polarization occurred within the infected cell, rather than towards it.

So, when an HTLV-I-infected T cell contacts another cell, microtubule rearrangements in the infected T cells occur, and the viral genome is subsequently transferred to the recipient cell. The identity of the molecules that initiate contact and polarization is unknown; the Env protein is one candidate for fusion, being the only HTLV-I protein that is expressed on the outside of the infected cell, but HTLV-I also upregulates the expression of some adhesion molecules that could favour cell–cell transmission. Other viruses that depend on cell contact for transmission, or that are lymphotropic — such as HIV-1 — might similarly subvert normal T-cell physiology to propagate between cells.

Katrin Bussell

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ORGANELLE TRAFFICKING

Breakdown to arrive

When you're travelling to a particular destination, there's always the risk that mechanical breakdown will thwart your arrival. However, Weisman and colleagues now report in *Nature* that transport-machinery breakdown can actually be essential for cellular organelles to reach their final destination.

For yeast vacuole inheritance to occur correctly, vacuoles must be transported from the mother cell to the growing bud. The yeast class V myosin Myo2 moves organelles along actin to different destinations during the cell cycle, and previous studies indicated that the yeast vacuole membrane protein Vac8 is needed for Myo2's role in vacuole inheritance. However, Vac8 and Myo2 had not been shown to interact directly. Weisman and co-workers therefore began by identifying Vac17 as the vacuole-specific receptor for Myo2. However, Vac17 is not a membrane-bound protein, so how does it link Myo2 to vacuoles?

The authors showed that a Vac17–Vac8 interaction is the missing link and that the regions of Vac17 that interact with Vac8 and Myo2 are distinct. Vac17 can therefore interact with both proteins simultaneously — Vac17 links Myo2 to Vac8 and, as a result, to the vacuole membrane.

Vacuole inheritance was found to be blocked by mutations that disrupted either Myo2–Vac17 or Vac17–Vac8 interactions, and the authors found that this block resulted in Vac17 accumulation. Furthermore, they showed that Vac17 protein levels and the levels of vacuole-associated Vac17 change during normal cell-cycle progression. The levels of vacuole-localized Vac17 increase on formation of the nascent bud, decrease with increasing bud size, and decrease further on vacuole-inheritance completion. So, are these changes in Vac17 levels due to increased synthesis, decreased breakdown, or both? And could changes in Vac17 levels control vacuole inheritance?

Sequence analysis allowed the authors to identify a predicted PEST sequence in Vac17, which is a signal for rapid protein degradation. They found that deletion of PEST resulted in increased Vac17-ΔPEST levels, although Vac17-ΔPEST supported normal vacuole inheritance. These results indicate that, in this case and in vacuole-inheritance mutants, Vac17 accumulation is a result of defective Vac17 degradation, rather than because of a significant increase in Vac17 synthesis.

Using immunofluorescence, Weisman and co-workers showed that, in *VAC17-ΔPEST* mutants, Vac17-ΔPEST accumulates in the bud, whereas, in vacuole-inheritance mutants, Vac17 accumulates in the mother cell. These results support the idea that Vac17 degradation occurs after it has arrived in the bud.

When vacuole inheritance is complete, vacuoles are localized near the centre of the bud, and the authors found that, in the *VAC17-ΔPEST* mutant, several vacuoles were localized to the mother–bud neck. Using time-course experiments, they showed that removal of the PEST sequence stabilizes the Myo2–Vac17 interaction, which causes the vacuoles to move 'backwards' from the bud centre to the mother–bud neck.

Together, these results support a model in which newly synthesized Vac17 binds to Vac8 and Myo2 in the mother cell to form the Myo2–Vac17–Vac8 transport complex, which moves the vacuole along actin to the bud. In the bud, Vac17 is degraded in a PEST-dependent manner, which releases Myo2 from the vacuole and results in the vacuole being deposited near the centre of the bud. So, transport breakdown doesn't always hinder arrival after all!

Rachel Smallridge

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WEB SITE

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http://bcaws.biochem.uiowa.edu/weismanlab/index2.html