



Smoking, Alcohol, Gene Variant Interact to Increase Risk of Chronic Pancreatitis

Genetic mutations may link smoking and alcohol consumption to destruction of the pancreas observed in chronic pancreatitis, according to a 12-year study led by McGowan Institute for Regenerative Medicine affiliated faculty member [David Whitcomb, M.D., Ph.D.](#), chief of gastroenterology, hepatology, and nutrition, and researchers at the University of Pittsburgh School of Medicine. The findings, published in Nature Publishing Group's online, open-access journal *Clinical and Translational Gastroenterology*, provide insight into why some people develop this painful and debilitating inflammatory condition while most heavy smokers or drinkers do not appear to suffer any problems with it.



The process appears to begin with acute pancreatitis, which is the sudden onset of inflammation causing nausea, vomiting, and severe pain in the upper abdomen that may radiate to the back, and is typically triggered by excessive drinking or gallbladder problems, explained senior investigator Dr. Whitcomb. Up to a third of those patients will have recurrent episodes of acute pancreatitis, and up to a third of that group develops chronic disease, in which the organ becomes scarred from inflammation.

“Smoking and drinking are known to be strong risk factors for chronic pancreatitis, but not everyone who smokes or drinks damages their pancreas,” Dr. Whitcomb said. “Our new study identifies gene variants that when combined with these lifestyle factors make people susceptible to chronic pancreatitis and may be useful to prevent patients from developing it.”

In the North American Pancreatitis Study II consortium, researchers evaluated gene profiles and alcohol and smoking habits of more than 1,000 people with either chronic pancreatitis or recurrent acute pancreatitis and an equivalent number of healthy volunteers. The researchers took a closer look at a gene called *CTRC*, which can protect pancreatic cells from injury caused by premature activation of trypsin, a digestive enzyme inside the pancreas instead of the intestine, a problem that has already been associated with pancreatitis.

They found that a certain variant of the *CTRC* gene, which is thought to be carried by about 10 percent of Caucasians, was a strong risk factor for alcohol- or smoking-associated chronic pancreatitis. It's possible that the variant fails to protect the pancreas from trypsin, leaving the carrier vulnerable to ongoing pancreatic inflammation and scarring.

“This finding presents us with a window of opportunity to intervene in the diseases process,” Dr. Whitcomb said. “When people come to the hospital with acute pancreatitis, we could screen for this gene variant and do everything possible to help those who have it quit smoking and drinking



alcohol, as well as test new treatments, because they have the greatest risk of progressing to end-stage chronic pancreatitis.”

Dr. Whitcomb’s team has been implementing more personalized approaches to pancreatic diseases in the Pancreas Center of Excellence within the Digestive Disorders Center at UPMC and hopes to learn whether use of genetic information can, in fact, reduce the chances of chronic disease in high-risk patients.

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[Abstract](#) (The common chymotrypsinogen C (CTRC) variant G60G (C.180T) increases risk of chronic pancreatitis but not recurrent acute pancreatitis in a North American population. Jessica LaRusch, Antonio Lozano-Leon, Kimberly Stello, Amanda Moore, Venkata Muddana, Michael O’Connell, Brenda Diergaard, Dhiraj Yadav and David C Whitcomb for the NAPS2 Consortium. *Clinical and Translational Gastroenterology* (2015), published online 8 January 2015.)

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