved outcomes for patients with pancreatic cancer.

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.’