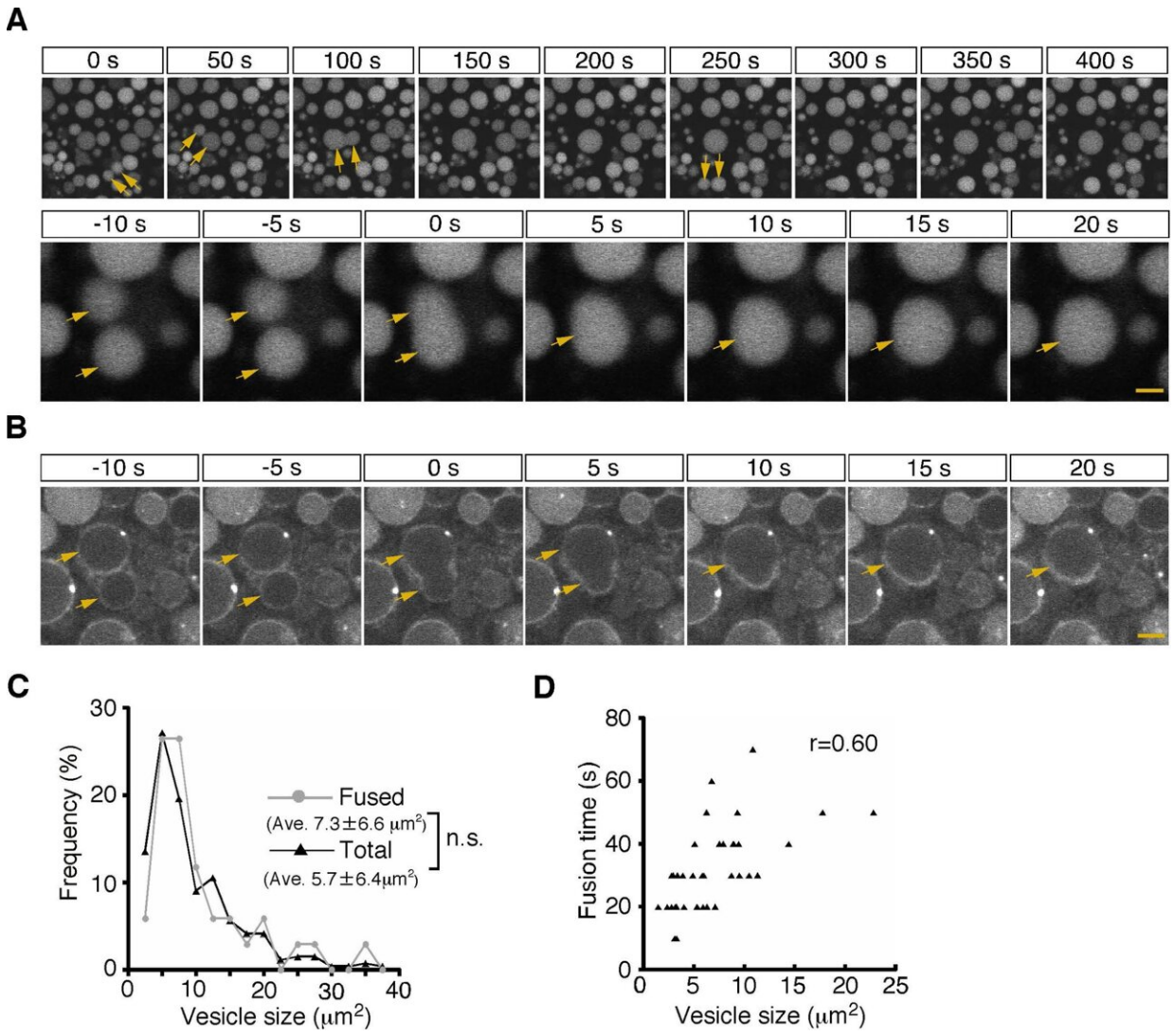
Researchers discover two vesicle fusion mechanisms while studying vesicle movement in living cells

