



# PEARL



The Pancreas Education and Research Letter

## Pancreas Disease Researchers and Leaders: The Next Generation

The Collaborative Alliance of Pancreatic Education and Research (CAPER) has made tremendous progress as a new non-profit organization. CAPER built on the successes of the Midwest Multicenter Pancreatic Study Group and has launched a new web site. You can find them at <http://caperpancreas.com/history.php>. Their focus is on developing the next generation of pancreas disease researchers and leaders – they are off to a terrific start!

Cancer Institute (R21CA138370, R21CA152935), the James F. Walsh Foundation and an award from the Wallace H. Coulter Foundation.

**Jessica LaRusch, PhD** – Dr. LaRusch, a post-doctoral fellow in Dr. Whitcomb's lab at the University of Pittsburgh, was a finalist for the Young Investigator Best Abstract in Basic Science Award at the 2010 Cystic Fibrosis (CF) Conference held in Baltimore, MD in October. The conference focuses on the diagnosis and treatment of CF, a lethal genetic disorder that impacts



multiple organs, including the pancreas and lungs, and is caused by two mutations in the *cystic fibrosis transmembrane conductance regulator (CFTR)* gene. *CFTR* mutation status has been identified as a risk factor for pancreatitis, and her recent work explores the relationship between CF and chronic pancreatitis. She has identified a link between atypical *CFTR* mutations, pancreatitis and bicarbonate conductance. Patients and controls from the NAPS2 and familial pancreatitis studies were screened for *CFTR* variants. The *CFTR* variant p.R75Q was found more frequently in pancreatitis patients than controls, but is not a CF causing mutation. Functional testing showed that p.R75Q causes a selective defect in bicarbonate conductance and increases risk for pancreatitis, but not CF. These findings have implications in the diagnosis and management of pancreatitis (Schneider and colleagues, *Gastroenterol*, Epub ahead of print Oct 25, 2010). ○

### Highlighting Young Researchers

**Yang Liu, PhD** – Dr. Liu and the bioengineering group at the University of Pittsburgh have recently developed a novel type of optical microscopy – Spatial-domain Low-coherence Quantitative Phase Microscopy – that allows us to detect very subtle changes in cell structures with a sensitivity one thousand times better than a conventional microscope. They are currently exploring the capability of this instrument to improve the early detection of pancreatic cancer. Initial results have shown great promise to detect the presence of pancreatic cancer even in patients who were labeled as "indeterminate" by expert pathologists but subsequently confirmed to have cancer upon surgery. Ongoing studies are being conducted to expand the patient population and further validate the technology. This impressive research is funded in part by grants from National



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### New Treatment Study Being Planned

Phase 2 of the Hereditary Pancreatitis treatment study has started. An initial study of a blood pressure medicine, amlodipine (marked as Norvasc, and as a generic medication) showed that this medicine did not cause obvious side effects in patients with hereditary pancreatitis and may be beneficial. Through a generous donation by one of the families, a formal study of amlodipine in hereditary pancreatitis is being planned. A notification to families who might benefit from this trial will be sent to them as soon as all of the approvals have been granted and additional funding has been received. ○

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## Family Time!

It's the holiday season! Time to spend with family and share memories is a wonderful way to pass along family lore, traditions and stories to younger generations. But we get more than traditions from our



ancestors. Our genes, the basic instruction code for how our bodies grow, develop and function, are also passed down from parent to child. Genes can determine traits like hair color and freckles. They can also predict health and disease risk. Genes have been linked with heart disease, cancer, Alzheimer's disease among other medical problems.

In some cases, pancreatic cancer and diseases like pancreatitis can be linked to inherited factors. About 5-10% of pancreatic cancer is hereditary, meaning that the risk for developing it is caused by a gene mutation, or a faulty gene. Genetic tests can personalize the cancer risk for each family member. In addition, these

tests can offer options for medical decision making and healthy lifestyle changes.

