NFPTR NEWS
national familial pancreas tumor registry

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FROM THE NFPTR TEAM

NFPTR (left to right): Zoe Norris (Coordinator), Sharon Varghese (Coordinator), David (Researcher), Dr. Alison Klein (NFPTR Director), Dr. Michael Goggins (CAPS Director), Evelina Mocci (Researcher)

We at the NFPTR would like to thank all of our families and friends for their continued participation and support of our research into understanding what causes certain individuals to develop pancreatic cancer and why pancreatic cancer clusters in certain families. With your support, we have made great progress in understanding some of the genetic and environmental causes of this disease. However, there is still much to learn before we achieve our goal of preventing the development of pancreatic cancer.

This past year, our team underwent some changes, as we said goodbye to our previous coordinators, and welcomed two new coordinators. We would like to thank both Ally Klann and Eric Miller, our previous research coordinators, for their ardent support and dedication to pancreatic cancer research. Ally is currently pursuing a masters in medical science at Boston University, and Eric started medical school at SUNY Upstate. We wish them the best of luck, and know they will continue to do great things in the fields of medicine and public health.

We are also excited to introduce our new coordinators, Sharon Varghese and Zoë Norris. Sharon graduated from Johns Hopkins University in 2015 with a BA in Public Health Studies. While studying at Johns Hopkins University, Sharon did research on the effects of community health workers on the health of underserved populations, and how varying levels of exercise affect obesity. After graduating, Sharon joined the Episcopal Service Corps to help educate Maryland communities on environmental factors harming human health. Sharon is excited to work with the NFPTR in helping families fight and prevent pancreatic cancer.

Zoë graduated from Temple University in 2013 with a BFA in Dance and BS in Kinesiology. After graduating, she served as a Peace Corps Volunteer from 2014-2016 in the Community HIV/AIDS Outreach Program in South Africa. While at Temple University, she participated in pancreatic cancer basic science research, and is excited to continue the fight to end this disease.

Both Sharon and Zoe work with the Pancreas Multidisciplinary Clinic (PMDC) at the Johns Hopkins Hospital, as well as communicating with patients and families online or by phone.

This year's newsletter includes ongoing research being performed by our team and our collaborators. On page two, we discuss some exciting developments in the screening and treatment of pancreatic cysts, led by Dr. Anne Marie Lennon, Director of the Multidisciplinary Pancreatic Cyst Program at Johns Hopkins. On page three we discuss a new grant awarded to Drs. Michael Goggins, Marcia Canto, Alison Klein, and Laura Wood. This award will be used will be used to improve the early detection of pancreatic cancer and its precursor lesions for better clinical outcomes. Also on page three, we talk about our work in establishing the genetic causes of pancreatic cancer

This year, Dr. Klein participated in the National Pancreatic Cancer Advocacy Day sponsored by the Pancreatic Cancer Action Network in Washington, DC. As part of this event, she led an educational session for the advocates on genetics and pancreatic cancer. In addition, along with fifteen other members of the Johns Hopkins Pancreatic research team, she met with representatives on Capitol Hill to raise awareness for the continued need to support cancer research.

As 2016 comes to a close, we would like to, once again, thank all of you who have participated in the National Familial Pancreas Tumor Registry. It is through the continued support of families like yours that our research is possible. Without your help, we would not be able to make advancements in how we prevent, diagnose, and treat pancreatic cancer. Please complete and return the enclosed update card (even if there have been no changes), and please contact us with any questions, concerns, or updates. On behalf of the NFPTR team, we would like to wish you all a happy holiday season!

- *The NFPTR Team*

Inside this issue:

NEW METHOD TO SORT PRECANCEROUS PANCREATIC CYSTS FROM BENIGN CYSTS

Dr. Anne Marie Lennon
(Director, Multidisciplinary Pancreatic Cyst Program

Adenocarcinoma of the pancreas, the most common form of pancreatic cancer, is considered to arise from both microscopic lesions in the pancreas called intraepithelial neoplasia, as well as certain types of pancreatic cysts. While there are several types of pancreatic cysts, many of which are benign, some cysts, including a small number of intraductal papillary neoplasms and mucinous cystic neoplasms, may warrant surgical removal. As imaging technology improves, many individuals who are undergoing imaging tests for a variety of reasons are found to have incidental pancreatic cysts.

