

NFPTR NEWS

December 2003

Important Contact

Information for NFPTR

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UPDATE FROM THE DIRECTOR

Welcome to the fourth volume of the NFPTR News. This has been an exciting year for us. The NFPTR continues to grow at a rapid pace. As of October 1, 2003, over 1,200 families have enrolled in the registry. Most of the families are from the United States, but we even have some families from Europe, Canada and Australia! As the NFPTR has grown, so too have the research studies that we conduct. With your help and cooperation we have: 1) Correlated the risk of pancreatic cancer with the number of relatives a person has with pancreatic cancer. For example, individuals with three first-degree relatives with pancreatic cancer (a first-degree relative is a brother/sister or parent/child) have a 32-fold increased risk of developing pancreatic cancer. This study has just been submitted for publication and is described in greater detail on page 3. It is important because it helps to quantify cancer risk, an important first step in applying screening tests for the early

detection of pancreatic cancer 2) Began a large follow-up research study of the role of the BRCA2 gene (the second breast cancer gene) in familial pancreatic cancer. Working with Drs. Fergus Couch and Gloria Petersen at the Mayo Clinic, we will use a new technique developed by Dr. Couch to further define the role of BRCA2 in familial pancreatic cancer (see page 3); 3) Dr. Scott Kern and colleagues have demonstrated that a small minority of pancreatic cancers, particularly those that occur at an early age, are caused by inherited changes in one of the "Fanconi anemia" genes. You can read more about this exciting study on page 2.

We are working on a number of other exciting research studies, including one of the first systematic studies of metastatic pancreatic cancer (see page 3).

I also want to congratulate Kieran Brune, Coordinator of the NFPTR. On

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FROM THE COORDINATOR

I hope that when you are looking through the various stories in this newsletter, you are able to get a sense of the many diverse projects that our group is working on. From trying to understand the genetic basis of pancreatic cancer to taking this knowledge and applying it to the counseling and screening for our families, our group is truly studying all aspects of pancreatic cancer. The pancreatic cancer researchers here at Hopkins form a tight team and we are all working together to further our understanding of pancreatic cancer.

If you have any questions regarding the studies described in this newsletter or regarding any of our research, please do not hesitate to either call me at 410-955-3502 or e-mail me at kbrune@jhmi.edu. I



Kieran Brune and Dr. Ralph Hruban

always enjoy speaking with our families and I will be happy to answer any of your questions.

Kieran A. Brune

FANCONI GENE ABNORMALITIES IN PC

Eight years ago while studying pancreatic cancer, the research laboratory headed by Dr. Scott Kern found mutations of a new gene. Soon, this laboratory and others working in other tumor systems found that mutations of this gene were often inherited, raising the risk for pancreatic, ovarian, and breast cancer when an individual inherits one bad copy of the gene. This was the second gene found to cause inherited breast cancer, thus leading to the gene name, BRCA2 (see page 3).

In a paper published recently in the journal *Cancer Research*, these scientists followed up on that earlier discovery. They knew that BRCA2 mutations can give rise to a rare syndrome, Fanconi anemia, when two defective copies (rather than just one bad copy) are inherited by an individual. Fanconi anemia causes skeletal abnormalities and progressive bone marrow failure. They also knew that Fanconi anemia is not usually caused by BRCA2, but is more often caused by a number of other genes that on occasion are also inherited in a mutant form. But what if an individual were to inherit only one bad copy of a Fanconi gene, a condition that was previously thought not to cause

The Kern Lab



disease? Was it possible that some of these other Fanconi genes might play a role in pancreatic cancer? They found the answer to be "Yes!"

Dr. van der Heijden, a postdoctoral fellow in Dr. Kern's lab, studied two of the Fanconi genes, FANCC and FANCG. New mutations were found in a number of pancreatic cancers. Some of these mutations are inherited, meaning that individuals were inheriting a risk for pancreatic cancer.

