

FROM THE DIRECTOR

Once again this has been another outstanding year for pancreatic cancer research and the NFPTR! First, I would like to thank all of the families whose continued participation over the years makes our research possible. I would also like to welcome new families who have joined our registry this year. In this newsletter, we will update you on some of the progress we have made over the past year.

A critical step in fighting pancreatic cancer is to detect this disease in its precancerous stage. Therefore, we are proud to announce two early detection studies that will begin this coming year. The third phase of Dr. Canto's study, Cancer of the Pancreas Screening Study (CAPS 3), will begin this year. A complementary study led by Dr. Goggins is aimed at identifying blood markers of pancreatic cancer, and will begin this winter. For details on how you can participate in these research studies, please see page 2.

In addition to the research that we highlight in the newsletter, there are numerous other ongoing studies. We continue to strive to identify the causes of pancreatic cancer, both through our independent studies and by collaborating with other institutes. For example, Dr. Maitra is leading a project examining expression of genes in individuals with pancreatic cancer in collaboration with Illumina, a biotechnology company (see page 3). Additionally, we continue to collaborate with other academic institutions through our participation in the Pancreatic Cancer Genetic Epidemiology Consortium.

I am looking forward to the progress we will make in the coming year in our fight against this disease.

- Alison Klein, Ph.D., MHS



NFPTR TEAM (left to right): Emily Palmisano (NFPTR Coordinator), Marian Raben (Research Coordinator), Dr. Alison Klein (NFPTR Director), and Dr. Ralph Hruban (Founder of the NFPTR)

UPDATE FROM THE COORDINATOR

My name is Emily Palmisano and I have been the coordinator of the NFPTR since July 2005. This past year has been extremely exciting and productive for us. The NFPTR continues to grow rapidly and has now reached a significant milestone of over 2,000 families! Our families are the real key to the success of our research and we are deeply grateful to each one of you for your participation. I especially would like to thank each family who has worked tirelessly to obtain death certificates, provide dates of birth, and get those extra details about your family. As always, if you have any questions for me, or would just like to say hello, feel free to contact me at 410-955-3502, or by email at epalmis1@jhmi.edu.

PLEASE REMEMBER TO RETURN YOUR UPDATE CARD.

THANK YOU!

The information you provide helps us to better understand this disease and its impact on families.

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THIRD PHASE OF SCREENING STUDY BEGINS FOR HIGH RISK FAMILY MEMBERS

Dr. Marcia Canto at the Johns Hopkins University School of Medicine is conducting a new multi-center research study to screen relatives of patients with pancreatic cancer. This research study, known as Cancer of the Pancreas Screening (CAPS 3) involves the use of endoscopic ultrasound (EUS) to look for signs of early pancreas cancer or precancerous changes in the pancreas.

This research study builds on the findings of CAPS 1 and CAPS 2, which were earlier successful phases of this study that have been highlighted in past newsletters. This year the findings of the CAPS 2 study were published (see page 4). In this study Dr. Canto screened 109 high-risk individuals for evidence of changes in the pancreas. Ten individuals with precancerous lesions were identified and underwent surgery at Johns Hopkins. These results suggest that early detection of pancreatic cancer may be possible!

While the first two phases of this study demonstrate that EUS can detect early pancreatic cancer, the goal for the next stage of this study, CAPS 3, is to compare EUS

to other potential screening tests to find the most effective test. The screening for pancreatic cancer in CAPS 3 will also involve a state-of-the-art CT scan, an MRI, and blood tests for tumor markers.

While Dr. Canto is leading this research, we are collaborating with researchers at four other centers around the United States. To be eligible to participate in the CAPS 3 research study, an individual must have at least 3 affected family members with pancreatic cancer (and have a sibling, parent, or child who has been diagnosed with pancreatic cancer) or have a diagnosis of Peutz-Jeghers syndrome.

