


THANK YOU FROM THE NFPTR TEAM!



NFPTR (left to right): David McKean (Researcher), Sharon Varghese (Coordinator), Dr. Alison Klein (NFPTR Director), Nancy Porter (Coordinator), Evelina Mocci (Researcher)

WAYS 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.

Participate as a “control”. 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

Through financial support. Those of you wishing to support the NFPTR pancreas cancer research at Johns Hopkins may do so by sending your tax-deductible contribution payable to NFPTR to our mailing address listed below. Or visit pathology.jhu.edu/pancreas/support.php

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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!

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.

1. Haycock PC...Klein AP... Davey Smith G. Association Between Telomere Length and Risk of Cancer and Non-Neoplastic Diseases: A Mendelian Randomization Study. *JAMA Oncology.* 2017 May 1;3(5):636–651. PMID: 5638008

2. Cohen JD, Javed AA, Thoburn C, Wong F, Tie J, Gibbs P, Schmidt CM, Yip-Schneider MT, Allen PJ, Schattner M, Brand RE, Singhi AD, Petersen GM, Hong S-M, Kim SC, Falconi M, Doglioni C, Weiss MJ, Ahuja N, He J, Makary MA, Maitra A, Hanash SM, Dal Molin M, Wang Y, Li L, Ptak J, Dobbyn L, Schaefer J, Silliman N, Popoli M, Goggins MG, Hruban RH, Wolfgang CL, Klein AP, Tomasetti C, Papadopoulos N, Kinzler KW, Vogelstein B, Lennon AM. Combined circulating tumor DNA and protein biomarker-based liquid biopsy for the earlier detection of pancreatic cancers. *Proceedings of the National Academy of Sciences of the USA.* 2017 Sep 19;114(38):10202–10207. PMID: 5617273

3. Shindo K, Yu J, Suenaga M, Fesharakizadeh S, Cho C, Macgregor-Das A, Siddiqui A, Witmer PD, Tamura K, Song TJ, Navarro Almario JA, Brant A, Borges M, Ford M, Barkley T, He J, Weiss MJ, Wolfgang CL, Roberts NJ, Hruban RH, Klein AP, Goggins M. Deleterious Germline Mutations in Patients With Apparently Sporadic Pancreatic Adenocarcinoma. *Journal of Clinical Oncology.* 2017 Oct 20;35(30):3382–3390. PMID: 5648172

4. Grant RC...Roberts NJ, Klein AP...Gallinger S. Exome-Wide Association Study Of Pancreatic Cancer Risk. *Gastroenterology.* 2017 Oct 23; PMID: 29074453

5. Fang J, Jia J, Makowski M, Xu M, Wang Z, Zhang T, et al. Functional characterization of a multi-cancer risk locus on chr5p15.33 reveals regulation of TERT by ZNF148. *Nature Communications.* 2017 May 2;8:15034. PMID: 5414179

6. Streicher SA, Klein AP, Olson SH, Amundadottir LT, DeWan AT, Zhao H, Risch HA. Impact of Sixteen Established Pancreatic Cancer Susceptibility Loci in American Jews. *Cancer Epidemiology, Biomarkers & Prevention.* 2017 Oct;26(10):1540–1548. PMID: 5626623

7. Shindo K, Yu J, Suenaga M, Fesharakizadeh S, Tamura K, Almario JAN, Brant A, Borges M, Siddiqui A, Datta L, Wolfgang CL, Hruban RH, Klein AP, Goggins M. Lack of association between the pancreatitis risk allele CEL-HYB and pancreatic cancer. *Oncotarget.* 2017 Aug 1;8 (31):50824–50831. PMID: 5584208


NFPTR

national familial pancreas tumor registry

NEWS

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GREETINGS FROM THE NFPTR TEAM



Alison Klein, PhD, MHS

We at the NFPTR are grateful to our families for the continued support you provide for our research and registry! Your participation has helped us make substantial strides this year in understanding the genetics of pancreas cancer. Every year, we make progress towards our goal of understanding the origins of this terrible disease, and this would not be possible without the help of our families. We still have much to learn before we reach our goal of preventing the development of pancreas cancer, and we look forward to your continued support as we work to achieve this.

Over the last year, we underwent a few changes to our team. We would like to thank Zoe Norris, one of our previous research coordinators, for her hard work and dedication to our pancreas cancer research team. Zoe started attending medical school at the NYU School of Medicine this past year, and we are confident in and excited for the strides she will make in medicine and global health.


We are also happy to introduce our new senior coordinator, Nancy Porter. Nancy graduated from The Pennsylvania State University with a BS in Biobehavioral Health in 2008, and then with a MS in Public Health Sciences in 2011. While at Penn State, Nancy worked with the Northern Appalachia Cancer Network pursuing her research interests of cancer prevention and survivorship. Nancy then went on to pursue a PhD in Cancer Epidemiology at the University of South Carolina; she plans to complete her doctoral dissertation next year. Nancy is excited to work with the NFPTR in helping families fight and prevent pancreatic cancer.