April 8 2024



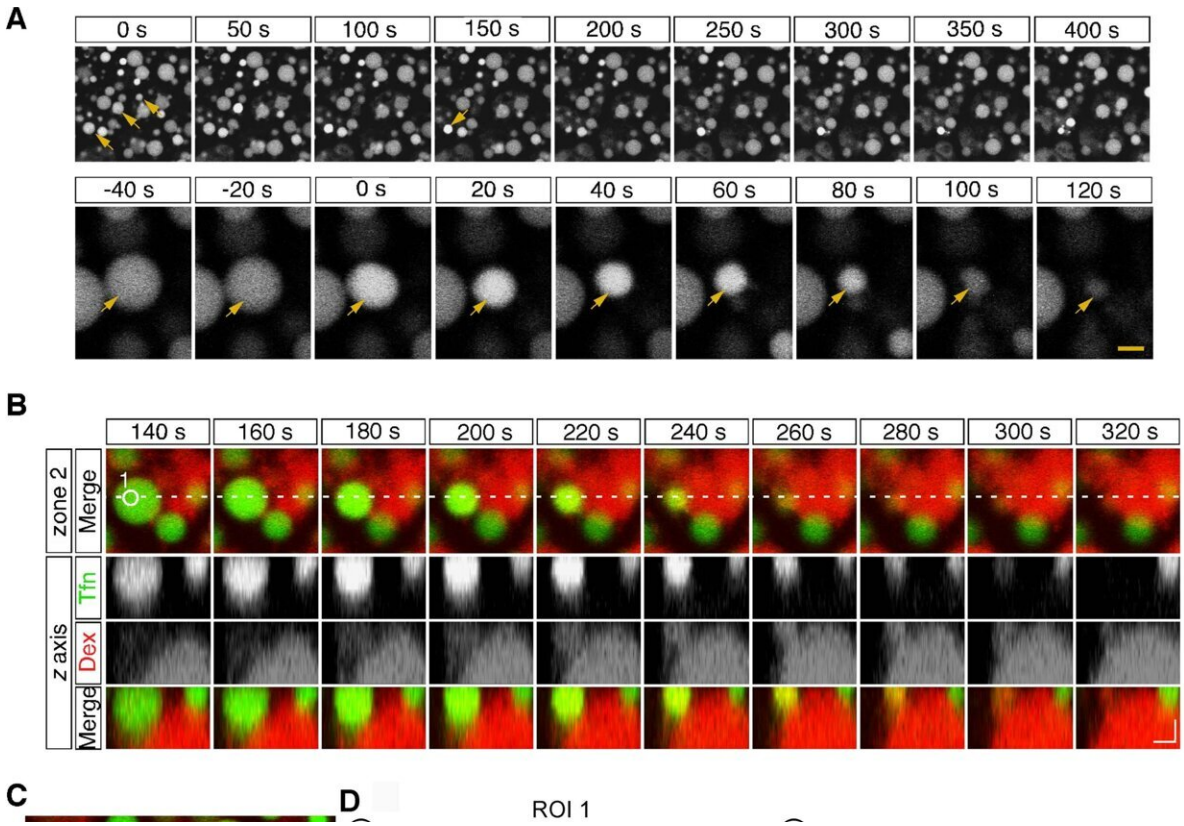
Homotypic fusion between late endosomes. (A) Time-lapse imaging of endocytic

vesicles in VE cells. (B) By labeling of VE cells with FM1-43, the fusion process of the cell membranes in zone 2 was observed. (C) Histograms showing the size distribution of total late endosomes (black line, n = 265) and the late endosomes that underwent homotypic fusion (gray line, n = 37). (D) Correlation between the size of the late endosomes that underwent homotypic fusion and the time required for completion of fusion. Credit: *eLife* (2024). DOI: 10.7554/eLife.95999

Cells intake substances from the outside world by encapsulating them in vesicles called endosomes, which are subsequently transported throughout the cell. During the transport process, vesicles fuse with other intracellular organelles. However, observing this process is challenging in many cells due to their small size and the complexity of underlying regulatory mechanisms.

In a new study published in *eLife*, the researchers focused on the outermost visceral endoderm cells of mouse embryos. By labeling endosomes with fluorescent markers, they successfully observed the fusion process under a microscope.

They identified two distinct modes of endosomal fusion: homotypic fusion, where two endosomes fuse rapidly to form a single vesicle, and heterotypic fusion, in which lysosomes slowly absorb endosomes.



Heterotypic fusion between late endosomes and lysosomes. (A) Time-lapse imaging of VE cells. After 15 min of pulse-labeling with Alexa 488-transferrin, heterotypic fusion of late endosomes was observed: they shrank gradually and disappeared from the focal plane (arrows). (B) Time-lapse imaging of late endosomes in VE cells. (C and D) Time course of the fluorescence intensity. (E) Electron microscopic image showing pore formation between a late endosome (LE) and a lysosome (Ly). (F) Correlation between the size of late endosomes that underwent heterotypic fusion and the time required for completion of fusion. (G) Histograms showing the size distribution of late endosomes at 5 min and 15 min. Credit: *eLife* (2024). DOI: 10.7554/eLife.95999

In addition, a mathematical analysis of the vesicle fusion process using a mechanical model of the vesicle membrane revealed that the vesicle size determines the fusion mode: homotypic fusion occurs in small vesicles

and heterotypic fusion happens in large ones. Moreover, the application of fluctuating forces to the vesicle membrane facilitated homotypic fusion even in large vesicles.

The binding of endosomes to the cytoskeletal protein called actin, which is believed to generate these fluctuating forces, appears to promote homotypic fusion. Furthermore, cofilin, which promotes actin turnover, and myosin, which interacts with actin, were crucial for vesicle fusion.

Using this observation system, the researchers expect to elucidate the regulatory mechanisms controlling the processes of intracellular vesicle fusion and trafficking.

More information: Seiichi Koike et al, Actin dynamics switches two distinct modes of endosomal fusion in yolk sac visceral endoderm cells, *eLife* (2024). DOI: 10.7554/eLife.95999

Provided by University of Tsukuba