One of the challenges facing doctors and patients is how to determine when these pancreatic cysts and neoplasms require surgery, or when they only need careful monitoring. Currently, patients undergo an endoscopic ultrasound-guided biopsy, a procedure in which a needle penetrates the pancreatic cyst and collects fluid. This fluid is then analyzed for biomarkers and atypical cells associated with cancerous cysts. The goal of this test is to determine whether the cyst is precancerous and needs to be removed surgically, or benign and should be monitored. Unfortunately, recent studies show that current tools are only accurate 63 percent of the time. This compelled a group of scientists at Johns Hopkins, led by Dr. Anne Marie Lennon, to develop a model to more accurately determine types of pancreatic cysts and their probability of harboring malignancy through the combination of genetic tests and clinical criteria, such as age, symptoms, and location and appearance of the cysts. Their discovery will hopefully help future patients avoid risky, unnecessary surgery to remove harmless cysts.

To demonstrate the effectiveness of their novel diagnostic method, the team at Hopkins carried out a retrospective analysis of 130 patients who had received surgery to remove pancreatic cysts. The patients' cyst fluid underwent genetic testing to identify molecular markers specific to each type of cyst (serous cystadenomas, solid-pseudopapillary neoplasms, mucinous cystic neoplasms and intraductal papillary mucinous neoplasms). The team was able to identify biomarkers and clinical characteristics that classified cyst type with a 92-98% specificity, a measure of accurately identifying individuals with a disease, and a 90-100% sensitivity, a measure of accurately identifying individuals without a disease. Their approach of combining an expanded panel of genetic markers with clinical acuity correctly identified 91% of the patients who did not require surgical removal of their cysts, and thus, this method could help prevent unnecessary operations in the future.

Although this study found promising results, further work is needed to validate the findings. They need to test the method on a greater number of patients, test the method's capability in identifying which cysts in newly-diagnosed patients require surgery, and assess its cost effectiveness.

CANCER OF THE PANCREAS SCREENING

We are currently screening individuals with a risk of developing pancreatic cancer at Johns Hopkins Hospital for Screening for Early Pancreatic Neoplasia (CAPS-5 Study). There are total of 8 sites in the United States recruiting for this study. Interested participants should not have pancreatic cancer or suspicious symptoms (chronic upper abdominal pain, unexplained weight loss, jaundiced eyes or skin). Dr. Michael Goggins is the principal investigator for this study and Dr. Marcia Canto is the lead clinician for the study. Drs. Goggins and Canto are widely recognized as authorities in the field of pancreatic cancer screening, and have been working together to evaluate the utility of pancreatic screening for approximately 15 years. For more information on screening or participating, visit our CAPS-5 ClinicalTrials.gov website or search for study **NCT02000089** at ClinicalTrials.gov.

HOW YOU CAN HELP

If you are interested in learning of future research studies please send us an email at pancreas@jhmi.edu and include your current contact information.

Spouses are eligible to serve as a "control" for us by donating a blood or saliva sample and completing a family history questionnaire. A control group is crucial for our research as it allows us to validate the significance of pancreatic cancer genes that we discover. If you are interested in enrolling as a spouse control, please email us at pancreas@jhmi.edu

A COLLABORATIVE APPROACH TO RESEARCH: THE PANCREATIC CANCER DETECTION CONSORTIUM (PCDC)

In early 2013, the Recalcitrant Cancer Act was signed by President Obama after passage through congress with strong bipartisan support. This act required the National Cancer Institute (NCI) to develop a strong framework to develop framework to support research on the deadliest cancers, including pancreatic cancer and lung cancer. In 2014 the NCI released the framework for pancreatic cancer that included a recommendation to dedicate funds to support the development of imaging and biomarker tests to advance the early detection of pancreatic cancer. We have made tremendous progress in understanding how pancreatic cancers develop at the molecular level and have shown that screening can detect early pancreatic cancer in high-risk individuals. However, we still need to develop better pancreatic screening tests that can accurately identify early pancreatic cancer and advanced precancerous changes of the pancreas. In 2016, Drs. Goggins and his colleagues Drs. Canto, Klein and Wood were awarded funding from of the NCI's new funding mechanism to improve early detection, namely the Pancreatic Cancer Detection Consortium (PCDC). The PCDC was created in response to the recalcitrant cancer act to fund the collaborative research of multi-disciplinary teams and clinicians in improving the detection of early stage pancreatic ductal adenocarcinoma and its' precursor lesions.

In collaboration with other institutions, the PCDC grant recipients will evaluate biomarkers to determine if they can improve early detection of pancreatic ductal adenocarcinoma over existing tests and improve our ability to evaluate pancreatic cysts which can sometimes progress to cancer. Research will also include evaluating new molecular/imaging approaches for screening high-risk populations; and the collection of biospecimens for future studies. Funding will also go toward collaborative activities among researchers and the sharing of ideas, specimens and data across pancreatic cancer research studies. We look forward to being a part of this new endeavor that we hope will rapidly lead to improvements in the early detection for pancreatic cancer.

