Genetic mutation may increase risk of pancreatic cancer in females

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Chris Pin, PhD, lead author on the study, has found that mutation of a gene called ATRX may lead to increased risk of developing pancreatitis and pancreatic cancer in females. Credit: Schulich School of Medicine & Dentistry

In a new study from Lawson Health Research Institute and Western

University's Schulich School of Medicine & Dentistry, researchers have found that mutation of a gene called ATRX may lead to increased risk of developing pancreatitis and pancreatic cancer in females. The study marks the first time a sex-specific genetic risk factor for pancreatic cancer has been identified.

The research team examined the effects of ATRX mutation in the adult pancreas using preclinical models. They deleted the ATRX gene and then studied its effect on susceptibility to pancreatic cancer. The team discovered that deleting the gene in females increased susceptibility to pancreatic damage associated with pancreatitis and increased progression to pancreatic cancer. In males, the mutation did not increase the risk of pancreatic injury and actually reduced progression to cancer.

The team's preclinical results were compared to human samples from the International Cancer Genome Consortium database, which includes whole genome sequence analysis for 729 patients. The research team found that 19 per cent of patients carried a mutation within the ATRX gene and that 70 per cent of them were female.

"Pancreatic cancer is a devastating disease that's often diagnosed very late. Patients don't often respond to available therapies and the average life span of patients is less than six months after diagnosis," says Chris Pin, Ph.D., a Lawson scientist and associate professor at Schulich Medicine & Dentistry. "We need to catch the disease much earlier."

Pancreatitis, a disease characterized by inflammation of the pancreas, is one of the most significant risk factors for developing pancreatic cancer. While further research is needed, females with pancreatitis could one day be identified as a high risk population that should be screened for this genetic mutation.

"For every patient and for every cancer, there's a specific set of gene

mutations and environmental conditions that make it very unique. Identifying those differences is very important because it will affect how we treat the disease," explains Pin. "Understanding the role of ATRX in pancreatic cancer could result in new female-specific targets for therapy and the development of new markers for early detection."

In a follow-up study, Dr. Pin will collaborate with researchers in France to study patient tumour samples in new preclinical models. Their goal is to better understand the mechanisms of ATRX mutation as a sex-specific risk factor.

"While the mutation might increase a female's risk of pancreatic cancer, it doesn't mean she will automatically develop the disease," says Pin. "We need to better understand the role of the mutation and how it interacts with other risk factors like inflammation to promote cancer. Only then can we harness our knowledge to develop better diagnosis and treatment methods for females carrying this mutation."

More information: Claire C. Young et al, The Loss of ATRX Increases Susceptibility to Pancreatic Injury and Oncogenic KRAS in Female But Not Male Mice, *Cellular and Molecular Gastroenterology and Hepatology* (2018). DOI: 10.1016/j.jcmgh.2018.09.004

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