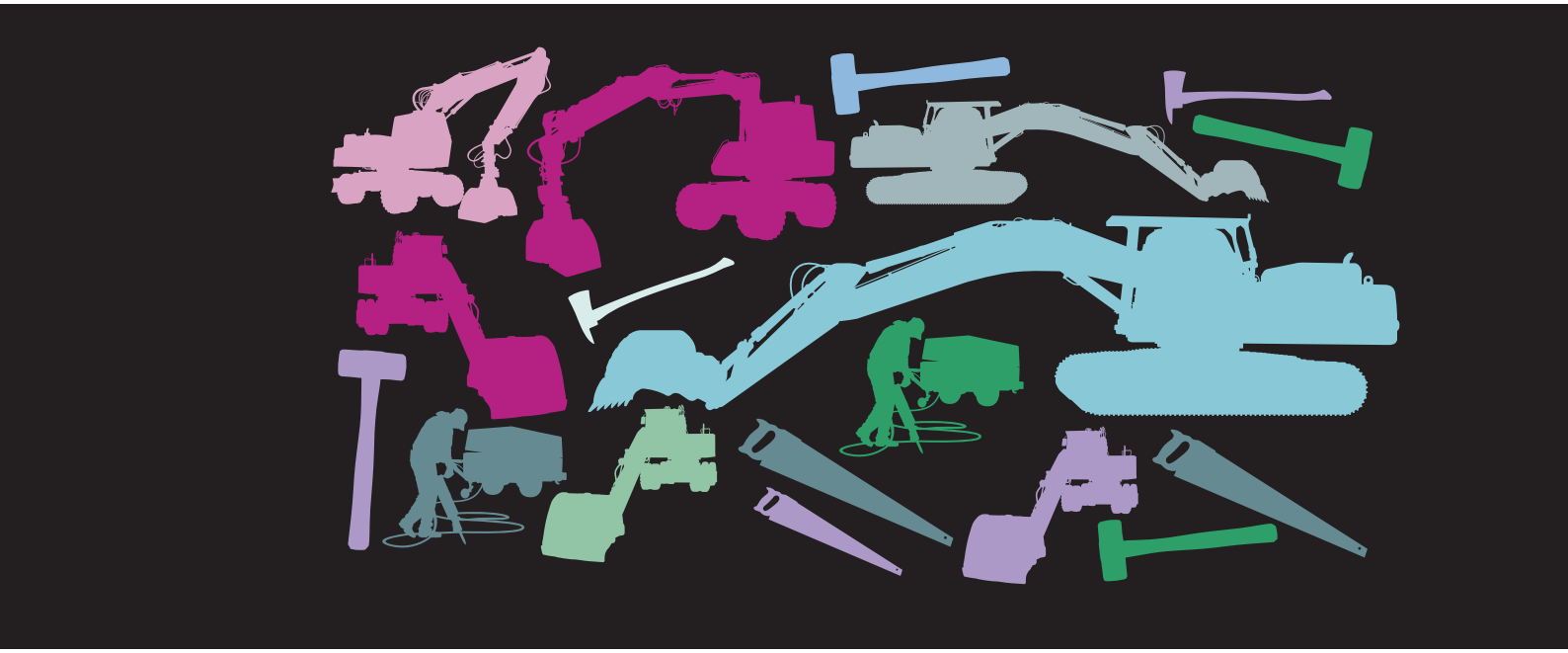

CELLULAR MICROBIOLOGY

Breaking up (the Golgi) is hard to do

Obligate intracellular parasites obtain nutrients from the host cell, but the mechanisms by which this occurs are often poorly understood. Writing in *Nature*, Heuer and colleagues now show that *Chlamydia trachomatis* induces breakdown of the Golgi to increase delivery of nutrients.

C. trachomatis grows inside eukaryotic host cells within membrane-bound compartments called inclusions. Following entry into host cells, the bacteria differentiate from an infectious form to a replicative form that divides multiple times and then converts back into an infectious form prior to lysis of the host cell. During growth, *C. trachomatis* requires Golgi-derived sphingolipids, which are incorporated into the inclusion membrane and the bacterial plasma membrane. However, the route of transport and regulation of sphingolipid acquisition are not understood. To understand the relationship between the inclusion and the Golgi during infection, Heuer and colleagues investigated Golgi morphology in infected cells. They report that the Golgi elongated and surrounded the inclusion. Electron microscopy revealed a decrease in both the normal stacking of the Golgi and the size of the individual stacks, which correlated with the formation of ministacks.

During cell division or apoptosis, several proteins that hold the Golgi stacks together are cleaved, causing Golgi dispersal. The authors checked whether a similar process occurs in *Chlamydia*-infected cells. They found that the protein golgin 84 was cleaved and that this cleavage was decreased by inhibitors of inflammatory caspases. Blocking golgin 84 cleavage led to a 100-fold decrease in the number of infectious progeny produced. Expression in host cells of a truncated version of golgin 84 that cannot be cleaved also decreased the number of progeny produced. Conversely, when Golgi fragmentation was induced prior to infection by knockdown of several proteins involved in tethering Golgi stacks, or with low doses of the microtubule depolymerizing drug nocodazole, bacterial growth increased up to tenfold.

Determination of the golgin 84 cleavage site revealed a possible calpain 2 recognition sequence, and treatment with a specific calpain 2 inhibitor led to the production of an intermediate cleavage product in infected cells. This suggests that cleavage is a two-step event that is catalysed by different host proteases.

How might Golgi dispersal increase progeny formation? Inhibiting golgin 84 cleavage reduces the transfer of sphingolipids to the vacuole. In golgin 84 knockdown cells, in which the stacks are disrupted, the life cycle of the bacteria was accelerated: infectious progeny were visible after 24 hours compared with 40 hours under normal conditions. A higher percentage of the bacteria might therefore convert to the infectious form prior to release from the host cell. The bacterial factors that induce golgin 84 cleavage and the mechanism by which Golgi stack breakdown promotes sphingolipid transfer remain to be elucidated.

Christiaan van Ooij

> “Blocking golgin 84 cleavage led to a 100-fold decrease in the number of infectious progeny produced.”

ORIGINAL RESEARCH PAPER Heuer, D. *et al.* *Chlamydia* causes fragmentation of the Golgi compartment to ensure reproduction. *Nature* 7 Dec 2008 (doi: 10.1038/nature075784–93)

© 2009 Macmillan Publishers Limited. All rights reserved