If you are interested in participating in this research or have any questions about whether you might be eligible for CAPS 3, you can contact the NFPTTR coordinator, Emily Palmisano at 410-955-3502, or by email at pancreas@jhmi.edu, or the CAPS 3 study coordinator Hilary Cosby, R.N. at 410-955-5274, or by e-mail at hcosby1@jhmi.edu, or Dr. Canto at 410-614-5388, or by email at mcanto1@jhmi.edu.

PURSUING NEW DIRECTIONS IN THE EARLY DETECTION LABORATORY

Dr. Michael Goggins' laboratory is working to develop a simple blood test for pancreatic cancer. In order to develop this test, researchers need to identify a blood marker that increases when precancerous changes develop in the pancreas, but does not increase in non-cancerous diseases of the pancreas (like pancreatic cysts or pancreatitis). Once this test is developed, it is our hope that clinicians could then monitor levels of this marker over time. If the marker levels begin to change, it would prompt clinicians to order additional medical tests to look for pancreatic cancer. This way we will detect the disease early, potentially saving lives!

To facilitate this work, Dr. Goggins recently received a

grant from the National Institutes of Health to identify these new blood markers. This research study will last five years, and during this period, he will collect blood samples at different points in time from both pancreatic cancer patients and their relatives. He will then look to see if he can detect changes in any marker levels in these samples.

In order to conduct this research study, we will need your help. We will be asking members of the NFPTTR if they would be willing to participate in this study. Participation in this early detection study is completely voluntary. You are a valued registry participant no matter what you decide! For more information, please contact Emily Palmisano at pancreas@jhmi.edu or 410-955-3502.

PANCAN CHAPTER VISITS OUR PANCREATIC CANCER RESEARCH LABS

On Saturday, September 9, 2006, 24 members of the Washington DC PanCAN group visited The Sol Goldman Pancreatic Cancer Research Center at Johns Hopkins. The visit was organized by Mary Zapor and Marsha Garil from PanCAN. The PanCAN visitors toured some of the labs, met with Dr. Alison Klein and Emily Palmisano from the NFPTTR, and listened to talks on the ongoing pancreatic cancer research and clinical treatment of pancreatic cancer at Johns Hopkins. After rotating through the labs, the group had an informal lunch with NFPTTR staff, the doctors and scientists.

Three members of the PanCAN group that had visited in 2003 returned to visit the new location in the Cancer Research Building II. Several of the doctors and scientists said that meeting patients and family members provides an inspiration for their work. Visit <http://pathology2.jhu.edu/pancreas/pancanvisit/index.htm> to see photos.

PANCREATIC CANCER IN THE ASHKENAZI JEWISH POPULATION

Dr. Alison Klein and Dr. Michael Goggins have recently begun a study aimed at determining the genetic basis of pancreatic cancer in individuals of Ashkenazi Jewish descent. This research complements our existing work to identify the genetic basis of pancreatic cancer in all families.

It has been recognized that individuals who are of Ashkenazi Jewish descent are at an increased risk of developing pancreatic cancer. While this increased risk could be due to a variety of factors such as diet and environmental exposures, a growing body of evidence suggests that a significant portion of the increased risk of pancreatic cancer in individuals of Ashkenazi Jewish descent is due to inherited ("germline") changes ("mutations") in specific cancer associated genes.

If we think of a gene as a single paragraph in a long book, a single typographical error ("mutation") in any word in that specific paragraph ("gene") can put someone at increased risk of developing pancreatic cancer. However, because many individuals of Ashkenazi Jewish descent have a common genetic ancestry, they are likely to have the exact same mutation which facilitates researchers' ability to find this mutation. For example, over 100 mutations have been identified in the second breast cancer gene, *BRCA2*. However, individuals of Ashkenazi Jewish descent who have a mutation in this gene almost always have the exact same mutation in this gene, known as the 6174delT mutation. But because different mutations in this same gene may also increase the risk of pancreatic cancer, the impact of this study will extend to all pancreatic cancer families, not only those of Ashkenazi Jewish descent. To be eligible for this research study, families needed to complete our questionnaire and join the NFPTR.

