



PEARL



The Pancreas Education and Research Letter

Genetic Discovery Links Alcoholic Pancreatitis with Chromosome X Factor

Volume Six
Number Four
Fall / Winter 2012

PEARL is a publication of the Pancreatic Studies Office in the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh

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Publication of PEARL is supported, in part, with support from Abbott

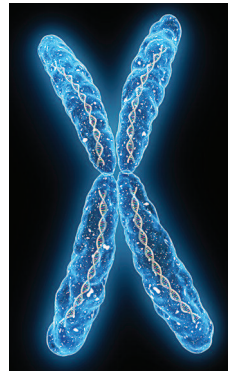
The North American Pancreatitis Group with collaborators from England and Germany reported the discovery of a genetic risk for chronic pancreatitis in men who are heavy drinkers. The report appeared as an advanced on-line report in *Nature Genetics* on November 12, 2012. The discovery was identified as a genetic variant located on the X chromosome near the claudin-2 gene (*CLDN2*). This breakthrough will now help doctors caring for patients with pancreatitis to know how likely a patient will be to progress to chronic pancreatitis in the future. It will also allow doctors to counsel specific high risk patients about preventing the progression of disease.

The factor on chromosome X does not appear to cause pancreatitis but if pancreatic injury occurs for any reason, such as gallstone pancreatitis or abdominal trauma, it is more likely that the person will develop chronic pancreatitis – especially if they also drink alcohol.

"The discovery that chronic pancreatitis has a genetic basis solves a major mystery about why some people develop chronic pancreatitis and others do not," said David C. Whitcomb, MD, PhD, the study's leading author. "We also knew there was an unexpected higher risk of men developing pancreatitis with alcohol consumption, but until

now we weren't sure why. Our discovery of this new genetic variant on chromosome X helps solve part of this mystery."

The link between men, alcohol and the factor on the X chromosome is very interesting. Researchers discovered that the high-risk DNA variant on the X chromosome was common, and present in 26 percent of men without pancreatitis, but jumps to nearly 50 percent of men diagnosed with alcoholic pancreatitis. Women have two X chromosomes, so most women with the high-risk DNA variant on one X chromosome appear to be protected from alcoholic chronic pancreatitis by the other X chromosome, if it is normal. Men have one X chromosome and one Y chromosome, so if they inherit a high-risk X chromosome, there is no protection.



The finding, among the many others we share with you in the **PeaRL**, was conducted on study samples from participants in the North American Pancreatitis Study II, or NAPS2. Samples from the Hereditary Pancreatitis study, PAGER study and PROOF study were also included. We thank you for your participation! ○

This research was supported by the National Institutes of Health (NIH) (grants DK061451, DK054709, DK063922, MH057881, CA117926, UL1 RR024153 and UL1TR000005).

HAPPENINGS

Sheila Solomon, MS, Certified Genetic Counselor at the University of Pittsburgh, Division of Gastroenterology, Hepatology and Nutrition, was invited to speak on the "Complexities of Hereditary Pancreatitis: Clinical Implications for Your Practice" at the National Society of Genetic Counselors' Annual Education Meeting in Boston, MA this October.



Ms. Solomon explained the details of this rare condition to more than 1,600 genetic counselors from across the country and the world in attendance. "Regardless of the rarity of the disease, it is critical to share this information with health care providers of all types," Solomon explained. "Many genetic counselors approached me after the talk with questions and comments about how they can now guide patient care based on this new information."

The learning never ends. ○



Sheila Solomon, MS, CGC speaks to the National Society of Genetic Counselors about Hereditary Pancreatitis.

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www.pancreas.org

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Be INSPPIRED This Holiday Season!

INSPPIRE (International Study Group of Pediatric Pancreatitis: In search for a cure) is a group comprised of 21 pediatric gastroenterology centers in the United States, Canada, Israel and Australia. INSPPIRE is the first-ever initiative to create a multi-center approach to systematically characterize pancreatitis in children, a poorly understood problem for which there are no clear diagnostic guidelines or therapeutic alternatives.



