HOW YOU CAN HELP:

Most importantly, please return your update card!

Spouses are eligible to donate a blood 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* are also eligible to donate a blood sample to aid our research. Contact us at pancreas@jhmi.edu.

Interested in Screening? Individuals with *at least two other family members with pancreas cancer* MAY be eligible for a research screening study (CAPS 4) 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.

NEW PANCREATIC CANCER BLOG!

We encourage you to visit the new *Johns Hopkins Pancreatic Cancer Blog* at http://apps.pathology.jhu.edu/blogs/pancreas/

The blog was created to facilitate communication with patients, their families, and friends as they face health issues related to the pancreas. Johns Hopkins experts will regularly post blogs on "hot issues." We hope that you find these blogs interesting and educational, and we encourage you to contribute your thoughts, experiences and expertise to the online blog.

Also, remember to follow our research progress throughout the year and keep up to date on exciting news by checking the "What's New" section of the Johns Hopkins Pancreatic Cancer Web: http://pathology.jhu.edu/pancreas/

LEARN MORE ABOUT OUR RESEARCH!

Below is a short bibliography of 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 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.

Berrington de Gonzalez A, Yun JE, Lee SY, Klein AP, Jee SH. Pancreatic cancer and factors associated with the insulin resistance syndrome in the Korean cancer prevention study. *Cancer Epidemiol Biomarkers Prev*. 2008 Feb;17(2):359-64. PMID: 18268120

Fu B, Guo M, Wang S, Campagna D, Luo M, Herman JG, Iacobuzio-Donahue CA. Evaluation of GATA-4 and GATA-5 methylation profiles in human pancreatic cancers indicate promoter methylation patterns distinct from other human tumor types. *Cancer Biol Ther*. 2007 Oct;6(10):1546-52. Epub 2007 Jul 7. PMID: 17912029

Jones S, Zhang X, Parsons DW, Lin JC, Leary RJ, Angenendt P, Mankoo P, Carter H, Kamiyama H, Jimeno A, Hong SM, Fu B, Lin MT, Calhoun ES, Kamiyama M, Walter K, Nikolskaya T, Nikolsky Y, Hartigan J, Smith DR, Hidalgo M, Leach SD, Klein AP, Jaffee EM, Goggins M, Maitra A, Iacobuzio-Donahue C, Eshleman JR, Kern SE, Hruban RH, Karchin R, Papadopoulos N, Parmigiani G, Vogelstein B, Velculescu VE, Kinzler KW. Core signaling pathways in human pancreatic cancers revealed by global genomic analyses. *Science*. 2008 Sep 26;321(5897):1801-6. Epub 2008 Sep 4.

Laffan TA, Horton KM, Klein AP, Berlanstein B, Siegelman SS, Kawamoto S, Johnson PT, Fishman EK, Hruban RH. Prevalence of unsuspected pancreatic cysts on MDCT. *AJR Am J Roentgenol*. 2008 Sep;191(3):802-7. PMID: 18716113

Pawlik TM, Laheru D, Hruban RH, Coleman J, Wolfgang CL, Campbell K, Ali S, Fishman EK, Schulick RD, Herman JM; Johns Hopkins Multidisciplinary Pancreas Clinic Team. Evaluating the impact of a single-day multidisciplinary clinic on the management of pancreatic cancer. *Ann Surg Oncol*. 2008 Aug;15(8):2081-8. Epub 2008 May 7. PMID: 18461404

Shi C, Daniels JA, Hruban RH. Molecular characterization of pancreatic neoplasms. *Adv Anat Pathol*. 2008 Jul;15(4):185-95. Review. PMID: 18580095

Tan AC, Fan JB, Karikari C, Bibikova M, Garcia EW, Zhou L, Barker D, Serre D, Feldmann G, Hruban RH, Klein AP, Goggins M, Couch FJ, Hudson TJ, Winslow RL, Maitra A, Chakravarti A. Allele-specific expression in the germline of patients with familial pancreatic cancer: an unbiased approach to cancer gene discovery. *Cancer Biol Ther*. 2008 Jan;7(1):135-44. Epub 2007 Oct 19. PMID: 18059179

CONTACT INFO

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- **Our phone number**
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- **Alison Klein, PhD, MHS**
  NFPTR Director
  *Email: aklein1@jhmi.edu
- **Emily Palmisano, BA**
  NFPTR Coordinator
  *Email: pancreas@jhmi.edu

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.

N F P T R
national familial pancreas tumor registry
NEWS
December 2008

GREETINGS FROM THE NFPTR TEAM!

The NFPTR has reached another significant milestone of over 3000 participating families! Many thanks go out to all of the families who made this a reality! Without your hard work in tracking down details about your family history, our study wouldn't be possible. Your continued involvement in the registry (by completing and returning the enclosed update card) is also an important part of our success.

This year, we are very excited to announce the completion of the Pancreatic Cancer Genome Sequencing project. In this landmark study, Drs. Bert Vogelstein, Ken Kinzler and Victor Velculescu, along with our pancreatic cancer research team from Johns Hopkins, sequenced the entire pancreatic cancer genome (see page 2). They identified the genetic changes that are acquired during a patient's lifetime that cause pancreatic cancer to develop. From a genetic standpoint, this makes pancreatic cancer one of the best understood cancers. Now the work begins to translate these findings into patient care, early detection, and a better understanding of why pancreatic cancer runs in some families.

