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## **Professor Youngsoo Jun's collaborative research team identifies protein complex structure that helps with autophagy**

- GIST (President Kiseon Kim) School of Life Sciences Professor Youngsoo Jun of the Cell Logistics Research Center led a collaborative research team with UNIST Department of Biological Sciences Professor Changwook Lee and discovered that autophagy is selectively regulated through the protein quaternary structure \* .

\* protein quaternary structure: Multiple polypeptides gather together to act as a protein because of hydrophobic bonds. It may not be present if one polypeptide plays a unique role as a protein. Like the tertiary structure, it is further stabilized by disulfide bonds, hydrogen bonds, and ionic bonds.

- This research revealed that the structure of the protein complex plays an important role in selecting which substances to break down and transfers them to the lysosomes. It is expected to provide a new direction for the study of autophagy related diseases.
- When waste builds up inside a cell or an external invader such as a virus enters, autophagy \* begins, which is a kind of "cleaning" that breaks down unwanted substances within the cell itself. This process takes place in the lysosome \*\* , which contains degradative enzymes.

\* autophagy: One of the reactions for cell survival when it consumes and reuses parts of itself. Problems with this process can lead to degenerative neurological diseases such as Parkinson's disease, dementia, inflammatory digestive diseases, cancer, and aging.

\*\* lysosome: A small pouch in the cell containing the protease. Generally, it destroys dead organelles or foreign substances such as viruses and bacteria that have been captured by external phagocytosis.

- Various proteins are involved in picking up unwanted substances in cells and transferring them to lysosomes. The Vacuole related 8 (Vac8) protein is well known, and the type of autophagy is determined by which protein it binds to. For example, when the Vac8 protein binds to the Nucleus-vacuole junction 1 (Nvj1) protein, Piecemeal microautophagy of the nucleus (PMN) occurs, which breaks down a portion of the cell nucleus, whereas binding to the Autophagy Related 13 (Atg13) protein transports cytosolic enzymes to the lysosomes and activates the Cytoplasm-to-vacuole targeting pathway (Cvt). However, the specific principle of how Vac8 binds to these proteins is unknown.
  - In this study, the X-ray crystallography and X-ray scattering methods using protein crystals revealed that the quaternary structure depends on the protein to which the Vac8 protein binds. The altered structure also determined the type of autophagy.
  - The team also used yeast to induce amino acid mutations involved in Atg13 protein binding. As a result of problems with the Atg13 binding structure, PMN autophagy was observed but Cvt related reaction was not found. Abnormalities in the quaternary structure of the protein demonstrated that no specific autophagy occurred.
- GIST Professor Youngsoo Jun said, "This research identified how a single protein can selectively mediate various forms of autophagy. The protein quaternary structure is expected to provide a new direction in discovering treatments for autophagy-related diseases such as Parkinson's disease, dementia, cancer, and aging."
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