

Pancreatic Cancer Research Update

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Thank You . . .

We are pleased to provide you with this new update of pancreatic cancer research. We have moved forward in a big way to better understand factors that can affect risk, with recent discoveries about body weight, the ABO blood group, and other genes. Mayo Clinic and the Pancreatic Cancer Genetic Epidemiology Consortium (PACGENE) research team are at the forefront. These exciting findings are the result of our continuing, focused effort. Most importantly, they could not have been done without your commitment to our research. Thank you for taking part and working with us!

ABO Blood Type and Pancreatic Cancer

The ABO blood group system, which is genetically determined, and its medical value have been known for decades. The four main blood types are: A, B, AB, and O. Several studies in the mid-20th century reported a relationship between ABO blood type and some cancers, including pancreatic cancer. In 2009, two studies have refined our knowledge, and we hope, using newer technologies, to apply this new knowledge to improve risk assessment.

Many universities and hospitals around the world, including Mayo Clinic, have worked together on a study of DNA from blood samples of pancreatic cancer patients that were compared with the DNA from people without pancreatic cancer. Using a method known as a genome-wide association study (GWAS), in which hundreds of thousands of genetic variants were analyzed in over 8,800 people, the variants that are in the ABO gene were found to significantly increase risk by 20 percent.

This finding led to a look at ABO blood types in a large number of United States health professionals in a study run since 1976 by Harvard University. Among this group, 316 had developed pancreatic cancer

over the years (out of 107,503 who have been in this study). They found increased risk by 30 percent to 70 percent in individuals with blood types A, B, or AB, compared to those with blood type O. They estimated that 17 percent of pancreatic cancers are attributed to non-O blood groups.

These studies will help us greatly as we develop a useful way to compute risk for pancreatic cancer.

References:

- Amundadottir L et al. Genome-wide association study identifies ABO blood group susceptibility variants for pancreatic cancer. *Nature Genetics*, September, 2009.
- Wolpin BM et al. ABO blood group and the risk of pancreatic cancer. *Journal of the National Cancer Institute*, 101:424-31, 2009.



Pancreatic Research Update

Higher Weight and BMI Can Influence Risk and Survival



Being overweight or obese is known to increase the risk of getting different cancers, including pancreatic cancer. A team in Texas has shown that obesity, as measured by body mass index (BMI), increases the risk of developing pancreatic cancer, after taking diabetes and cigarette smoking into account.

This study also pointed to greater risk from a higher BMI in early adulthood.

The study compared 841 patients with pancreatic cancer to 754 patients without cancer. Compared to patients with normal BMI, those who reported being overweight (BMI 25-29.9) at ages 14 to 39 years had 0.7 times higher risk, while those who reported being obese at ages 20 to 49 had 2.6 times higher risk. The team also found that patients who reported a higher BMI in early adulthood developed pancreatic cancer younger, by 2 to 6 years, than patients with normal weight.

Once patients are diagnosed with pancreatic cancer, those with a higher adult BMI had lower rates of survival. This finding is similar to our Mayo study in which a higher usual adult BMI predicts lower survival.

References:

- Li D et al. *Body mass index and risk, age of onset, and survival in patients with pancreatic cancer.* JAMA. 301:2553-62, 2009. Editorial: McWilliams RR and Petersen GM. *Overweight, obesity, and pancreatic cancer: Beyond risk alone.* JAMA 301:2592-3, 2009.
- McWilliams RR et al. *High usual adult body mass index is an independent predictor of worse survival in pancreatic adenocarcinoma.* Presented at AGA-ASCO Gastrointestinal Cancer Symposium Annual Meeting, January 2009.

To calculate your own BMI, please visit this link:

<http://www.mayoclinic.com/health/bmi-calculator/nu00597>

Variation in Genes Related to DNA Repair Can Increase Risk of Pancreatic Cancer



Our body normally repairs damage to DNA caused by carcinogens or mistakes in DNA when cells divide. Many different genes encode each step of this process. Cancer can develop when the DNA of a normal cell is not repaired properly, and uncontrolled growth follows. We and

others have found that the genes involved in the DNA repair process are important in pancreatic cancer. We chose specific variants in dozens of DNA repair genes. We then compared these variants in the DNA from over 1,000 Mayo Clinic pancreatic cancer patients to a similar number of healthy controls. We found that

some variants increase risk and others are protective. One gene that is of great interest is *MMS19L*, as it was significantly associated with increased risk for pancreatic cancer.

References:

- McWilliams RR et al. *Polymorphisms in DNA repair genes, smoking, and pancreatic adenocarcinoma risk.* Cancer Research 68:4928-35, 2008.
- McWilliams RR et al. *Nucleotide excision repair pathway polymorphisms and pancreatic cancer risk: evidence for role of MMS19L.* Cancer Epidemiology Biomarkers and Prevention 18:1295-302, 2009.