ATTITUDES TOWARD GENETIC COUNSELING FOR PANCREATIC CANCER

Jennifer Axilbund, M.S., CGC, provided genetic counseling to the participants in Dr. Canto's endoscopic ultrasound screening study called "CAPS" (see page 4). As a follow-up to the genetic counseling session, she mailed a survey to each participant to determine if the genetic counseling session was deemed "useful," even though the major gene that is believed to cause familial pancreas cancer has not yet been discovered. Participants were overwhelmingly in favor of genetic counseling, even though only limited information was available. The survey found that a large majority of participants would be interested in another genetic counseling session when more information is learned, and most would want to be genetically tested once a predisposing gene has been discovered. This study

confirmed that family members at increased risk for pancreas cancer wish to be apprised of current information, even if informative genetic testing is not yet available.

We also hope that these results will be applicable to other cancers for which the major causative gene has yet to be identified. If you have questions regarding genetic counseling, please contact Jennifer Axilbund at 410-614-0378.



Jennifer Axilbund

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 purpose of life is to live it, to reach out eagerly and without fear for newer and richer experience."

Eleanor Roosevelt

AN END OF LIFE CHOICE

One way that patients with terminal pancreatic cancer can greatly assist pancreatic cancer research is by agreeing to undergo an autopsy for research purposes.

In 2003, the Gastrointestinal Cancer Rapid Medical Donation Program (GICRMDP) was initiated at The Johns Hopkins Medical Institutions to supplement ongoing research of pancreatic cancer. The principal investigator of this research program, Dr. Christine Iacobuzio-Donahue, is committed to studying pancreatic cancers that have spread ("metastasized") to organs beyond the pancreas. Information gathered from the pancreatic cancer tissues collected at autopsy will form the basis for

research directed towards the creation of new drugs to specifically target late stage pancreatic cancers.

There is no monetary benefit to the patient or their family for consenting to an autopsy as part of the GICRMDP, and there are no direct health benefits to the patient by joining this research study. However, we strongly believe that any patient willing to undergo a research autopsy at the time of death will be making the single most important contribution any individual could make to help researchers better understand and treat metastatic cancer. Participation in this study is purely voluntary and it may help other patients and their families in the future.



Dr. Christine Iacobuzio-Donahue and Lab

If this research study is something you would like to learn more about, please contact Dr. Iacobuzio-Donahue at ciacobu@jhmi.edu or call 410- 955-3511 Monday through Friday from 8 a.m. to 5 p.m. (EST).

PROSPECTIVE RISK OF DEVELOPING PANCREATIC CANCER

Dr. Alison Klein recently completed a large study of families enrolled in the NFPTR. The purpose of her study was to calculate the risk of pancreatic cancer in individuals with a family history of pancreatic cancer. Dr. Klein studied over 800 families enrolled in the NFPTR.

Dr. Klein found that individuals from families where there was at least a pair of first-degree relatives (first-degree relatives are parents, siblings, and children) had a significantly increased risk of developing pancreatic cancer. This risk increased with the number of first-degree relatives each person had with pancreatic cancer. For example, individuals with three first-degree relatives with pancreatic cancer had a 32-fold increased risk of

developing pancreatic cancer. In addition, the risk of developing pancreatic cancer was higher in smokers than in non-smokers.

The results of this study will be important for genetic counselors (see page 2) as well as for identifying individuals who are in need of screening (see Dr. Canto's study on page 4).



Dr. Alison Klein

ROLE OF THE BRCA2 GENE IN FAMILIAL PANCREATIC CANCER

As those of you who have received previous issues of the NFPTR News will know, inherited ("germline") mutations in the second breast cancer gene, called BRCA2, are believed to account for 17% of familial pancreatic cancers. This percentage is higher in individuals of Ashkenazi Jewish heritage and somewhat lower in other groups.

Most studies of the BRCA2 gene in familial pancreatic cancer have examined only a relatively small number of pancreatic cancer families. In collaboration with the Mayo Clinic, we are in the process of studying a large number of families from the NFPTR and from the Mayo Clinic. Close

to 150 families will be studied in this research protocol. A new technique developed by Dr. Fergus Couch at the Mayo Clinic will allow us to study many families. When this exciting collaborative research study is completed it should provide more definite information on the role of inherited BRCA2 gene mutations in familial pancreatic cancer.