In addition, we continue to make progress in our efforts to better understand the inherited changes which cause clustering of pancreatic cancer in some families. As part of this work, we are using novel technologies such as those featured on page 3, as well as working with researchers around the world as part of our involvement in the PACGENE and PanScan consortiums. We are leaving no stone unturned in our work to find the causes of familial pancreatic cancer.

In the coming weeks we will be welcoming some new faces to the NFPTR as coordinator Emily Palmisano will be leaving her position in January to enroll in a Master's in Nursing program. Good luck Emily, we will miss you! We also would like to thank our Hopkins coordinator, Marian Raben, for her work on the registry. Marian stepped down to accept a clinical position in prostate cancer at Hopkins.

November 22, 2008 marked the second anniversary of the multidisciplinary pancreatic cancer clinic (PMDC) at Hopkins. In one single day, a patient with a suspected pancreas problem is offered a comprehensive evaluation encompassing all the resources available at Hopkins for the education, diagnosis, treatment and research of pancreatic cancer. Two new medical oncologists have joined the Hopkins pancreatic cancer team. To learn about Dr. Le and Dr. Azad, see page 3. For more information about this clinic, please see the Web: http://pathology.jhu.edu/pancreas/MDC/index.html

As always, if you have any questions, feel free to contact us at 410-955-3502, or by email at pancreas@jhmi.edu. Thanks again to all our wonderful families who make our research a success!

With appreciation,
Dr. Alison Klein, Director

We've updated and redesigned the NFPTR webpage! Check it out for information on the purpose of our research, insights gained, and new research studies you may be eligible to participate in!

http://pathology.jhu.edu/pancreas/nfptr

NFPTR TEAM (left to right): Dr. Alison Klein (NFPTR Director), Dr. Ralph Hruban (NFPTR Founder), Emily Palmisano (NFPTR 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 CANCER GENOME SEQUENCED

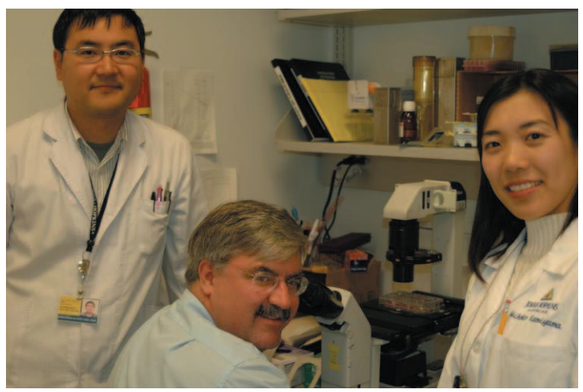
Johns Hopkins has long been a site of revolutionary pancreatic cancer research. In an exciting advance, the complete genetic blueprint (the "genome") for pancreatic cancer was decoded by the pancreatic cancer research team at The Sol Goldman Pancreatic Cancer Research Center at Johns Hopkins. The study, led by Dr. Bert Vogelstein, Dr. Kenneth Kinzler and Dr. Victor Velculescu, is reported in the Sept. 26, 2008 issue of the journal *Science*.

This project had three main components: sequence analysis, copy number analysis, and expression analysis. After sequencing more than 20,000 genes in a series of 24 well-characterized pancreatic cancers, the team discovered over 1,500 DNA mutations in these cancers. Believed to be the most comprehensive genetic study to date for any tumor type, the new map evaluated mutations in virtually all known human protein-encoding genes in 24 pancreatic cancers. An average of 63 mutations was found in each cancer, supporting the growing body of evidence that cancer is fundamentally a disease caused by alterations in the DNA. The scientists identified 12 core cell signaling pathways and processes that were each altered in more than two-thirds of the cancers. These 12 core pathways provide the basis for novel diagnostic and therapeutic approaches in pancreatic cancer.

"This perspective changes the way we think about solid tumors and their management, because drugs or other agents that target the physiologic effects of these pathways, rather than individual gene components, are likely to be the most useful approach for developing new therapies," says Bert Vogelstein, M.D., co-director of the Ludwig Center at Johns Hopkins and a Howard Hughes Medical Institute investigator.

What does this mean for the average person? It means that we are making great strides in better understanding the basic science behind the development of pancreatic cancer. As director of The Sol Goldman Pancreatic Cancer Research Center, Dr. Ralph Hruban, said, "This landmark study characterizes the fundamental genetic components of pancreatic cancer and will guide research on this disease for the next decade. The enhanced understanding of pancreatic cancer gained from these studies and their follow-up work will hopefully lead to dramatic improvements in the prevention, detection, or treatment of pancreatic cancer." Your participation in the NFPTR gives us even more crucial information about the development of pancreas tumors in families.

