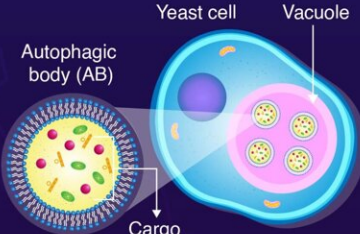


# New study sheds light on the molecular mechanisms underlying lipid recycling within cells

November 2 2023

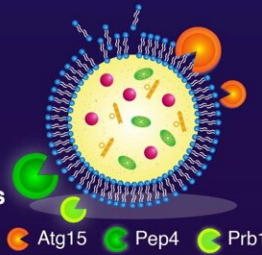
## Atg15-Mediated Mechanism Underlying Autophagy

Autophagy is a cellular process involving the degradation and recycling of cellular components within the vacuoles



Yeast cell    Vacuole  
Autophagic body (AB)    Cargo

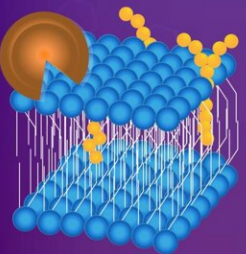
The phospholipase Atg15 and proteases Pep4 and Prb1 are necessary to disrupt ABs and release their cargo, but the underlying mechanisms remain unclear



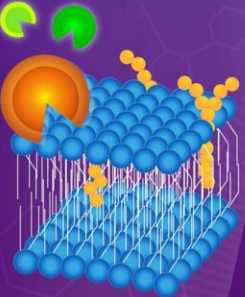
Atg15    Pep4    Prb1

**Mechanism of AB membrane disruption mediated by Pep4- and Prb1-processed Atg15 within the vacuole**

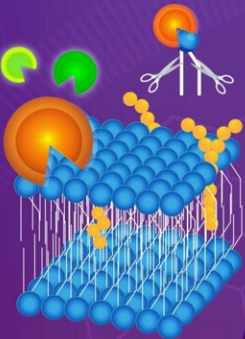
Atg15 binds to the phospholipid bilayer of ABs



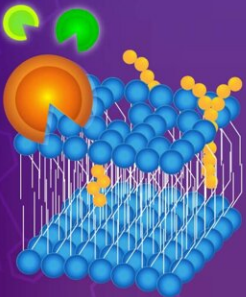
Pep4 and Prb1 activate Atg15



Atg15 cleaves phospholipids through the phospholipase B activity



Phospholipid degradation



**This study provides new insights into autophagy and membrane lipid recycling that have potential applications in metabolic disorder research**

The Mechanism of Atg15-Mediated Membrane Disruption in Autophagy  
 Kagohashi et al. (2023) | *Journal of Cell Biology* | DOI: 10.1101/2023.06.26.546516



This study provides new insights into autophagy and membrane lipid recycling that have potential applications in metabolic disorder research. Credit: Tokyo Tech

Recycling is just as essential in cells as in our more familiar macroscopic world. Cells continuously generate waste products and accumulate damaged components while performing regular functions. Various recycling mechanisms have evolved to ensure efficient use of these resources and help maintain homeostasis, with autophagy being one of the most well-preserved among countless animal, plant, and fungal lineages.

In the main form of autophagy, materials floating in the cell are transported to specialized organelles, such as lysosomes or vacuoles, within small capsule-like structures called autophagosomes. Once these autophagosomes reach inside the lysosomes or vacuoles, they are called autophagic bodies (ABs).

To degrade the cargo contained in ABs—a process called autophagy—the proteins within the lysosome or vacuole begin by breaking down the phospholipid bilayers enveloping the ABs. Previous research identified a few key players in this process, namely the proteins Atg15, Pep4, and Prb1. However, the interrelation between these proteins and underlying mechanisms is still unclear.

A research team from Tokyo Institute of Technology, Japan, has made [substantial progress](#) toward solving this puzzle. In a study published in the [Journal of Cell Biology](#) and led by 2016 Nobel laureate Professor Yoshinori Ohsumi and Assistant Professor Kawamata, they used yeast as

a [model organism](#) to shed light on some of the intricacies of autophagy.

"The relative simplicity of yeast vacuolar enzymes was particularly advantageous for our study as it allowed us to clarify the relationship between protein- and lipid-breaking activity in the vacuole," explains first author Kagohashi.

By applying *in vitro* assays involving lipid-degradation, the researchers demonstrated that Pep4 and Prb1 transform Atg15 into an 'activated' form. This step is necessary to enable Atg15 to break the phospholipid bilayer of ABs.

The team confirmed these findings by testing various Atg15 mutants and [yeast](#) strains lacking the genes coding for Pep4 and Prb1. By tagging Atg15 with a probe, they also pinpointed the modifications that Pep4 and Prb1 make to Atg15 within the vacuole.

The team delved deeper into how Atg15 breaks down the phospholipid bilayer through further experiments using isolated ABs. These analyses revealed, for the first time, that Atg15 has phospholipase B activity—this allows Atg15 to cleave phospholipid molecules at two specific locations, thus efficiently disrupting the phospholipid membrane.

In summary, this work deepens our understanding of crucial cellular processes, remarks Dr. Kawamata. "Characterization of lipid-breaking activity in the vacuole/lysosome is essential to understand how lipids are recycled. This study provides insights into the recycling of membrane lipids and informs work on a range of metabolic disorders." As she notes, [autophagy](#) is implicated in many diseases and can also be an attractive drug target for new therapies.

**More information:** Yoko Kagohashi et al, The mechanism of

Atg15-mediated membrane disruption in autophagy, *Journal of Cell Biology* (2023). [DOI: 10.1083/jcb.202306120](https://doi.org/10.1083/jcb.202306120)

Provided by Tokyo Institute of Technology

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