We should emphasize that this is a research study. If you have questions about your own cancer risk, you may want to speak with a cancer genetic counselor in your area or you may contact Jennifer Axilbund here at Johns Hopkins at 410-614-0378 or solleje@jhmi.edu.

(*FANCONI GENES Continued from page 2*)

Fanconi anemia gene mutations are found in about 1 in 300 persons in the general population, and in about 1 in 75 individuals of Ashkenazi Jewish descent.

It remains to be determined how much the risk of cancer is increased for such persons, and whether cancers other than pancreatic cancer would also occur more frequently. Dr. van der Heijden and colleagues had another interesting finding: three of the nine persons whose pancreas cancer had young-onset (less than 50 years of age) had such mutations. He perhaps has discovered one of the causes of young-onset pancreatic cancer, although more work needs to be done to see if this genetic change is indeed a cause of young-onset pancreatic cancer.

There are no easy tests for the kinds of Fanconi gene mutations now being studied, but such tests may become available in the future. Cells that are defective in the Fanconi genes are known from other research to be highly sensitive to certain chemotherapy drugs. It may be possible in the future to recommend a different therapeutic regimen for patients with these mutations. More research in this exciting new area is needed.

(*FROM THE DIRECTOR continued from page 1*)

October 18, 2003, Kieran ran the half Marathon here in Baltimore. She finished in less than two hours and placed 161 out of the 1,307 female runners. Congratulations Kieran!

As always, your participation in the NFPT makes this exciting research possible, and it is sincerely appreciated by all of us.

Finally, please take a moment to complete the enclosed research update card.

Ralph H. Hruban, M.D.

NUTRITION AND PANCREATIC CANCER

Many questions about diet and exercise arise once a patient is diagnosed with pancreatic cancer. Pancreatic cancer and its treatment can place extra demands on the body, increasing a patient's caloric and nutrient needs. With so many sources of dietary advice, it is difficult to comprehend the latest dietary regulations and therefore make an informed decision.

The American Cancer Society Guidelines on diet, nutrition, and cancer prevention provide a good basis for a healthy diet. The ACS recommends that you choose most of the foods you eat from plant sources and that you strive to eat five fruits and vegetables per day. Frozen and canned fruits and vegetables are often a good source of nutrients and are an easy way to get your five servings of fruits and vegetables. These fruits and vegetables should be supplemented with breads, cereals, and grain products. It is also recommended that you limit your intake of high fat foods, particularly from animal sources. In addition, it is recommended that you try and stay physically active.

Weight loss can be a common symptom associated with cancer diagnosis and it is often difficult to combat this weight loss. Weight loss can cause fatigue and can lengthen a patient's recovery from cancer treatments. Eating smaller more frequent meals may be easier for a patient to tolerate than three large meals. In addition, choosing foods that are easy to chew, swallow, and digest may help. If it is difficult to meet nutritional needs through diet alone, nutritional supplements such as Ensure may help to increase the caloric intake.

Patients with pancreatic cancer may also face sensory changes that interfere with eating. Their sense of smell may be affected and they may find that they are more sensitive to food odors. Serving foods cold instead of hot may cut down the unpleasant aromas. In addition, when cooking, using covered pots, boiling bags, or a kitchen fan may minimize the unpleasant smells. A patient may also experience taste changes. Using plastic utensils and non-metal cooking containers may help to reduce this problem.

Having so much information regarding diet and nutrition can be overwhelming and can make it difficult to make a good decision. If the patient continues to experience problems with eating, they should consult with their primary care physician or a registered dietician to see if these individuals can help them.

CAPS CONTINUES

As part of an ongoing research protocol, Dr. Canto is still recruiting relatives from high-risk families to participate in her Cancer Prevention Study (CAPS) for the early detection of pancreatic cancer. In this research study, Dr. Canto is using endoscopic ultrasound (EUS) to screen healthy individuals from families in which there have been three or more pancreatic cancers.

If you would like more information about this research study, please contact Dr. Canto at 410-614-5388 or her study coordinator, Brenda Brehon, at 410-955-3821.

Please Remember To
Complete and Return Your
Research Update Card.

Thank You for Your
Assistance!