The group is led by Dr. Aliye Uc, *(photo, above right)* an Associate Professor of Pediatrics and a pediatric gastroenterologist at the University of Iowa Children's Hospital. Dr. Uc recently received a grant from the National Institutes of Health (R21 grant, \$275,000 in 2 years) to build a consortium that includes 15 academic institutions, with centers in the US, Canada, Australia, and Israel. The University of Iowa is the coordinating center.

The INSPPIRE group created task forces to define pediatric acute pancreatitis, acute recurrent pancreatitis

and chronic pancreatitis; conducted a survey of INSPPIRE members to examine the number of patients followed at each institution, the scope of the problem and the current practice; identified the most important questions in pediatric pancreatitis; and formed a subcommittee to develop standardized patient and physician questionnaires.

The immediate goal of INSPPIRE is to develop a database of children with acute recurrent pancreatitis and chronic pancreatitis and to understand the epidemiology, etiologies, natural history and outcome in a well-studied group of children with these disorders. The initial project will define pediatric acute recurrent pancreatitis and chronic pancreatitis, understand its epidemiology and build a patient registry and sample repository. The group's long-term goal is to develop new, effective therapies for these diseases in children.

We wish them the best as they make an important effort to help children with pancreatitis. ○



Turkey Winter Vegetable Stew

Wondering what to do with your extra turkey meat from the holidays? This richly flavored stew is full of vitamins, minerals, and protein. It can be served as soup or over a whole grain for a heartier meal.

Ingredients:

- 1-1/2 tablespoons olive oil
- 1 pound cooked turkey white meat, diced
- 2-1/3 cups reduced-sodium chicken or vegetable broth
- 2/3 cup dry red wine
- 2 cloves garlic, minced
- 2 shallots, thinly sliced
- 1 tablespoon fresh thyme, chopped
- 1/4 teaspoon each ground sea salt and freshly ground black pepper
- 1 bay leaf
- 2 cups butternut squash, peeled, seeded, and diced
- 1 cup parsnips, peeled and sliced
- 1 medium-large yam, peeled and chopped
- 3 ribs celery, chopped
- 1 medium yellow onion, thinly sliced
- 1/2 cup reduced-fat sour cream
- 3 tablespoons whole wheat flour

Instructions:

Place a large saucepan over medium heat. Add oil and heat about 1 minute. Add chicken and brown on all sides. Stir in broth and wine. Add garlic, shallots, thyme, salt, pepper, and bay leaf. Bring mixture to a boil. Reduce heat, cover, and simmer 20 minutes. Mix in squash, parsnips, yam, celery, and onion. Bring to a boil; reduce heat to low and simmer 30 minutes, or until vegetables are tender. In a small bowl, blend together sour cream and flour. Gradually stir 1/2 cup of the hot stew into the sour cream/flour mixture. Add the sour cream mixture to the saucepan. Remove bay leaf and continue to cook, stirring occasionally, until soup has thickened, about 6-8 minutes. Makes 6 servings.

Nutritional information per serving:

- Calories: 298
- Fat: 4 g
- Saturated fat: 1 g
- Carbohydrate: 20 g
- Total sugars: 3 g
- Protein: 20 g
- Sodium: 260 mg
- Cholesterol: 50 mg
- Dietary fiber: 3 g



PancreasFest 2012 Highlights

Each year physician-scientists meet in Pittsburgh to discuss advances and ways to work together as national and international teams of scientists to bring scientific advances to the patients as fast as possible. PancreasFest 2012, held on July 26, 27, 2012 on the campus of the University of Pittsburgh, boasted one of the largest and most widely successful meetings of its history. The focus for PancreasFest 2012 was to highlight pancreatic cancer and chronic pancreatitis advancements ranging from cancer prevention and early detection strategies, to treatment advancement implications for chronic and acute pancreatitis care as well as applying concepts of personalized medicine to pancreas disease treatment. New this year was a discussion of treatment implications and options through case discussion,

whereby participants used a handheld wireless device to measure attendee education as well as to vote on recommendations for chronic pancreatitis care options. Integrating this high tech function

Oncology at The Johns Hopkins University School of Medicine. He is currently the Director of the Sol Goldman Pancreatic Cancer Research Center, and Director of the Division of Gastrointestinal/Liver Pathology.

