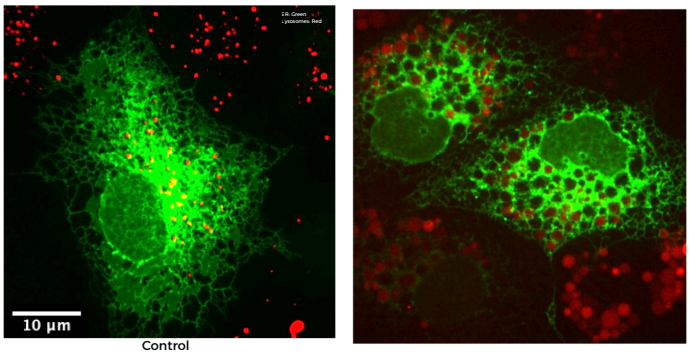
How Our Cells Stay Connected: Discovering a new role for PIKfyve in Cellular Communication

Scientists at Toronto Metropolitan University have uncovered an unexpected role for the lipid kinase PIKfyve in coordinating communication between lysosomes and the endoplasmic reticulum, providing new insight into how disruptions in organelle communication may contribute to human disease.



Control

Eukaryotic cells have always been depicted as having compartmentalized organelles, each performing distinct biochemical functions in response to environmental and developmental stimuli. However, in recent years, scientists have shown that organelles communicate and integrate their biochemical processes through membrane contact sites.

These interactions allow organelles to exchange lipids, coordinate movement, and respond to changes in the cellular environment. One of the most important partnerships occurs between lysosomes, the cell's recycling centres and the endoplasmic reticulum (ER), a network responsible for protein and lipid synthesis. Maintaining communication between these organelles is essential for healthy cell function. When one organelle stops functioning properly, the effects can ripple throughout the entire cell.

PIKfyve is a lipid kinase already known for its role in maintaining lysosome size and function When PIKfyve activity is disrupted, lysosomes become enlarged because they are unable to divide normally. but these researchers wondered if this impact extended beyond just the lysosome. Could this impact the way other organelles like the ER function?

An Unexpected Connection

The lab utilized high-resolution fluorescence microscopy, live-cell imaging, and molecular biology techniques, to examine how inhibiting PIKfyve affected interactions between lysosomes and the endoplasmic reticulum. This study found that inhibiting PIKfyve altered the structure and movement of the ER in two important ways. First, lysosomes became clustered near the nucleus and lost much of their mobility. Because the ER often extends through a process known as "ER hitchhiking," in which lysosomes help pull ER tubules throughout the cell, reduced lysosome movement also limited ER dynamics. Second, excess levels of a lipid called phosphatidylinositol-3-phosphate caused increased binding between lysosomes and the ER through the protein protrudin. Rather than promoting healthy communication, these excessive contacts disrupted normal ER organization. Together, these findings demonstrate that PIKfyve helps regulate not only lysosome biology but also the physical interactions between organelles that are essential for cellular organization.

Although this research focuses on fundamental cell biology, discoveries like these provide the foundation for future advances in medicine. This work reinforces an important concept in modern cell biology: organelles do not function in isolation. Instead, they operate as an interconnected network, where communication is just as important as the individual jobs each organelle performs. By understanding these connections, researchers can better uncover how disease develops and identify new opportunities for therapeutic intervention.

Read the full publication: *PIKfyve influences inter-organelle contacts with lysosomes to modulate the endoplasmic reticulum*, *Journal of Cell Biology* (2026).