NFPTR national familial pancreas tumor registry

NEWS

NOVEMBER 2010

# GREETINGS FROM THE NFPTR TEAM!

This year has been another remarkable year for pancreatic cancer research and we hope to continue to make progress against this terrible disease. We want to extend our continued thanks to our families and express our appreciation for their willingness to stay in touch with us by email, phone and through our newsletter update cards. The return of the update cards enclosed in the newsletter enables us to conduct studies such as our recent study looking to see if relatives of young-onset pancreatic cancer cases are at a higher risk of developing pancreatic cancer than relatives of patients who develop pancreatic cancer later in life (see page 3).

In 2010, we were able to launch a new pancreatic cancer research consortium with the support of the Lustgarten Foundation. The NFPTR at Johns Hopkins is leading an international team of investigators, including researchers from MD Anderson, Mt. Sinai, Mayo Clinic, Dana Farber and Karmanos Cancer Center in a study which seeks to leverage recent technological advances in genome sequencing to identify new familial pancreatic cancer genes (see page 2).

In addition to our research efforts at the NFPTR, we always like to highlight a member of our pancreatic cancer clinical team. This year we focus on Dr. Joseph Herman, who is the director of the Johns Hopkins Pancreatic Cancer Multidisciplinary Clinic. In the three years since this clinic began, over 900 patients with suspected pancreatic cancer have been evaluated. As part of his work to offer the best clinical care to patients with pancreatic cancer, Dr. Herman is interested in novel treatments for pancreatic cancer including combining vaccine therapy with stereotactic radiation therapy (see page 3).

Recently, in a pivotal research study lead by Dr. Christine Iacobuzio-Donahue, researchers at Johns Hopkins demonstrated that pancreatic cancer develops more slowly than previously believed. By studying the primary tumors as well as metastatic tumors of patients who participated in the Gastrointestinal Cancer Rapid Medical Donation study, Dr. Iacobuzio-Donahue and colleagues demonstrated that it takes at least two decades from when a normal pancreatic cancer cell acquires the first genetic cancer until it develops into a large metastatic pancreatic cancer. This study demonstrated there is a larger window in which early detection for pancreatic cancer may be possible than was previously expected (see page 2).

The research studies described in the newsletter are just some of our research highlights this year. For more information about some of our other studies check out the "Pancreas Cancer News" section of our website as well as our publication list on page 4.

We always look forward to hearing from our NFPTR families, so please **return your update card** and feel free to contact us at 410-955-3502, or by email at pancreas@jhmi.edu throughout the year.

**NFPTR TEAM (left to right): Dr. Alison Klein (NFPTR Director), Sarah Wiegand (Coordinator), Diane Echavarria (Coordinator)**

**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. Thank you!

## Inside this issue:

# PANCREATIC CANCERS PROGRESS TO THE LETHAL STAGE MORE SLOWLY THAN PREVIOUSLY BELIEVED

Once again, Johns Hopkins is at the center of ground-breaking pancreatic cancer research. The Hopkins work, published in the October 31 issue of the journal *Nature* and led by Dr. Christine Iacobuzio-Donahue, suggests that it takes at least two decades from the time the very first cancer-causing mutation occurs in a cell in the normal pancreas until it is a large pancreatic cancer that has spread (metastasized) to other organs. The results contradict the idea that pancreatic cancers metastasize very early in their development.

For the study, Dr. Iacobuzio's lab collected tissue samples during autopsies of seven patients who died from pancreatic cancer that had metastasized to other organs. In all patients, metastatic deposits were found in two or more sites in the body, most often the liver, lung and peritoneum (lining of the abdomen). Because the tissue samples were taken within six hours of each patient's death, her lab was able to keep some of the cells alive long enough to extract the DNA and sequence the series of chemical "letters" that form genes in each sample. This approach led to the identification and classification of two types of mutations in pancreatic cancers – those that occur before metastasis and others that happen after the cancer has spread. Most mutations in a pancreatic cancer have occurred before it metastasizes to other organs.

Based on the sequencing data, Dr. Iacobuzio's collaborators used mathematical models to study the timing of pancreatic cancer progression. These models conservatively estimated an average of 11.7 years before the first cancer cell develops to a high-grade pancreatic lesion, then an average of 6.8 years as the cancer grows and at least one cell develops the potential to metastasize, and finally, an average of 2.7 years from then until a patient's death.

