NFPTR national familial pancreas tumor registry

NEWS

DECEMBER 2013

FROM THE NFPTR TEAM

As 2013 comes to a close, we once again get the pleasure of updating all of the families in our registry of the progress we have made to understand why some individuals develop pancreatic cancer and why pancreatic cancer clusters in some families. These are critical steps to achieving our ultimate goal of preventing pancreatic cancer from developing.

The success of our research efforts depends on the ongoing support and involvement of all of the families in the registry. Without your ongoing participation we would not be able to keep making progress against pancreatic cancer! Despite our efforts, we still have a long road ahead of us. However, we have many exciting new studies on the horizon that will hopefully move the field forward. We continue to work towards our ultimate goal – saving lives.

Our recent success using DNA sequencing approaches to discover the genes that cause pancreatic cancer allowed us to expand this work to a much larger scale. On page 3 of the newsletter we detail a new effort led by the NFPTR team here at Johns Hopkins, working in collaboration with many other familial pancreatic cancer registries in North America. This study will comprehensively sequence the genomes of familial pancreatic cancer patients to find new familial pancreatic cancer genes.

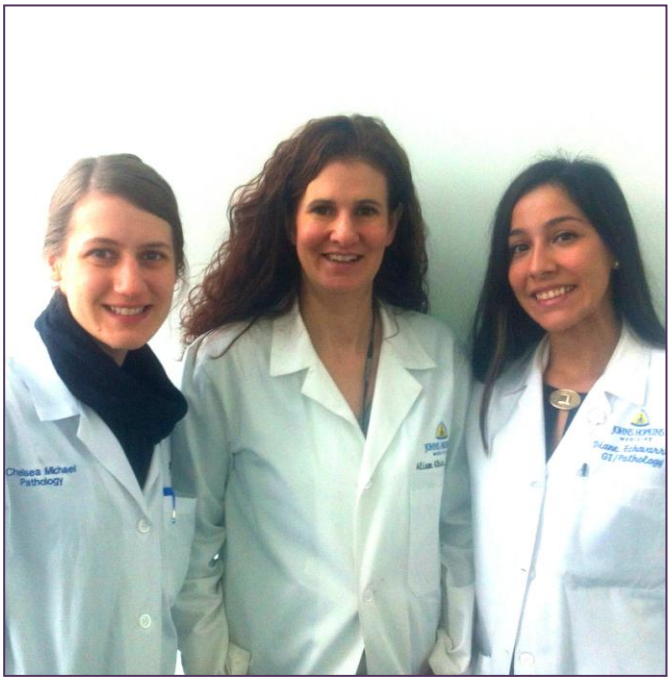
Inside this issue:

On page 3, we profile NFPTR collaborating physician-scientist Luis Diaz. Dr. Diaz is leading some exciting studies to develop new ways to detect pancreatic cancers early as well as a clinical trial to improve how we treat patients with metastatic pancreatic cancer.

For those of you who have an iPhone or an iPad, you may wish to download the free app developed by the team at Hopkins for pancreatic cancer patients and their families. (See: https://itunes.apple.com/us/app/icarebook-hd/id697194060?mt=8)

As always, please contact us with any questions, suggestions or updates as we're happy to hear from you throughout the year. On behalf of our NFPTR team we thank you for your continued participation in the registry and wish you and yours a very happy and healthy holiday season.

-Dr. Alison Klein, Diane and Chelsea



NFPTR Team:
(Left to right): Chelsea Michael (Coordinator), Dr. Alison Klein (NFPTR Director), Diane Echavarria (Coordinator)

SOL GOLDMAN PANCREATIC CANCER RESEARCH TEAM WINS AACR TEAM SCIENCE AWARD

Pancreatic Cancer Research Team:
(Left to right) Back row: Scott Kern, N. Volkan Adsay, Alison Klein, Christine Iacobuzio-Donahue.
Middle row: David Klimstra, Christopher Wolfgang, Joseph Herman, Laura Wood.
Front row: Kenneth Kinzler, Ralph Hruban, Bert Vogelstein, Nicholas Papadopoulos, Michael Choti, Victor Velculescu.
(Not pictured: Peter Allen, Luis Diaz, James Eshleman, Michael Goggins, Anirban Maitra and Alan Meeker)

We are proud to announce that the Pancreatic Cancer Sequencing Team of the Sol Goldman Pancreatic Cancer Research Center at Johns Hopkins received the 2013 American Association of Cancer Research (AACR) Team Science Award. The award was given:

> "***In recognition of having discovered a new cancer pathway and new familial pancreatic cancer genes. They have defined the time course for the development of pancreatic neoplasia, and have shown that each of the four cystic tumors of the pancreas has a unique mutational profile. These sequencing efforts have revolutionized the understanding of the fundamental genetic changes that characterize pancreatic cancer. Importantly, the team's work has immediate clinical implications." -AACR***

The team, led by Dr. Ralph Hruban, includes NFPTR Director Dr. Alison Klein, as well as NPFTR collaborating investigators Drs. Christine Iacobuzio-Donahue, Michael Goggins, James Eshleman, Scott Kern, Joseph Herman, Christopher Wolfgang, Anirban Maitra, Bert Vogelstein and Laura Wood.