PALB2: A New Cancer Susceptibility Gene for Familial Pancreatic Cancer (FPC)

Collaborators at Johns Hopkins University have found yet another gene for pancreatic cancer that runs in families. Based on a project that finished sequencing the genome of pancreatic tumors last year, the team focused on the PALB2 gene, a part of the BRCA2 pathway. The PALB2 gene was sequenced in 96 FPC patients' DNA. Around 3 percent had an inherited mutation in the gene. Collaborators in Canada found that one out of 104 FPC patients carried a PALB2 mutation. More research by the PACGENE team is underway on hundreds more FPC patients to help understand the best way to develop genetic tests.

References:

- Jones S et al. *Exomic sequencing identifies PALB2 as a pancreatic cancer susceptibility gene.* Science 324:217, 2009.
- Tischkowitz M et al. *Analysis of the gene coding for the BRCA2-interacting protein PALB2 in familial and sporadic pancreatic cancer.* In press, Gastroenterology, 2009.



Message from the Study Coordinators



Jodie Cogswell and Cindy Chan
Study Coordinators

We have enjoyed working with you and your families on our pancreas research. Thank you for the time and dedication you put into taking part and providing us with information and blood or tissue samples. If you learn of any relevant updates to your personal or family medical history in the future, we would be grateful if you let us know by mail or by calling us at 1-800-914-7962. These updates may include new diagnoses of cancers, pancreatic conditions, or genetic testing results.

PACGENE Consortium



The Pancreatic Cancer Genetic Epidemiology (PACGENE) Consortium includes seven medical centers in the U.S. and Canada that are gathering information and blood samples from families with a history of pancreatic cancer. Doctors and

scientists are studying why pancreatic cancer seems to run in some families. They are looking for new genes that increase the risk of developing this disease.

People who wish to join the family registry must be 18 years of age or over and meet one of the following criteria:

- At least two family members who ever had pancreatic cancer, or
- At least one family member who ever had pancreatic cancer and at least one family member who ever had melanoma.

If you or someone you know might be interested in taking part, please contact the Pancreas Research Team at 1-800-914-7962.

Cancer of the Pancreas Screening (CAPS 3) Study Update

The goal of this study was to find the best way to screen for pancreatic cancer. The study included a genetic counseling session, blood tests, an MRI, a CT scan and an endoscopic ultrasound (EUS). Five medical centers across the U.S. worked together on this study, and they are now finished recruiting participants. Mark Topazian, M.D. examined about 50 people from the Family Pancreas Registry at Mayo Clinic. The study is currently in follow-up phase and analysis. We would like to thank everyone who took part in this study at Mayo Clinic.



Who's Doing Pancreatic Cancer Research?

The Pancreatic Cancer Research Map

<http://www.cancermap.org/pancreatic/index.jsp>
This website provides comprehensive information about pancreas research studies in the U.S.

ClinicalTrials.gov

<http://www.clinicaltrials.gov/>
This website is a detailed and current registry of federally and privately supported clinical trials for many different diseases and conditions in the U.S. and around the world.

Clinical Trials at Mayo Clinic

<http://clinicaltrials.mayo.edu/>
This website provides information about research studies for many different diseases and conditions at Mayo Clinic.

Specialized Program of Research Excellence (SPORE)



SPOREs are funded by grants from the National Cancer Institute (NCI) to promote cancer research by translating discoveries from the laboratory to the clinic. The goal is to develop new ways to prevent, diagnose, and treat cancer.

Medical centers, universities, and other organizations may work together towards this common goal. Researchers may be from many different backgrounds, including biologists, epidemiologists, statisticians, and physicians.

Patient advocates also play a key role in SPOREs in many ways, including:

- Identifying and finding solutions to the needs and issues of patients and their families and friends.
- Supporting and guiding SPOREs and its research studies by providing feedback and advice.
- Promoting education and awareness of current knowledge about cancer and cancer research.

Mayo Clinic received a SPORE grant in pancreatic cancer in 2008 which provides funding for research for an additional five years. Gloria Petersen, Ph.D. is the director of this SPORE.

For more information about SPOREs, please visit the NCI SPORE website at: <http://spores.nci.nih.gov>

Resources

The Lustgarten Foundation for Pancreatic Cancer Research

<http://www.lustgarten.org>

Non-profit organization for supporting pancreatic cancer research and education.

Pancreatic Cancer Action Network, Inc.

<http://www.pancan.org>

National advocacy and patient support organization for pancreatic cancer.



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Representing Advocacy for Pancreas Patients with Outreach and Research Teams (RAPPORT)



RAPPORT is a group of patient advocates in Minnesota established in October 2008 as an affiliate of the Pancreatic Cancer SPORE at Mayo Clinic. The group consists of pancreatic cancer survivors, caregivers and other stakeholders, and its current mission is to determine the critical issues facing those affected by pancreatic cancer and to serve as a resource to both the pancreas research community and outreach efforts, starting in Minnesota. For more information about RAPPORT, please visit their website at: <http://rapport-pancreas.org>.

Past Newsletters...

For more information about PACGENE, CAPS 3, and family registries, please refer to previous volumes of this newsletter, which may be requested by contacting the Pancreas Research Team and also can be found online at:

<http://www.mayo.edu/pmts/mc1100-mc1199/mc1185-66.pdf>

<http://www.mayo.edu/pmts/mc1100-mc1199/mc1185-0209.pdf>

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