Findings may help keep pancreatic disease off the menu

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Timing is everything. That's especially true when it comes to the activation of enzymes created by the pancreas to break down food. When the timing is right, those enzymes are activated only when they reach the gut, where they get to work releasing and distributing nutrients that we need to survive. If the timing is wrong and the enzymes are activated too soon, they break down the pancreas itself, which is painful and sometimes fatal.

Fortunately, most of the time the body is a master timekeeper and has a game plan for what to do if a signaling misfire activates those enzymes too soon. But sometimes even those natural defense mechanisms aren't enough to thwart pancreatitis, making the pursuit of a better understanding of the enzymes' behavior a high priority for patients and physicians.

On Wednesday, April 13, an international research team determined to figure out and eventually manipulate the activation of such enzymes will present an important new finding at the Experimental Biology 2011 meeting in Washington, D.C.

"Acute pancreatitis is the most frequent disease of the pancreas, diabetes is the most prevalent chronic disease of the pancreas and pancreatic cancer is one of the most devastating cancers. Our finding could in the future arm us to better battle or to prevent these serious diseases," explains María I. Vaccaro, who oversaw the team's work and who will give a talk about their finding at 10:25 a.m. in Room 207A of the Walter

E. Washington Convention Center.

Writing in a Journal of Biological Chemistry "Paper of the Week" last month, Vaccaro's team identified for the first time a cellular process that the pancreas uses to selectively detect and degrade activated enzymes before they can digest the organ, avoiding the progression of disease.

The research team, which included participants from the University of Buenos Aires, the National Institute of Health and Medical Research in France and the Mayo Clinic in Rochester, Minn., has dubbed the cellular process "zymophagy."

"Our results showed that there is a refined mechanism that the pancreas switches on to avoid the progression of the disease to a lethal condition. The paradoxical and amazing fact is that this protective process is a form of autophagy," Vaccaro says.

Autophagy is an evolutionarily preserved process during which a cell degrades its own components, essentially by eating them. It occurs for a number of reasons, but it's particularly important under conditions of starvation, when the cell eats up less important components to nourish more important ones to keep an organism alive. In this case, autophagy functions as a defense strategy that the cell uses to fight against the disease.

The team coined the new form of autophagy "zymophagy" because the dangerous components that get gobbled up are called zymogen granules.

"Therefore, a self-eating event within the cell protects the pancreas from self-digestion," Vaccaro says.

Acute pancreatitis is a painful disease that ranges from a mild and autolimited process to a severe and eventually lethal condition. Vaccaro

says this protective cell-defense strategy could explain, at least in part, the autolimited form of the disease that seen in many patients.

"Hence, the more efficient zymophagic response by the pancreatic acinar cell, the less severity of the disease," she says. "Our study also identified the molecules that mediate the zymophagy. Therefore, it would be possible that in the future, a kind of test to evaluate zymophagy capacity in patients could help to predict the progression of the disease and modify the therapeutic approaches."

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