National Familial Pancreas Tumor Registry
http://pathology.jhu.edu/pancreas

NFPTR NEWS

December 2002

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UPDATE FROM THE DIRECTOR

This year the National Familial Pancreas Tumor Registry (NFPTR) has achieved a significant milestone. As of August 15, 2002, over 1,000 families have joined the NFPTR! These families form the foundation of our research into why pancreatic cancer runs in some families. We very sincerely appreciate your continued participation.

A number of you have asked for periodic updates on the research being conducted by the NFPTR. We have created this issue of the NFPTR News to give you a sense of some of our ongoing projects.

On page 3, Dr. Anirban Maitra reports his work developing a new "familial pancreatic cancer gene chip" that researchers can use to simultaneously sequence five of the genes thought to cause some forms of familial pancreatic cancer. These genes are called p16, BRCA2, hMLH1, STK11, and PRSS1. This gene chip is for research purposes only, but it represents a significant advance in our ability to study the role of these five genes in the familial aggregation of pancreatic cancer. Dr. Maitra plans to make this wonderful resource available to investigators at other centers.

This year the NFPTR also joined forces with five other familial pancreatic cancer research registries to form a new consortium (called "PACGENE") dedicated to the hunt for the familial pancreatic cancer gene. The other centers participating in PACGENE include The Mayo Clinic, the Karmanos Cancer Center in Detroit, the University of Toronto, MD Anderson Cancer Center, and Creighton University. The joining together of these familial registries gives the PACGENE Group more statistical power in the hunt for the familial pancreatic cancer gene. PACGENE has received a large grant from the federal government for these studies.

The laboratory of Dr. Goggins here at

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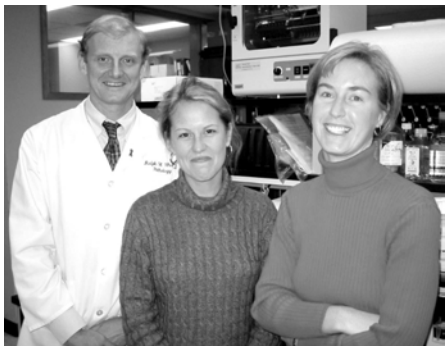
Inside this issue

FROM THE COORDINATOR

I am very pleased to announce the addition of Alice Martien to the NFPTR team. Ms. Martien will assist me with the day-to-day operations of the registry as well as interacting with the members of our registry. Ms. Martien is very excited about her new role with the NFPTR and we know that she will be a great addition to the NFPTR team! If there is ever a time when you cannot reach me with your questions, please call Ms. Martien at 410-955-3502 and she will be happy to assist you.

I always enjoy hearing from the members of our registry and I welcome phone calls and e-mails from the participants in the NFPTR with any questions or comments that you may have.



Dr. Ralph Hruban, Alice Martien, and Kieran Brune

Best wishes for a very happy holiday season and a healthy 2003!

Kieran A. Brune

THE EARLY DETECTION LABORATORY

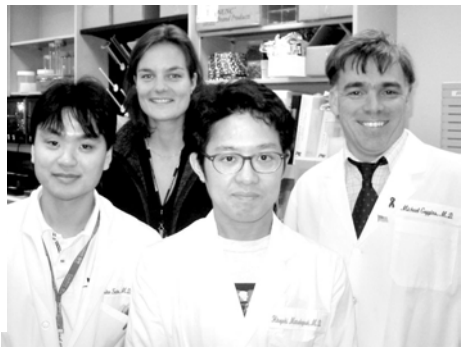
One of the most important research priorities in the war against pancreatic cancer is the discovery of new tests to detect pancreatic cancer early, before it has spread beyond the gland. Dr. Michael Goggins' Early Detection Laboratory is dedicated to this goal. The researchers in the Early Detection Lab are systematically identifying changes in pancreatic cancer that could potentially be used as new markers for the early detection of pancreatic cancer.

Our genes are determined by the DNA code in our cells and many DNA changes occur during pancreatic cancer development. These DNA abnormalities, in turn, give rise to changes in the RNA that are known as "gene expression changes." The RNA expression patterns in turn generate protein abnormalities that could be detected in the blood or other types of patient samples.

To look at the thousands of genes and proteins in a pancreatic cancer cell, the Goggins' lab is using a variety of cutting-edge molecular approaches including gene chips, protein chips, and DNA sequencers. These molecular tools are used to examine the pancreatic cancers from all "angles" in order to find the best new target for the early detection of pancreatic cancer. The scientists in the Early Detection Lab have been successful in identifying a number of DNA alterations, as well as RNA and protein changes that appear to be specific for pancreatic cancer and therefore could serve as the basis for future diagnostic tests for pancreatic cancer. Some of these changes have been detectable in the blood samples and pancreatic fluids of patients with pancreatic cancer. The researches are now investigating if these new markers can detect silent pancreatic cancer.

