Mutant CTRC gene has a new way to trigger pancreatitis

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(PhysOrg.com) -- The CTRC gene is a lot like your baby brother—mutant and annoying. Drs. Miklos Sahin-Toth and Richard Szmola of the Department of Molecular & Cell Biology at Boston University Henry M. Goldman School of Dental Medicine (GSDM) have found yet another way that CTRC mutants trigger pancreatitis.

Drs. Sahin-Toth and Szmola already knew from their previous work that CTRC gene mutations lead to pancreatitis. They showed in a Journal of Biological Chemistry paper that the activity of mutant digestive enzymes damages acinar cells—those that make and give out digestive enzymes. In this new study, they show that the misfolding of mutant digestive enzymes also kills acinar cells.

“Thus, different mechanisms converge onto a common endpoint, acinar cell death,” says Dr. Sahin-Toth. “This can suggest that perhaps we should target this endpoint for therapy rather than the individual pathways leading there, which may be many and more difficult to treat.”

The new way CTRC mutants are attacking acinar cells may not be unique, either. Dr. Sahin-Toth says other mutant digestive enzymes may be doing the same thing—misfolding in the endoplasmic reticulum (ER), causing ER stress, and killing the cell.

The GSDM researchers are the first to show that a mutant digestive enzyme can harm acinar cells through ER stress.

The research is part of Dr. Sahin-Toth's ongoing investigation of the role of chymotrypsin C in digestive physiology and the role of chymotrypsin C mutations as risk factors for chronic pancreatitis in humans. He holds a grant, Chymotrypsin C in pancreatitis, and recently received two American Recovery and Reinvestmant Act (ARRA) supplements.

You can read an abstract of the study, Pancreatitis-associated chymotrypsinogen C (CTRC) mutant elicits endoplasmic reticulum stress in pancreatic acinar cells, online in the November 30 Gut, the journal of the British Society of Gastroenterology.

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