To educate individuals about pancreatic cancer in the Ashkenazi Jewish population, we developed a webpage: (http://pathology2.jhu.edu/pancreas/ashkenazi_jewish_ancestry.cfm).

If you would like more information about our ongoing research studies, please contact Emily Palmisano at 410-955-3502 or pancreas@jhmi.edu.

INNOVATIVE APPROACH TO FIND THE GENETIC BASIS OF PANCREATIC CANCER

Dr. Anirban Maitra is leading a collaborative study with Drs. Klein, Hruban and Goggins, as well as investigators at the Johns Hopkins Institute of Genetic Medicine, on a novel screening tool for the discovery of new genes in familial pancreatic cancers using allele specific



Dr. Anirban Maitra in the Lab

expression (ASE). It is now being increasingly recognized that even though we all carry two alleles, one from each parent, both alleles do not necessarily express message RNA (mRNA) at the same level. While this phenomenon of imbalanced allelic expression was well known in a limited set of genes ("imprinted genes"), it has now become evident that allele specific expression (ASE) is far more common in the human genome than previously recognized. More importantly, using novel array-based technologies, it is not only possible to identify normal patterns of ASE in the population, but also identify those rare abnormal ASE events that are associated with a deleterious germline mutation in patients with familial pancreatic cancer.

Dr. Maitra and colleagues are looking to discover cases of "extreme ASE" in pancreatic cancer patients not observed in the apparently normal set. However, if ASE is found, additional work is needed to determine if these changes are involved in increasing the risk of pancreatic cancer. This study will help identify individuals at high risk of pancreatic cancer who may benefit from early detection tools such as those being developed by Drs. Goggins and Canto (see page 2).

CERTIFICATE OF CONFIDENTIALITY

We want to remind the participants in our registry 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 to our registry and affords us legal protection from having to involuntarily release any information about you or your family. With

this certificate, our investigators cannot be forced by court order to disclose any information which may identify our participants in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

If you have any questions regarding this certificate or would like a copy, please contact Emily Palmisano at 410-955-3502 or Dr. Klein at 410-955-3511.

CONTACT INFORMATION

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MEDICAL DONATION PROGRAM

Dr. Christine Iacobuzio-Donahue's Gastrointestinal Cancer Rapid Medical Donation Program (GICRMDP) continues to gather crucial information about metastatic pancreatic cancer. Since this research program began in 2003, 54 cancer patients from around the United States have participated by volunteering to undergo a rapid, research autopsy during which tissues from the pancreas and other organs are collected.

Participation in this research is purely voluntary and it may help other patients and their families in the future. If this research study is something you would like to learn more about, feel free to contact Dr. Iacobuzio at ciacobu@jhmi.edu or call Marian Raben, Clinical Coordinator at (410) 955-3512. Patients willing to undergo a research autopsy at the time of death will be making one of the most important contributions to help researchers better understand and treat metastatic cancer.

YOU CAN HELP!

To continue our studies, we are now enrolling spouses of pancreatic cancer patients as "controls" (people without pancreatic cancer to serve as comparisons). Other close contacts including family members who are not biologically related to the patient are also eligible. For more information on participating in this research, please contact us at pancreas@jhmi.edu.

SELECTED NFPTR BIBLIOGRAPHY-2006

Although we would like to be able to write about each and every study conducted by all of the NFPTR investigators, we simply do not have the space to do so. We have therefore put together a brief bibliography of some of the other published research conducted by investigators working with the NFPTR. We hope that this list helps you see the wide variety of research that we are conducting. If you have any questions about any of the studies discussed in this newsletter or listed here, please do not hesitate to contact the NFPTR at 410-955-3502 or pancreas@jhmi.edu and we will do our best to answer your questions.

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Congratulations Dr. Hruban! Recipient of the 2006 PanCAN Medical Visionary Award

Follow our research progress throughout the year and keep up to date on exciting news such as this by checking the "What's New" Section of the Johns Hopkins Pancreatic Cancer Webpage:
<http://pathology.jhu.edu>