NOVEL STRATEGY EMPLOYED IN THE HUNT FOR THE PANCREATIC CANCER GENE



Drs. Hirohiko Kamiyama, Jim Eshleman and Mihoko Kamiyama

Discovery of the gene(s) predisposing one to familial pancreatic cancer is an important goal of the NFPTR. As part of this ongoing work, Drs. Hirohiko and Mihoko Kamiyama in Dr. Jim Eshleman's lab here at Johns Hopkins have been employing a novel strategy to find these genes.

With the help of Drs. Ralph Hruban, Anirban Maitra, and Christine Iacobuzio-Donahue, they have isolated 9 new familial pancreatic cancer cell lines, which are cancers that can be grown "in vitro" in the laboratory. Prior to their efforts, there was only a single pancreatic cancer cell line reported in the literature.

Using a technique called GINI discovered at Johns Hopkins by Dr. Hal Dietz, they have screened these 9 lines to identify candidate familial pancreatic cancer genes. Over 95 candidate genes have been identified. Dr. Eshleman's laboratory, in collaboration with Drs. Klein, Goggins, Hruban and Kinzler, will now use these data in conjunction with DNA sequencing and family data collected as part of the NFPTR to narrow this list to the few genes important in familial pancreatic cancer. This is an important next step in our efforts to identify the "familial pancreatic cancer gene."

IN THE NFPTR SPOTLIGHT

We would like to welcome some new faces to the Pancreatic Cancer research team at Johns Hopkins. This year, two medical oncologists have joined the team, Drs. Nilo Azad and Dung Le.

Dung Le, M.D. is an oncologist whose primary focus is the treatment of patients with pancreatic cancer. She received her BS from Yale University and received all of her medical training at Johns Hopkins, including medical school, internal medicine residency, and medical oncology fellowship.

She has a special interest in immunotherapeutic approaches to pancreatic cancers. In the laboratory, she is studying immune effects in the tumor microenvironment to better understand the barriers to effective vaccination strategies. She works closely with Drs. Elizabeth Jaffee and Dan Laheru to translate various cancer vaccine approaches that have been developed in the laboratories at Hopkins into clinical trials. This includes evaluation of genetically modified Listeria monocytogenes that aim to prime an immune response to a protein (mesothelin) expressed on a majority of pancreatic cancers, as well as developing protocols that combine vaccines in a synergistic manner.

By working with a team of dedicated laboratory and clinical researchers, she is working to test the most efficient and effective vaccines in combination strategies that have strong scientific foundation in the hopes of providing more effective treatment options to her patients.

Nilofer Azad, M.D. is an Assistant Professor of Oncology. She obtained her M.D. degree and Internal Medicine Fellowship from Baylor College of Medicine in Houston, Texas, followed by a fellowship in Medical Oncology at the National Cancer Institute.

Her research centers around finding new treatments for gastrointestinal malignancies using molecularly targeted drugs. The hope is that that these targeted agents can attack cancer cells based on biological changes that are preferentially found in tumor cells over normal cells. The promise of targeted therapy is that we will be able to attack cancer cells while sparing normal tissue.

Dr. Azad has been pivotally involved in multiple trials of targeted agents alone and in combination. At the National Cancer Institute, Dr. Azad was instrumental in the design and implementation of a study using PARP inhibitors, agents that target the DNA repair pathway, with platinum-based chemotherapy in patients with *BRCA* gene mutations. Impaired DNA repair is an important characteristic of many GI malignancies, and Dr. Azad's clinical research will continue to explore agents that target DNA repair in treatment of GI cancers.

Both Dr. Le and Dr. Azad are a pivotal part of the pancreas cancer team at Johns Hopkins. To make an appointment with Dr. Le or Dr. Azad, contact the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Hospital at 410-955-8964.

BRCA1 GENE MUTATION IS NOT A COMMON CAUSE OF FAMILIAL PANCREATIC CANCER

A recent study led by genetic counselor Jennifer Axilbund and Dr. Alison Klein examined if inherited mutations in the first breast cancer gene, BRCA1, were a common cause of the familial clustering of pancreatic cancer. Several previous studies conducted have shown that individuals who inherit a mutation in the first breast cancer gene BRCA1 have a 2-fold increased risk of developing pancreatic cancer; this translates to about a 2% lifetime risk of developing pancreatic cancer.

Our investigators were interested in determining the frequency of BRCA1 mutations in families with 3 or more pancreatic cancers enrolled in the NFPTR. They sequenced DNA from 66 pancreatic cancer patients in these families. Overall, no deleterious mutations were detected. In contrast, in a similar study conducted by Drs. Kathy Murphy and Scott Kern in 2004 reported 17% of families with 3 or more pancreatic cancer carried deleterious mutations in BRCA2, the 2nd breast cancer gene.

These studies combined indicate that BRCA2 is a much more common cause of the familial clustering of pancreatic cancer than is BRCA1. Overall, we are continuing our efforts to look for the gene(s) responsible for the majority of the familial clustering of pancreatic cancer.

Dr. Alison Klein and Jennifer Axilbund, MS

CERTIFICATE OF CONFIDENTIALITY

We want to remind participants that the NFPTR is 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 certificate or would like a copy, please contact us at 410-955-3502.