Bert Vogelstein, M.D., Clayton Professor and Director of the Ludwig Center for Cancer Genetics & Therapeutics at the Johns Hopkins Kimmel Cancer Center and an investigator at the Howard Hughes Medical Institute, collaborated with Dr. Iacobuzio in this work. Dr. Vogelstein said the results show that "many pancreatic cancer cases have a long lag time before they are detected through conventional tests. This leaves room to develop new early, diagnostic tools and intervene with potentially curative surgery."

Why is this important? This work is the first to show how long it takes to develop a pancreatic cancer, and indicates there is a very long window of opportunity for early detection and cure of pancreatic cancer, but that patients are often not diagnosed until after this window of opportunity has passed. Now that we have a better understanding of the time to intervene, we can begin to optimize screening approaches to diagnose more pancreatic cancers in the curative stage.

*For full citation, see #1 on page 4.*

# NFPTR LEADS NEW INTERNATIONAL PANCREATIC CANCER RESEARCH CONSORTIUM

**Dr. Ralph Hruban**

In February 2010 a new familial pancreatic cancer research consortium was launched supported by The Lustgarten Foundation. The foundation is supporting this work as part of their efforts to advance the most promising research initiatives aimed at finding a cure for pancreatic cancer. As part of this effort NFTPR researchers at Johns Hopkins, led by Drs. Ralph Hruban, Bert Vogelstein and Alison Klein are leading an international team of researchers including investigators from the Mayo Clinic, Memorial Sloan Kettering Cancer Center, Karmanos Cancer Center, MD Anderson, Dana Farber and Mt. Sinai Hospital in Toronto.

The goal of this study is to identify novel familial pancreatic cancer susceptibility genes. Using a new approach, investigators will conduct genome sequencing of all 20,000 genes of patients with familial pancreatic cancer to look for the genetic mutations that may be responsible for the occurrence of pancreatic cancer in these families.

# IN THE NFPTR SPOTLIGHT: JOSEPH M. HERMAN, M.D.

In 1994, Dr. Joseph M. Herman graduated from Salisbury State University with a Bachelor of Science in Biology and Chemistry. Dr. Herman received his medical degree from The University of Maryland in Baltimore and completed his post doctoral internship and residency in the University of Michigan Health System. He served as Chief Resident in Radiation Oncology in the University of Michigan Health System from 2004-2005. In 2005, he joined the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins as Lecturer in the Department of Radiation Oncology and Molecular Radiation Sciences and was promoted to Assistant Professor in 2007.

Dr. Herman's clinical research interests focus on improving the quality and quantity of life for patients diagnosed with pancreatic cancer. He is specifically interested in vaccine therapy because it adds little toxicity to standard treatments. Dr. Herman is involved in efforts to improve survival and quality of life of patients with pancreatic cancer by combining vaccine and targeted therapy with stereotactic radiation and chemotherapy. He is currently the principal or co-principal investigator of three clinical trials that combine radiation with chemotherapy and/or targeted agents for use in pancreatic cancer patients with resected, unresectable, and metastatic disease.

Dr. Herman developed and currently directs a pancreatic multidisciplinary clinic (PMDC) which was the first step towards translational research and improving patient care. Over the past three years the clinic has evaluated over 900 pancreatic patients and has noted a major increase in the pancreas cancer familial registry and clinical trial enrollment.

Dr. Herman has been honored with numerous awards including the Letter of Commendation from the National Institutes of Health, Graduate Merit Award from the University of Maryland, Outstanding Student Achievement Award in Radiation Oncology from the University of Maryland, Resident of the Year from the University of Michigan Health Systems, the AACR Career Development Award for Pancreatic Cancer Research, and the JHU Oncology Center Teaching Award.

# AGE OF ONSET PREDICTS RISK OF PANCREATIC CANCER IN FAMILY MEMBERS

When one or more family members develop pancreatic cancer, it is only natural for the other members of the family to wonder what their chances are of developing pancreatic cancer. This is especially true when an individual develops pancreatic cancer at a young age (less than age 50). A study published this year in the *Journal of the National Cancer*, led by Dr. Alison Klein, Director of the National Familial Pancreas Tumor Registry helps to answer this question.

