Bacterial and host cell proteins interact to regulate Chlamydia's 'exit strategy'

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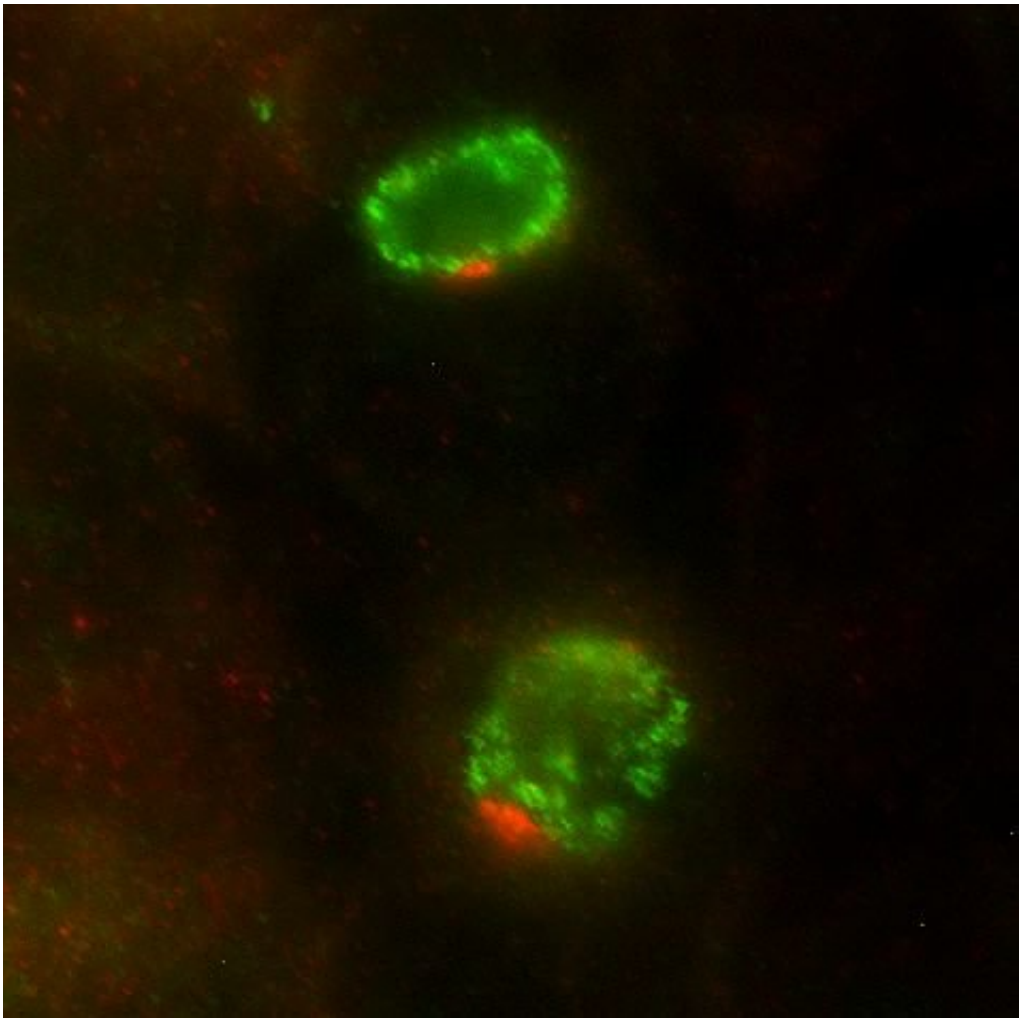

Chlamydia trachomatis inclusion showing recruitment of the inositol 1,4,5-trisphosphate receptor type 3 to microdomains on the inclusion membrane (red). Chlamydia are counterstained in green. Credit: Nguyen PH, et al. (2018)

Interactions between *Chlamydia trachomatis* proteins and host cell proteins help determine whether the bacterium leaves an infected cell via breakdown of the cellular membrane (lysis) or in a membrane-bound package, according to new research published in *PLOS Pathogens* by Phu Hai Nguyen of the National Institutes of Health, U.S., and colleagues.

C. trachomatis exists in different variants that can cause human and veterinary infections, such as infectious blindness or sexually transmitted diseases. Within an infected cell, the bacterium develops and multiplies inside a membrane-bound compartment known as the inclusion. At the end of its development cycle, *C. trachomatis* is released from the cell, freeing it to infect additional cells in the infected person or animal.

Previous studies have shown that *C. trachomatis* leaves a cell either via lysis or in the membrane-bound inclusion, which is extruded intact from the cell and may serve to protect *C. trachomatis* on its way to infect new cells. However, the mechanisms that determine which exit strategy is used are poorly understood.

In the new study, experiments with genetically modified *C. trachomatis* and host cell lines showed that a *C. trachomatis* protein found in the inclusion membrane, myosin regulatory complex subunit A (MrcA), interacts with the host proteins ITPR3 and STIM1. ITPR3 is a calcium channel; it enables passage of calcium ions across cellular membranes, which can serve as a signal to trigger different cellular events. STIM1 helps regulate calcium ion signaling.

Additional experiments showed that genetic disruption of MrcA, depletion of ITPR3, and depletion of STIM1 all significantly inhibited extrusion in infected cells, as did chemical disruption of calcium ion signaling. In these experiments, the scientists also observed significant effects on multi-protein "motor" structures involving the protein myosin, which were already known to play a major role in extrusion.

These findings suggest an important role for calcium ion signaling in regulating extrusion and could help improve understanding of how the bacterium leaves an infected cell and spreads within the body of an infected person of animal.

"One of the important points to come out of this work is that it implies a complex of multiple chlamydial proteins that function together to regulate exit mechanisms from host cells," the authors further explain. "Understanding how these work in conjunction with host proteins to control this aspect of chlamydial development should provide useful insights into pathogenesis."

More information: Nguyen PH, Lutter EI, Hackstadt T (2018) Chlamydia trachomatis inclusion membrane protein MrcA interacts with the inositol 1,4,5-trisphosphate receptor type 3 (ITPR3) to regulate extrusion formation. *PLoS Pathog* 14(3): e1006911. doi.org/10.1371/journal.ppat.1006911

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