The Early Detection Lab Pictured at Right:

Dr. Norihiro Sato
Dr. Hiroyuki Matsubayashi
Dr. Tjarda van Heek
Dr. Michael Goggins



ATTITUDES TOWARD SMOKING AND PANCREATIC CANCER RISK

We recently conducted a survey of smoking behavior and attitudes about smoking and pancreatic cancer risk among NFPTR participants. Surveys were mailed out in June 2002 and to date we have received back over 1,100 completed surveys! We are extremely pleased with and appreciative of this high response rate, and would like to express our gratitude to all who participated. Our goal is to use this data to develop a smoking cessation program specifically for individuals with a family history of cancer. We have therefore invited Dr. Laura Juliano, an expert in smoking treatment development, to join our research team to work on this exciting research project.

Dr. Juliano received her Ph.D. in Clinical Psychology from the State University of New York at Binghamton and subsequently completed a fellowship at The Johns Hopkins University School of Medicine. She is currently an Assistant Professor at American University in Washington D.C. where she is also the Director of Smoking Treatment and Research Services (STARS). She has been conducting research and providing treatment for tobacco dependence for more than a decade. We will keep you informed about the outcome of her research and the future development of any smoking treatment research studies that might develop from her work. In the meantime we would like to welcome Dr. Juliano to the NFPTR.

CERTIFICATE OF CONFIDENTIALITY

We want to remind the participants in our registry that The NFPTR continues to be protected by a Confidentiality Certificate (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 Kieran Brune at 410-955-3502.

"The future depends on what we do in the present."
Mahatma Ghandhi

FAMILIAL PANCREATIC CANCER GENE CHIP

Over the last year, Dr. Anirban Maitra has continued his exciting research efforts to understand familial pancreatic cancer. He has used a technology called "conversion" (discovered by Dr. Bert Vogelstein, a world famous cancer researcher at Hopkins) to study patients who belong to high-risk pancreatic cancer families. Why use this technique? Each cell in our body contains 23 pairs of chromosomes. If there is an abnormality in one chromosome from a pair (in other words, a "gene mutation" that would predispose an individual to developing pancreas cancer), this abnormality may be masked (hidden) by the second normal copy of that chromosome. Conversion is a technique that separates the pairs of human chromosomes, so that an abnormality in one chromosome can be detected without being masked by the "sister" chromosome. Dr. Maitra has combined conversion with revolutionary "gene chips" (called snp chips) that can be used to analyze thousands of genes in one single experiment in order to detect mutations. This is the first time such an approach has been taken for the study of familial pancreas cancer, and we hope that it will greatly speed up our search for the "familial pancreatic cancer gene."

In addition, Dr. Maitra has embarked on collaboration with Affymetrix, Inc., the largest company in the world manufacturing gene chips, to design a "familial pancreatic cancer" gene chip. This chip will be used for research

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Dr. Anirban Maitra

FAMILY CANCER STUDY

Alison Klein, Ph.D., is studying the family health information that we have collected from each of the families enrolled in the registry to examine the occurrence of different types of cancers that develop in these families. Through this important research study, we hope to gain further understanding of the risk of new pancreatic cancers developing in families in which there has already been at least one case of pancreatic cancer. Additionally, her work will help to establish if there are cancers, other than pancreatic cancer, that occur with increased frequency among individuals who have a family history of pancreatic cancer. For example, melanoma occurs more frequently in families with a history of pancreatic cancer and this finding led to the discovery of the importance of the p16 gene in familial pancreatic cancer.

We hope the results of this research study will help us to improve the counseling, screening, and treatment options for pancreatic cancer patients and their families. We look forward to interesting results from Dr. Klein's study.

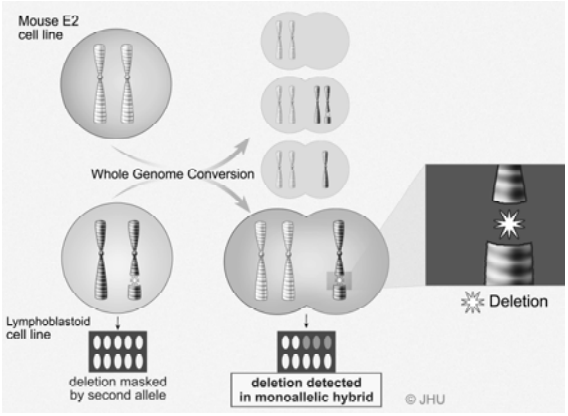
PANCREATIC CANCER GENETIC EPIDEMIOLOGY (PACGENE)

We are pleased to announce that investigators in the National Familial Pancreas Tumor Registry have agreed to participate in a multi-center consortium to study familial pancreatic cancer. This consortium, called "PACGENE," will include physicians, scientists, and registry coordinators from the Mayo Clinic, the Karmanos Cancer Center in Detroit, the University of Toronto, MD Anderson, and Creighton University. Through shared expertise and streamlining of efforts, it is hoped that the joining together of research efforts from these multiple centers will greatly facilitate the hunt for the causes of familial pancreatic cancer. For example, Dr. Goggins at Johns Hopkins will help coordinate any initial genetic screening that may be needed by any of the participating centers. The PACGENE consortium has already applied for and received a large 5-year grant from the federal government.

