Researchers uncover new function for cell master regulator

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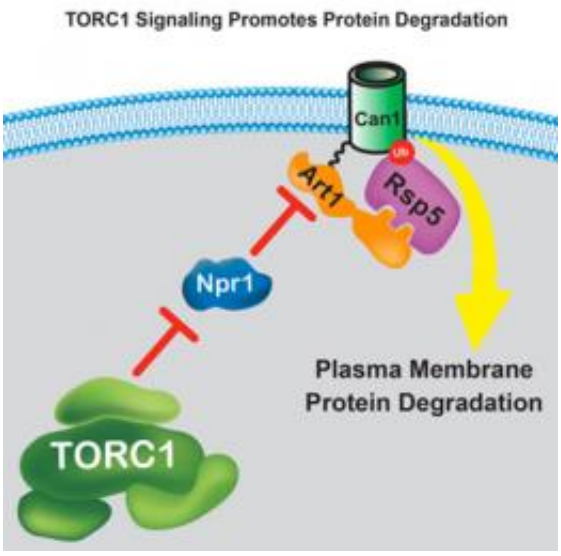

Art1 controls the abundance of resident plasma membrane proteins by targeting them for modification with ubiquitin (in red), a small chemical tag that marks proteins for degradation. Cornell researchers determined that the master cell growth regulator TORC1 controls protein degradation by activating Art1. Image: Emr Lab

(PhysOrg.com) -- TORC1 is a master regulator in cells, playing a key role in such diverse processes as gene expression and protein synthesis. While previous studies have described the role that TORC1 plays in these processes, a new Cornell study has discovered yet another process where the molecule is a central player: It maintains the composition of proteins in a cell's plasma membrane, the organelle that defines the outer

surface of the cell.

Proper turnover of proteins in the plasma membrane is critical for development and for day-to-day functions of every cell. The researchers sought to determine exactly how cells control the remodeling of these proteins at their surfaces.

The study is published in the Nov. 23 issue of the journal *Cell*.

"The problem is you have hundreds of different proteins at the cell's surface, and all of them must be turned over in a certain, regulated way," said Jason MacGurn, a postdoctoral researcher in the Weill Institute for Cell and Molecular Biology, who co-led the study with graduate student, Pi-Chiang Hsu. MacGurn and Hsu work in the lab of Scott Emr, the paper's senior author and Weill Institute director.

"We've found a new role for TORC1 in coordinating protein turnover," added Emr.

In the paper, the researchers describe a cellular system that responds to changes in nutrient availability by degrading plasma membrane proteins. The study shows how TORC1 controls this process: When cells have access to nutrients, TORC1 is "on," and signals to inhibit an enzyme called Npr1. The inhibition of Npr1 activates a second protein called Art1, which facilitates the removal of specific proteins at the cell's surface. When cells are starving, TORC1 is "off," causing Npr1 to inhibit protein degradation by ejecting Art1 from the plasma membrane. This mechanism for regulating the degradation of plasma membrane proteins is a key feature of the cell's growth-control program.

Disruption of this process can lead to uncontrolled cell growth that contributes to the progression of many types of cancer. The type of control mechanism described by Emr and colleagues may also contribute

to the control of obesity, since the proteins that correspond to Art1 in mice have also been shown to regulate body mass.

MacGurn received the first Sam and Nancy Fleming Research Fellowship from Cornell's Weill Institute for Cell and Molecular Biology in 2008. Marcus Smolka, assistant professor of molecular biology and genetics in the Weill Institute, is a co-author of the paper.

Provided by Cornell University