Cellular self-eating promotes pancreatitis

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To survive tough times, cells sometimes resort to a form of self-cannibalism called autophagy. But as Hashimoto et al. reveal, autophagy can have a down side, destroying the pancreas by prematurely activating a digestive enzyme.

In autophagy, a vesicle swallows a portion of cytoplasm and ferries it to the lysosome for digestion. The process is often beneficial, allowing hungry cells to recycle molecules, for example. However, the researchers previously discovered that in mice with pancreatitis the level of autophagy in pancreatic cells surges.

Pancreatitis occurs when the enzyme trypsin dissolves cells from within. Normally, pancreatic cells fashion and discharge an inactive form of trypsin called trypsinogen, which remains inert until it reaches the small intestine. But if trypsinogen converts to trypsin before its release, it can damage or kill a pancreatic cell. Hashimoto et al. tested whether autophagy promotes this early activation by delivering trypsinogen to the lysosome, where enzymes turn it on.

The researchers gave mice injections of the compound cerulein, which spurs pancreatitis. Control animals suffered severe damage to the organ, which harbored numerous deteriorating cells. But rodents that lack a gene necessary for autophagy displayed almost no symptoms. To determine whether autophagy promotes trypsinogen activation, the team dosed pancreatic cells from both types of mice with cerulein. Cells from the autophagy-impaired animals carried much less activated trypsinogen than did cells from controls.

In rodents capable of autophagy, cerulein injections triggered much higher levels of trypsin activity in pancreatic tissue than did shots of saline, confirming that autophagy switches on the enzyme. The study is the first to reveal that autophagy can initiate a disease. The next step, the researchers say, is determining what triggers pancreatic cells to start eating themselves.

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