We are also excited to announce several new initiatives this year. First, in collaboration with the MD Anderson Cancer Center, Dana Farber Cancer Center, Mayo Clinic, and University of San Diego we were awarded a Stand Up to Cancer Interception Grant (see page 2 for more detail). The goal of this study is to improve the early detection of pancreatic cancer through expanding genetic testing of pancreatic cancer patients and their family members, early detection studies, and prevention studies. We hope to launch these studies in early 2018.

This past August, our director Alison Klein joined the Pancreatic Cancer Action Network’s (PanCAN) Scientific and Medical Advisory Board (SMAB) and attended their annual meeting in San Diego, CA. The SMAB consists of 29 pancreatic cancer scientists, clinicians, and other healthcare professionals who assist PanCAN in the planning and implementation of their research initiatives. Dr. Klein remarked about how much she enjoyed not only hearing about the exciting science but also her interactions with the exceptional volunteers from all over the country dedicating their time to raising awareness and fighting this deadly disease.

As 2017 comes to a close, we would like to thank all of you who have participated over the years. 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, and please contact us with any questions, concerns, or updates. We would like to wish you all a happy holiday season!

- Dr. Alison Klein, & the NFPTR Team



WE’RE GOING ELECTRONIC!

Starting this year, we will also be offering an electronic newsletter!

Please add pancreas@jhmi.edu to your e-mail contacts to ensure that you receive our annual newsletters. If you would like to receive electronic newsletters from us in the future, check ☐ “Yes, I would like to only receive electronic newsletters in the future” at the bottom of the enclosed update card.

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STAND UP TO CANCER LAUNCHES “DREAM TEAM” TO DETECT PANCREATIC CANCER IN EARLY STAGES



Dr. Michael Goggins

Cancer interception, or finding cancer at its earliest stages, has the potential to improve survival in cancer patients. Early detection of pancreatic cancer particularly in those individuals at higher risk because of the family history of cancer, has been a longstanding focus of the NFPTR. It is our continued hope, with the right chemoprevention, vaccines, and more sensitive screening, cancer interception can help us block pancreas cancer early, while it is still treatable.

The Stand Up To Cancer (SU2C) Cancer Interception initiative was created to make this possible, dedicated to finding both the technologies and treatments needed to find early pre-cancerous markers and stop its progression. In October 2017, SU2C, along with the Lustgarten Foundation for Pancreatic Research, LUNGevity, and the American Lung Association announced four teams of top researchers to be awarded grants for cancer interception research projects on cancers of the lung and pancreas.

We are proud to announce that one of the research teams awarded is the SU2C-Lustgarten Foundation Pancreatic Cancer Interception Dream Team is co-lead by NFPTR team members. The Dream team is led by Dr. Anirban Maitra at the University of Texas MD Anderson Center, Dr. Scott

Lippman of University of California, San Diego, and Dr. Michael Goggins, the Johns Hopkins PI. Dr. Alison Klein will serve as co-PI with Dr. Goggins. A total of \$7 million will be awarded to the team’s multi-disciplinary research efforts, spanning six institutions: Johns Hopkins University, The University of Texas MD Anderson Cancer Center, University of California, San Diego, Mayo Clinic, Dana-Farber Cancer Institute, and MIT.

The team’s research will focus on intercepting pancreas cancer through targeted immune prevention and careful early detection, as well as developing an early detection screening test by searching for distinct characteristics of the blood. As part of this study we will also be exploring the utility of offering genetic testing for inherited pancreatic cancer genes to all pancreatic cancer patients, regardless of their family history of cancer and how best to reach out to the family members of pancreatic cancer patients found to have a mutation in a pancreatic cancer susceptibility gene. We anticipate over 2,000 newly diagnosed pancreatic cancer patients will be tested across the 5 cancer centers as part this endeavor.

In addition to the genetic testing study described above, relatives carrying a mutation but are cancer-free will be eligible to enter an active screening protocol, involving computer-based “deep learning” imaging algorithms to detect smaller cancers hidden from human eye. Relatives without cancer, but with pre-cancerous lesions, will be invited to a novel clinical trial of a vaccine in order to help induce their body’s immune system to fight and prevent pancreas cancer.

Through these studies, the team hopes to broaden the current guidelines for genetic testing of pancreatic patients with pancreatic cancer, and to ultimately save many lives by intercepting this disease as early as possible.

IN THE SPOTLIGHT: MARY HODGIN

For 10 years, the Pancreas Multidisciplinary Care Clinic (PMDC) at Johns Hopkins has been dedicated to providing patients with the highest quality of care. Patients seen here at the PMDC receive a comprehensive single day evaluation from our top-notch team, which includes medical, radiation, surgical oncology, gastroenterology, pathology, radiology, pain management, and research teams. We would like to highlight one member of the team in particular who helps make it all possible.