The ongoing support of NFPTR families in advocating for increased funding for pancreatic cancer research and raising awareness for this deadly disease continues to have a profound impact on the war against pancreatic cancer.

IDENTIFYING THE CAUSES OF FAMILIAL PANCREATIC CANCER

One of the major research goals of the NFPTR is to find why pancreatic cancer clusters is some families. While some families have a clustering of pancreatic cancer due to shared non-genetic factors, including tobacco exposure, our research has demonstrated that inherited factors play a major role in familial clustering of pancreatic cancer. Our past studies have demonstrated that mutations in the *BRCA2*, *PALB2* and *ATM* genes are explain about 6-10%, 1%, and 3-4% of pancreatic cancer families respectively. While another 2-5% of cases are explained by mutations in the, *BRCA1*, *STKL11*, *PRSS1*, *SPINK1 CDKNA2*, *MLH1*, *MSH2*, *MSH6*, and *PMS2.* To continue our work to understand the causes of familial pancreatic cancer*,* in 2013, The NFPTR, along with other investigators in The Sol Goldman Pancreatic Cancer Research Center, launched a consortium to identify the genes that cause familial pancreatic cancer. The consortium also includes Mayo Clinic, University of Toronto, Mt. Sinai Hospital, Dana-Farber Cancer Institute, Memorial Sloan-Kettering Cancer Center, University of Pittsburgh, Karmanos Cancer Institute, McGill University, University of Pennsylvania, and University of Michigan. As part of this project, we sequenced the genomes 638 of patients with familial pancreatic cancer.

The results or our initial analysis of these data were published early this year (Roberts et al 2016; see publication #4 on page 4). Our study provided strong evidence supporting previously reported susceptibility genes increasing a person's risk of developing pancreatic cancer, including the *ATM, BRCA2, PALB2*, and *CDKN2A* genes.

In addition, mutations in the following candidate genes *BUB1B, CPA1, FANCC*, and *FANCG* were also found to be more common in patients with familial pancreatic cancer. However, it will take many more years of work to determine if mutations in these candidate genes explain the occurrence of pancreatic cancer in these families or if they are chance findings.

We are continuing our work to compare the sequenced patient genomes to the genomes of patients without pancreatic cancer. Dr. Klein was awarded a 5-year grant from the NCI in April 2016 to continue to examine the data from this study, including studying candidate genes identified in these analysis in over 6,000 pancreatic cancer patients and 6,000 healthy "control" individuals. Given that, on average, each person has over 6 million changes in their DNA many of which are unique to that individual, identifying the genetic changes which lead to pancreatic cancer vs those benign variants that are unique to each individual is an ongoing challenge, not only faced by pancreatic cancer researchers, but common to all genetics researchers. The challenge for our researchers will be to identify the single genetic change amidst these 6 million that increases a person's chances of developing pancreatic cancer.

*Under a licensing agreement between Myriad Genetics Inc. and the Johns Hopkins University, Drs. Klein, Eshlelman, Hruban and Goggins, are entitled to a share of royalty received by the University on sales of products described in this newsletter. The terms of this arrangement are being managed by The Johns Hopkins University in accordance with its conflict of interest policies.

PLEASE REMEMBER TO RETURN YOUR UPDATE CARD ENCLOSED WITH THIS NEWSLETTER.

Even if there have been no changes in your family, this information is very important to our research!

CERTIFICATE OF CONFIDENTIALITY

We want to remind the participants that the NFPTR continues to be protected by a Certificate of Confidentiality (NCI-01-062) from the National Institutes of Health, Department of Health and Human Services. This certificate further helps us protect the confidential information that you have provided by giving us legal protection from being required to involuntarily release any information about you. With this certificate, we cannot be forced by court order to disclose any information for criminal, administrative, legislative, or other proceedings.

If you have any questions regarding this or would like a copy, please contact Sharon or Zoë: (410) 955-3502 or (410) 955-3512

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LEARN MORE ABOUT OUR RESEARCH

Below is a short list of citations of key discoveries made by the NFPTR over the past twenty years as shown on page two. Due to space limitations, we can only show a few of our publications, but we hope that this conveys some of the progress we have made. To view abstracts and full versions of these publications, please visit the NCBI PubMed website (http://www.ncbi.nlm.nih.gov/pubmed) and search by the **PMID** number.

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9. Masica DL…Goggins M…Lennon AM. A novel approach for selecting combination clinical markers of pathology applied to a large retrospective cohort of surgically resected pancreatic cysts. *Journal of the American Medical Informatics Association.* (2016) Jun 21. PMID: 27330075