Previous studies in the NFPTR have shown that individuals with a family history of pancreatic cancer are at higher risk of developing pancreatic cancer themselves. The goal of this study was to see if relatives of patients who developed pancreatic cancer at a young age (<50) were at a higher risk of developing pancreatic cancer than relatives of patients who developed cancer later in life. In this study Dr. Klein and colleagues followed over 1,718 families who had participated in the NFPTR. Families were followed for an average of five years per family. Forty-one of the people being followed developed pancreatic cancer during this time.

This study found that individuals who had at least two relatives with pancreatic cancer and where their relatives with pancreatic cancer developed disease at a young age (<50) had a 9.3-fold increased risk of developing pancreatic themselves. For individuals with at least two relatives with pancreatic cancer where all pancreatic cancers occurred after the age of 50, had a 6.3-fold increased risk.

In contrast, for individuals who had only a single relative develop pancreatic cancer, risk was increased 2.4-fold. This risk was the same whether the relative developed cancer at a young age or not.

This study demonstrates that individuals who have had more than one family member develop pancreatic cancer, especially when one of those family members developed pancreatic cancer at an early age, have a higher risk of developing pancreatic cancer themselves. Risk of pancreatic cancer depends on many factors including family history. Those concerned about their personal risk should discuss this concern with their personal physicians or with a genetic counselor.

*For full citation, see #2 on page 4.*

# HOW YOU CAN HELP:

**Most importantly, please return your update card!**

**Spouses** are eligible to donate a saliva sample as a "control" (a person without pancreatic cancer to serve as a comparison) for our research studies. Contact us at pancreas@jhmi.edu.

**Family members** with *at least one first-degree relative* with pancreatic cancer (sibling, parent, or child) *as well as one other family member with pancreatic cancer* MAY also be eligible to donate a blood sample to aid our research. Contact us at pancreas@jhmi.edu.

**Interested in Screening?** Individuals with *two or more family members with pancreas cancer* MAY be eligible for a research screening study (CAPS4) using endoscopic ultrasound here at Hopkins. For information, please contact the study coordinators, Hilary Cosby or Verna Scheeler at **caps4@jhmi.edu** or 410-502-9795.

# 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**

# UPDATES

Johns Hopkins experts continue to post educational blogs on the web. We hope that you find these blogs enlightening, and we encourage you to contribute your thoughts, experiences and expertise to the blog.
**Website:** http://apps.pathology.jhu.edu/blogs/pancreas/

**Also, remember to follow our research progress throughout the year and keep up to date on exciting news by checking "Pancreatic Cancer News" on the Johns Hopkins Pancreatic Cancer Website: http://pathology.jhu.edu/pancreas/news.php**

# CONTACT INFO

- **Our Website** http://pathology.jhu.edu/pancreas/nfptr
- **Our phone number** (**410) 955-3502**
- **Email:** pancreas@jhmi.edu
- **Alison Klein, PhD, MHS** NFPTR Director
- **Diane Echavarria, BA** Coordinator
- **Sarah Wiegand, MS** Coordinator

# LEARN MORE ABOUT OUR RESEARCH!

Below is a short bibliography of our most interesting, recently published research conducted by investigators working with the NFPTR.

You can view abstracts of most or all of these articles by visiting www.pubmed.com and copying and pasting the title of the article into the search field. If you have any questions about any of the studies discussed in this newsletter or listed here, please contact the NFPTR at 410-955-3502 or pancreas@jhmi.edu.


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7. Wang L, Brune KA, Visvanathan K, Laheru D, Herman J, Wolfgang C, Schulick R, Cameron JL, Goggins M, Hruban RH, Klein AP. Elevated cancer mortality in the relatives of patients with pancreatic cancer.Cancer Epidemiol Biomarkers Prev. 2009 Nov;18(11):2829-34.


# MEDICAL DONATION RESEARCH PROGRAM

Dr. Iacobuzio-Donahue's Gastrointestinal Cancer Rapid Medical Donation Program (GICRMDP) continues to gather crucial information about metastatic gastrointestinal cancer by participants who volunteer prior to their death to undergo a rapid, research autopsy. If this research study is something you or a family member would like to learn more about, feel free to contact Dr. Iacobuzio-Donahue at ciacobu@jhmi.edu or call her at (410) 955-3511.