In 2004, the Family Health Portrait was developed by a collaboration between the Office of the Surgeon General and the National Human Genome Research Institute, a part of the National Institutes of Health, Department of Health and Human Services. The Family Health Portrait is an easy online tool for families to collect health information about their relatives. It provides a hard copy for you to print and take to your healthcare provider. Better yet, share your Family Health Portrait with a genetic counselor.

Genetic counselors are healthcare professionals who work with families to understand their options for healthy living and disease prevention. There are over 2,600 genetic counselors in the US and around the world. Visit National Society of Genetic Counselors at <http://www.nsgc.org> for more information.

Learning about the past can be the backbone to seeing what the future may bring. Visit the "My Family's Health Portrait" at <https://familyhistory.hhs.gov/fhh-web/home.action>. ○

## Healthy Eating:

### Broccoli and Tomato Halibut

Few vegetables rival broccoli and tomatoes in nutritional value. If you are watching your sugar and carbohydrate intake, this dish is perfect for you because it contains fewer than 10 grams of carbohydrates per serving. This recipe's allicin (garlic) and lycopene (tomatoes) are potent antioxidants that may help reduce the risk of pancreatic, esophageal, prostate and colon cancer.



#### Ingredients:

- 2 tablespoons olive oil
- 2 cups fresh broccoli florets, chopped
- 2½ cups fresh ripe tomatoes, diced
- 2 tablespoons lemon juice
- 1½ tablespoons garlic, minced
- 1 teaspoon dried tarragon
- ½ teaspoon sugar
- ¼ teaspoon each—salt and freshly ground black pepper
- 4 halibut steaks (about 5 to 6 ounces each)

#### Preparation:

Heat oil in a large skillet over medium heat about 1 minute. Add broccoli and heat 5 minutes. Add all remaining ingredients except halibut; cook 5 minutes, stirring occasionally. Add halibut; cover and cook about 5 minutes on each side. Divide halibut and vegetables among 4 dinner plates. Makes 4 servings.

#### Nutritional information per serving:

Calories: 218.0	Fat: 7.6 g
Saturated fat: 1.0 g	Carbohydrate: 8.5 g
Total sugars: 3.6 g	Protein: 28.9 g
Sodium: 85 mg	Cholesterol: 40.8 mg
Dietary fiber: 1.5 g	



#### Pancreasfoundation.org

The National Pancreas Foundation (NPF) has launched a new website.

The NPF is adding many local chapters which support local and national objectives. Visit their web site at <http://pancreasfoundation.org/> to find a chapter near you and to find out how you can get involved.

## North American Pancreatitis Study 2 (NAPS2) Update

The second phase of the NAPS2 study is almost complete with nearly 1,500 participants. The study is the largest of its kind ever developed in the United States. A study this large takes careful comparison of millions of possible factors to understand which combinations give the highest risk for developing pancreas disease.

There are already some major advances now coming from the NAPS2 research:

- **Smoking and drinking.** The combination of excess alcohol and smoking was much worse than either risk factor alone. We have urged physicians to warn their patients to stop smoking and drinking at the first sign of pancreas problems. (Coté and colleagues, *Clin Gastroenterol Hepatol*, online Oct 25, 2010)

- **Pancreatic pain.** Almost all of the disability from pancreatitis comes from constant pain, mild or

severe. Constant pain is also linked to alcohol use. Pain is different in women than in men. Smoking is a major link to severe pain in women. (Mullady and colleagues, *Gut*, in press)

- **Antioxidants.** Patients in NAPS2 with pancreatic insufficiency (failure to properly digest food) were helped by pancreatic enzymes more often than patients who did not have pancreatic insufficiency.

*continued on page 4*

### RESEARCH ADVANCES

**Vitamin D.** Over the last few years, the High Risk Pancreas Clinic at the University of Pittsburgh Medical Center (UPMC) has recommended a daily intake of Vitamin D as high as 2,000 International Units (IU) to patients at increased risk for pancreatic cancer due to family history.