The NFPTR team's discoveries, including the identification of *PALB2* and *ATM* as familial pancreatic cancer genes, were some of the key findings acknowledged by this award. Thus, by partipating in the Registry, each and every family in the NFPTR is a critical component to the success of our research efforts – and we thank you for your ongoing participation and support.

IN THE NFPTR SPOTLIGHT: LUIS DIAZ, M.D.

As Director of Translational Medicine at the Ludwig Center for Cancer Genetics and Therapeutics at Johns Hopkins, Associate Professor of Oncology, Luis Diaz, M.D. develops ways to apply findings made in the research laboratories to improve patient care, including the care of the many pancreatic cancer patients he sees in the clinic. One of Dr. Diaz's main research goals is to develop a new blood test that could be used as an early detection screening tool for pancreatic cancer. Pancreatic cancers, like all cancers, arise when the DNA in healthy cells become mutated or damaged. Some of this mutated DNA may be shed from the tumor into a patient's blood stream. This shed DNA is called circulating tumor DNA, or ctDNA.

Dr. Luis Diaz, M.D.

Dr. Diaz is developing methods to find ctDNA in a patient's blood. While the preliminary results are promising, additional evaluation of the test is needed. Tests for ctDNA and similar tests for circulating tumor cells that are being developed by other groups may be used in the future to predict tumor recurrence after surgery, to monitor tumor response to treatment, and to detect pancreatic cancer before it has spread.

Dr. Diaz is also collaborating with Dr. Dung Le, a colleague at Johns Hopkins, to lead a clinical trial to treat patients with pancreatic cancer that has metastasized to other parts of the body. This trial at the Johns Hopkins Hospital combines low doses of existing chemotherapy drugs to treat metastatic pancreatic cancer. They hope that by combining treatments at lower doses, they will reduce treatment-related side effects while maintaining patient response. In addition to working with pancreatic cancer patients, Dr. Diaz is the Director of the Swim Across America Lab and is board-certified in medical oncology. He completed his residency and medical oncology fellowship at the Johns Hopkins Hospital. Before coming to Hopkins, he earned his undergraduate and medical degrees at the University of Michigan. He is also a member of the Pancreatic Cancer Sequencing Team (see page 2).

GENOME SEQUENCING PROJECT SEEKS TO FIND NEW FAMILIAL PANCREATIC CANCER GENES

The NFPTR team is leading a new multi-center consortium to identify new genes that cause familial pancreatic cancer. The consortium also includes investigators at the Mayo Clinic, Mt. Sinai Hospital in Toronto, Dana-Farber Cancer Institute, Memorial Sloan-Kettering Cancer Center, University of Pittsburgh, Karmanos Cancer Institute, McGill University, University of Pennsylvania and the University of Michigan.

For the project, we are sequencing the genomes, or the complete genetic code, of hundreds of patients with familial pancreatic cancer. The DNA sequences of the patients will then be compared to the sequences of people without pancreatic cancer, in order to identify genetic changes that cause pancreatic cancer. On average, every individual has over 6 million changes in their DNA compared to the "reference genome." The overwhelming majority of these differences do not cause disease, but instead contribute to what makes each individual unique (i.e. height, hair color, eye color, etc.). The challenge for researchers will be to identify the single genetic change amidst these 6 million that increases a person's chances of developing pancreatic cancer. It will take many years of analysis and laboratory work to identify the changes that are responsible for placing a person at a higher risk for pancreas cancer. The project is, however, a critical first step in the process.

We are excited by this project because it has worked before when we studied a smaller number of familial pancreatic cancer patients (only tens, rather than hundreds), and found two previously unknown familial pancreatic cancer genes, *PALB2* and *ATM*, that play an important role in pancreatic cancer risk. It is important to note that variations in these genes account for less than 4% of familial pancreatic cancer cases. While only another 5-10% of cases are explained by mutations in the known pancreatic cancer genes- *BRCA2*, *BRCA1*, *STKL11*, *PRSS1*, *SPINK1* CDKNA2, *MLH1*, *MSH2*, *MSH6*, and *PMS2* genes. Therefore, the genetic basis of most familial pancreatic cancers still remains unknown. We hope that by studying more families we can find what causes the clustering of pancreatic cancer in these "unexplained" families.