The participation of the NFPTR researchers in the PACGENE consortium highlights the willingness of investigators in the NFPTR to collaborate and share their expertise with investigators at other centers. We look forward to hearing positive results from the PACGENE consortium. In the meanwhile, if you have any questions, please do not hesitate to give us a call (410-955-3502).

(GENE CHIP Continued from page 3)
purposes only and it will allow researchers to examine mutations in the most commonly involved genes known to be associated with an increased risk for familial pancreatic cancer (p16, BRCA2, hMLH1, STK11, and PRSS1). Although the genetic abnormality underlying the vast majority (about 80%) of familial pancreas cancers is not known yet, this "familial pancreatic cancer gene chip" will help researchers to identify mutations in one of the above known genes.
(Please see illustration below describing how the conversion technique works)

Illustration of Conversion Technique



The Role of Surgery in Palliative Care for Pancreatic Cancer
By: JoAnn Coleman, R.N.

Presently, only a minority of patients are candidates for surgical removal of their pancreatic cancer. Thus it becomes important for physicians to ease the symptoms associated with unresectable pancreatic cancer and therefore maximize the quality of life for these patients. Surgery on patients with unresectable pancreatic cancer is aimed at relieving three major symptoms associated with this cancer: obstructive jaundice resulting from blockage of the biliary tree, duodenal or gastric outlet obstruction, and tumor-related pain. Surgery is a means of providing relief for these three symptoms and is indicated in patients found to have unresectable pancreatic cancer at the time of their diagnosis.

The relief of obstructive jaundice and its related itching can provide improvement in a patient's overall well being. The surgical relief of obstructive jaundice is performed by creating a bypass of the blocked biliary tree to the intestines (called a "choledochojejunostomy" or "hepaticojejunostomy").

Cases in which the cancer has progressed, obstruction of the bowel (the duodenum) occurs in a significant percentage of patients. This obstruction prevents the passage of food or fluids from the stomach into the intestine. This obstruction can be surgically bypassed by creating a passage from the stomach to the intestines (called a "gastrojejunostomy"). Patients may undergo one or both bypass procedures at the time of initial surgery. If both procedures are done at the same time the patient will have undergone a "double bowel bypass."

The appropriate management of pain related to pancreatic cancer may provide the greatest improvement in a patient's quality of life. One option for pain management in patients undergoing a surgery is an alcohol nerve block, called a "chemical splanchnicectomy." This procedure is performed by injecting alcohol into an area with a lot of nerves for the pancreas. The alcohol may numb the nerves for up to four months. This procedure may reduce pain or delay the onset of pain in those patients who don't have pain at the time of surgery. An alcohol nerve block may be repeated if needed and can also be done as an outpatient procedure by pain management specialists using CT scan guided techniques.

Although there are effective nonoperative and minimally invasive palliative techniques available for unresectable pancreatic cancer, in many instances surgical management can best treat obstructive jaundice, treat or prevent bowel obstruction, and reduce the significant pain associated with extensive disease in a single procedure.

(FROM THE DIRECTOR Continued from page 1)
Johns Hopkins will help in the analysis of DNA samples for PACGENE. On page 2, Dr. Goggins describes some of his other ongoing research on the early detection of pancreatic cancer.

I also want to call your attention to page 3, where Dr. Alison Klein describes an exciting research study she is conducting on the other types of cancer that occur in families with pancreatic cancer. For example, the finding that melanoma (a form of skin cancer) also runs in some families with pancreatic cancer led to the discovery of the importance of the p16 gene in familial pancreatic cancer and familial melanoma. Dr. Klein's study should prove a major advance in our understanding of which cancers run in families with pancreatic cancer.

Also in this issue of NFPTR News, Dr. Laura Juliano describes a research study she is conducting on smoking behavior and attitudes in families with pancreatic cancer (page 2). We look forward to the results of this important research.

We are very excited by the remarkable success of the NFPTR and by the important research studies being performed. We sincerely thank you for your continued participation in this research and, as always, we welcome your feedback.

Ralph H. Hruban, M.D.
Director, NFPTR