In December 2010, the Institute of Medicine, a non-profit organization that provides health information and advice to the public, published new information regarding Vitamin D intake. The Institute now recommends daily intake of 400IU for the general population. **Now, the recommendation from UPMC is daily intake of 600–1,000 IU for patients at increased risk for pancreatic cancer.** Too much Vitamin D is not recommended (over 4,000 IU). Therefore, individuals at high risk for developing pancreatic cancer are encouraged to calculate the amount of dietary Vitamin D intake before adding other supplements. It is important to consider the amount of Vitamin D in a daily multi-vitamin and then add a Vitamin D supplement, if needed.

**Leaky blood vessels and severe acute pancreatitis.** In severe cases of acute pancreatitis the blood vessels become leaky so that proteins and fluid leave the blood and go into the tissue. This complication is called the Vascular Leak Syndrome (VLS). VLS leads to a dangerous drop in blood pressure, fluid accumulation in the lungs and thick blood with too high a concentration of red blood cells. Multiple studies have shown that patients with VLS are more likely to have the failure of multiple organs including the cardiovascular system, lungs, kidneys, etc. A recent study from the United States



and Germany showed that Angiotensin-2 (Ang-2), a molecule that is released from blood vessels after injury to cause local swelling (edema) is released in very high levels in patients that go on to develop leaky blood vessels. This finding is important because it helps scientists understand why some patients develop leaky blood vessels. This information is also critical because it can be used as a warning sign to physicians that fluid resuscitation and other treatments will be needed immediately. (Whitcomb and colleagues, *Am J Gastroenterol*. 2010 May 11;(epub May 21, 2010)).

**Blood type is linked to risk of pancreatic cancer.** Blood type is important to know before receiving a transfusion because getting the wrong type of blood can cause a serious reaction. The three major blood types are A, B and O, with further typing by Rh factor + or -. Although blood type is important in transfusions, it still is not clear what the blood types mean to a person's health. A series of papers was recently published by different research groups that showed that people with blood groups A and B are at somewhat higher risk of pancreatic cancer, and that patients with type O seem to have some protection. These findings provide new clues rather than new answers. Regardless of blood type, healthy lifestyle is the best defense against pancreatic cancer (Amundadottir and colleagues *Nat Genet*. 2009 Sep;41(9):986-90; Risch and colleagues, *J Natl Cancer Inst*. 2010 Apr 7;102(7):502-5, Greer and colleagues, *World J Gastroenterol*. 2010 Nov 28;16(44):5588-91.) ○



## NAPS2 Update *continued from page 3*

Some with unexplained chronic pancreatitis or an obstruction had less pain after taking antioxidants and vitamins. (Burton and colleagues, *Aliment Pharmacol Ther.* online Oct 29 2010)

- **Links to Cystic Fibrosis Gene.** A common change in the cystic fibrosis gene (CFTR) is a risk factor for pancreatitis, without classic cystic fibrosis symptoms, especially when it is linked with SPINK1 gene changes. See page 1 article on Dr. LaRusch for more details. (Schneider and colleagues, *Gastroenterol.* online Oct 25, 2010)

In addition to these important scientific and medical

papers there are a number of new findings that are being evaluated in more detail. Physicians and scientists from around the world will meet in Chicago, IL in May 2011 to discuss new approaches for diagnosis and treatment of pancreatic diseases.

**CALL US.** If you participated in the NAPS2 study, the NAPS2 team needs to update your information. If one of your family members was in the NAPS2 or Hereditary Pancreatitis study and passes away, please call as well so that we can update their files and learn from their life. Call the pancreatitis study office at **1-888-Pitt-DNA**. The call should take less than 10 minutes. ○



## ~ P r e s e n t a t i o n ~

In November, David C. Whitcomb, MD, PhD, (left) presented his pancreas genetics research findings as the inaugural Giant Eagle Foundation Professor of Cancer Genetics. In 2006, he received the honor of the first endowed chair in the University of Pittsburgh's Division of Gastroenterology, Hepatology and Nutrition. The University of Pittsburgh provost, Dr. Patricia Beeson, presented him with a medallion and welcomed Dr. Whitcomb to the podium.

During his talk, Dr. Whitcomb highlighted his lab's genetics findings and discussed the future of personalized medicine regarding genetics and pancreas disease as they relate to clinical research, patient care and public health awareness. ○

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