Dr. Hruban has dedicated his career to understanding the development of pancreatic cancer and has been hugely influential in the progress of identifying at risk patients and clarifying the pathology and genetics of pancreatic cancer.

At PancreasFest, Dr. Hruban received the Ruth C. Brufsky Award for Excellence in Clinical Research on Pancreatic Cancer and spoke

to the group on the "Pancreatic Pathology and Whole Genome Sequencing: Implications for Diagnostics and Therapeutics".

Congratulations and thank you, Dr. Hruban. ○



From left to right: David Whitcomb, MD, PhD, Ralph Hruban, MD, and Randall Brand, MD

into the program was well received and results will be published soon.

One of the highlights of PancreasFest 2012 included honoring Ralph Hruban, MD, Professor of Pathology and

First Total Pancreatectomy for Islet Autotransplantation

A team of University of Pittsburgh Medical Center pancreatic cancer surgeons led by Herbert Zeh, MD and transplantation surgeons led by Abhinav Humar, MD performed the first total pancreatectomy with islet autotransplantation (TPIAT) using minimally invasive robot-assisted surgery. This highly advanced procedure for total pancreatectomy was designed for pancreatic cancer surgery because the traumatic effect on the body is much less, leading to a shorter recovery time and more strength to combat the cancer and cancer therapy. The surgeons use the Da Vinci robot, which gives the surgeon a more clear vision of the tissue and high magnification to do very delicate cutting and suturing.

TPAIT is a procedure used for severe pain and disability in patients with recurrent acute pancreatitis and chronic pancreatitis to remove the source of pain while retaining the specialized islet cells that make insulin and prevent diabetes. Dr. Humar's team are experts at autotransplantation, but in the past the procedure required a major incision across the abdomen and resulted in a long recovery time.



Dr. Zeh using the Da Vinci robot during a pancreatic surgery.

Combining the robotic-assisted approach to the pancreas with the methods of islet autotransplantation is a win-win. Dr. Zeh's team was able to complete the procedure with no complications. Dr. Humar's team assured that the islet cells had minimal damage during the removal phase, and retained the maximal number of islet cells. Both teams of surgeons confirmed that the new approach in this case was a total success. ○



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Pancreatic Clinicians Honored by National Pancreas Foundation

Each year the Pittsburgh and Boston chapters of the National Pancreas Foundation (NPF) identify and honor physician-scientists who have dedicated their lives to treating patients with pancreatic diseases.

On October 26, 2012 the Pittsburgh chapter of the NPF honored **Herbert Zeh, MD**, a pancreatic surgeon at the University of Pittsburgh who has pioneered the use of minimally invasive pancreatic surgery for pancreatic diseases using robotic-assisted methods (*see feature article on page 3*). Dr. Zeh also directs a basic science laboratory focused on pancreatic inflammation.

On November 29, 2012 the Boston chapter of the NPF honored **Darwin Conwell, MD**, a clinical pancreatologist at Harvard University who practices at the Brigham and Woman's Medical Center in Boston, MA. Dr. Conwell has pioneered better methods of evaluating the function of pancreas as a diagnostic test. He is also recognized as a teacher and mentor of physicians who are interested in advanced training in managing pancreatic diseases. ○



Darwin Conwell, MD (right) with his senior partner, Peter Banks, MD at the NPF Gala in Boston, MA.

For more information, contact **Sheila Solomon, MS** at 1-888-PITT-DNA or solomonsr@upmc.edu