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An unexpected link between coronavirus replication and protein secretion in infected cells

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Coronavirus replication is critically linked to two factors within the early secretory pathway, according to new findings by a team of Dutch researchers that are published June 13th in the open-access journal *PLoS Pathogens*.

Coronaviruses, a group including the well-known SARS virus, are the causative agents of many respiratory and enteric infections in humans and animals. As with all viruses, virtually every step of their infection cycle depends on host cellular factors.

As the first, most crucial step after their penetration into cells, coronaviruses assemble huge RNA replication "factory" complexes in association with characteristic, newly induced double membrane vesicles. The cellular pathways hijacked by these plus-strand RNA viruses to create these "factories" have thus far not been elucidated.

The researchers, led by Cornelis A. M. de Haan, showed that RNA replication of mouse hepatitis coronavirus (MHV) was inhibited by a drug — brefeldin A — that disrupts the central station in the cell's secretory pathway, the Golgi complex. Consistently, depletion of both the cellular target of brefeldin A, a factor called GBF1, and its downstream target, ARF1, was also shown to negatively affect coronavirus infection.

The researchers conclude that "an intimate association exists between the early secretory pathway and MHV replication." They speculate that, while GBF1 and ARF1 are not involved in the formation of the viral replication structures, they probably play a key role in their maturation or functioning. As this work was limited to the mouse hepatitis coronavirus, an interesting next step would be to study the importance of GBF1 and ARF1 in the replication of other coronaviruses.

Source: Public Library of Science