Mary Hodgin has spent the last half of her 20 year (and counting) career here at Johns Hopkins working with the PMDC. Mary’s job is to organize patients’ visits to PMDC, ensuring that each patient is exactly where they need to be and that they have all the tools necessary to navigate this difficult time of their lives. Mary and her team spend countless hours on the phone with physicians’ offices, tracking down every report, every image, and every detail necessary. However, it is clear that the part of Mary’s job that she feels is most important is educating patients on their diagnosis and their road ahead.

It is not just Mary’s incredible work ethic that makes her so great; it is her compassion and level of understanding that makes her truly wonderful. Growing up, Mary never thought

she would be a nurse; in fact, her major in college was German literature. Mary met her husband in college and together they had four children. It was through tragedy that Mary found nurs-ing. After losing her husband to cancer, and inspired by the nurses who deeply cared for her family while her husband was receiving treatment, Mary went on to earn a BS and MS in nurs-ing. Mary says she tries to treat her pa-tients with the same respect that her and her family were given. She feels that it is so important to educate patients and give them a plan, so that she can “take away their fear of the diagnosis and have them run the cancer, rather than the cancer run them.”



Mary Hodgin, BSN, MS

Thank you Mary for your compassion and dedication to making every patient, family, and this hospital feel cared for.

DNA PROTEIN MARKERS IN BLOOD MAY HELP SPOT EARLY PANCREATIC CANCER

While a blood based screening test for the early detection of pancreatic cancer is not yet available, recent work by investigators at Johns Hopkins, including Dr. Anne Marie Lennon and Joshua Cohen have made significant progress in developing such a test. Earlier this year, our scientists published an initial study on a blood test that spots tumor-specific DNA and protein biomarkers for pancreatic cancer. Pancreatic tumors are most often found late, when treatment options are limited. This new blood test builds on previous research, combining what we know about tumor DNA and biomarkers. Biomarkers are different types of molecules that can inform us about a patient’s current health status. They can be in the form of DNA, proteins, or hormones, which can be produced by the cancer or by other cells in your body. A popular protein biomarker is the carbohydrate antigen 19-9 (CA19-9). Although it is not sensitive enough on it’s own to be used for screening, we are hopeful that it can be combined with other biomarkers to be used for screening. Recently, mutant tumor DNA shed into a patient’s blood stream has been explored as a biomarker (so called “liquid biopsy”). Cancer cells have a high turn-over rate, and these dying cells release this mutant DNA which then escapes into bodily fluids such as urine, stool, and blood plasma. This mutant DNA is referred to as circulating tumor DNA (ctDNA). Over 85% of patients with advanced cancers have elevated levels of ctDNA, and patients with earlier stages of cancer (although, a

much smaller percentage, than those with advanced cases) have detectable levels of ctDNA in their plasma. This new blood test combines ctDNA with protein biomarkers, like CA19 -9, to increase the chances of detecting pancreatic cancer.

This study looked at 221 patients with surgically treatable pancreatic cancer (patients with stage III or IV disease were excluded) and 182 persons with no known history of cancer. This new blood test detected pancreatic cancer among 141 (64%) patients. Most notably, 45 of the patients in this study had no symptoms of pancreatic cancer; among these non-symptomatic patients, the blood test identified cancer in 27 (60%) of these patients. This new blood test also showed promising results among those with the earliest stages of disease, identifying 12 of the 29 cases (41%). While these results are exciting, this potential screening test is not yet ready to be used outside of a research setting. “While we are hopeful that this work will help lead us to a blood-based early detection test, more work is needed, including evaluating the test in a large series of individuals to see if this test correctly identifies individuals with early stage, asymptomatic cancer and does not result in a large number of false positive findings” says study co-author and NFPTR director Alison Klein. Researchers are hopeful that they are getting closer to developing a screening test that can detect pancreatic cancer at an earlier stage and help to lessen the burden of this awful disease.

JOHNS HOPKINS HOSTS RESEARCH DAY FOR PANCAN



On Sunday, November 12th, the Baltimore and Washington D.C. affiliates of PanCAN, the national pancreas cancer advocacy group, joined us at Johns Hopkins for an informational seminar on our work in the research and treatment of pancreas cancer. Visitors were able to meet with clinicians and scientists in small group sessions to learn about recent advances in pancreatic cancer. This was a wonderful opportunity for the Johns Hopkins Pancreatic Cancer Team to meet with the patients and families affected by this disease. In addition to working with the local PANCAN chapter. We are thankful for the valuable opportunity we had to share what we are doing and chat with each of you individually.

Thank you for your support!

Research Discussions Included:

- ◆ Dr. Lei Zheng: Chemotherapy for pancreatic cancer
- ◆ Dr. James Eshleman: New approaches to discovering novel therapies
- ◆ Dr. Elliot Fishman: Recent advances in radiology
- ◆ Dr. Michael Goggins: Early detection of pancreatic cancer
- ◆ Dr. Jin He: Minimal invasive surgery in the management of pancreatic cancer
- ◆ Dr. Jody Hooper: Rapid Autopsy program
- ◆ Dr. Alison Klein, Nancy Porter & Sharon Varghese: Familial pancreatic cancer – The NFPTR
- ◆ Dr. Papadopoulos: Genetic discoveries