HOW YOU CAN HELP:

Spouses are eligible to donate a blood or saliva sample as a "control" (a person without pancreatic cancer to serve as a comparison). Email us at pancreas@jhmi.edu with "Control" in the subject line to receive more information.

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 having 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 Diane Echavarria: (410) 955-3502

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LEARN MORE ABOUT OUR RESEARCH!

Below is a short bibliography of our most recently published research conducted by investigators working with the NFPTR. You can view abstracts of these articles by visiting www.pubmed.com and searching by **PMID**. If you have any questions about any of the studies, please call or email the NFPTR directly at pancreas@jhmi.edu or 410-955-3502.

1. Klein AP, Lindström S, Mendelsohn JB, Steplowski E, Arslan AA, Bueno-de-Mesquita HB, Fuchs CS, Gallinger S, Gross M, Helzlsouer K, Holly EA, Jacobs EJ, Lacroix A, Li D, Mandelson MT, Olson SH, Petersen GM, Risch HA, Stolzenberg-Solomon RZ, Zheng W, Amundadottir L, Albanes D, Allen NE, Bamlet WR, Boutron-Ruault MC, Buring JE, Bracci PM, Canzian F, Clipp S, Cotterchio M, Duell EJ, Elena J, Gaziano JM, Giovannucci EL, Goggins M, Hallmans G, Hassan M, Hutchinson A, Hunter DJ, Kooperberg C, Kurtz RC, Liu S, Overvad K, Palli D, Patel AV, Rabe KG, Shu XO, Slimani N, Tobias GS, Trichopoulos D, Van Den Eeden SK, Vineis P, Virtamo J, Wactawski-Wende J, Wolpin BM, Yu H, Yu K, Zeleniuch-Jacquotte A, Chanock SJ, Hoover RN, Hartge P, Kraft P. An absolute risk model to identify individuals at elevated risk for pancreatic cancer in the general population. PLoS One. 2013 Sep 13;8(9):e72311. doi: 10.1371/journal.pone.0072311. PMID:24058443

2. Wolfgang CL, Herman JM, Laheru DA, Klein AP, Erdek MA, Fishman EK, Hruban RH. Recent progress in pancreatic cancer. CA Cancer J Clin. 2013 Sep;63(5):318-48. doi: 10.3322/caac.21190. Epub 2013 Jul 15. Review. PMID:23856911

3. Leenders M, Bhattacharjee S, Vineis P, Stevens V, Bueno-de-Mesquita HB, Shu XO, Amundadottir L, Gross M, Tobias GS, Wactawski-Wende J, Arslan AA, Duell EJ, Fuchs CS, Gallinger S, Hartge P, Hoover RN, Holly EA, Jacobs EJ, Klein AP, Kooperberg C, LaCroix A, Li D, Mandelson MT, Olson SH, Petersen G, Risch HA, Yu K, Wolpin BM, Zheng W, Agalliu I, Albanes D, Boutron-Ruault MC, Bracci PM, Buring JE, Canzian F, Chang K, Chanock SJ, Cotterchio M, Gaziano JM, Giovanucci EL, Goggins M, Hallmans G, Hankinson SE, Hoffman-Bolton JA, Hunter DJ, Hutchinson A, Jacobs KB, Jenab M, Khaw KT, Kraft P, Krogh V, Kurtz RC, McWilliams RR, Mendelsohn JB, Patel AV, Rabe KG, Riboli E, Tjønneland A, Trichopoulos D, Virtamo J, Visvanathan K, Elena JW, Yu H, Zeleniuch-Jacquotte A, Stolzenberg-Solomon RZ. Polymorphisms in genes related to one-carbon metabolism are not related to pancreatic cancer in PanScan and PanC4.
Cancer Causes Control. 2013 Mar;24(3):595-602. doi: 10.1007/s10552-012-0138-0. Epub 2013 Jan 19.PMID:23334854

4. Klein AP. Identifying people at a high risk of developing pancreatic cancer. Nat Rev Cancer. 2013 Jan;13(1):66-74. doi: 10.1038/nrc3420. Epub 2012 Dec 6. Review.

5. Roberts NJ**,** Klein AP. Genome-wide sequencing to identify the cause of hereditary cancer syndromes: With examples from familial pancreatic cancer. Cancer Lett. 2013 Nov 1;340(2):227-33. doi: 10.1016/j.canlet.2012.11.008. Epub 2012 Nov 27.