Researchers identify mechanism that helps bacteria avoid destruction in cells

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Infectious diseases currently cause about one-third of all human deaths worldwide, more than all forms of cancer combined. Advances in cell biology and microbial genetics have greatly enhanced understanding of the cause and mechanisms of infectious diseases. Researchers from Thomas Jefferson University, the Pasteur Institute in Paris, and Yale University reported in *PLoS ONE*, a way in which intracellular pathogens exploit the biological attributes of their hosts in order to escape destruction.

Intracellular pathogens include *Chlamydia*, which causes infertility in women, and *Legionella*, which causes Legionnaire's disease. These pathogens are able to escape destruction and remain in the cells. Until now, it was unclear how they were able avoid the destruction process. The team of researchers, led by Fabienne Paumet, Ph.D., assistant professor of Microbiology and Immunology at Jefferson Medical College of Thomas Jefferson University, found that it appears to be due to SNARE-like proteins expressed by the pathogen.

SNARE proteins are necessary for eukaryotic cells to fuse to their intracellular compartments. These proteins, which are present on the surface of almost all intracellular compartments, interact to form a stable complex, triggering fusion of the membranes. Intracellular pathogens, like *Chlamydia* and *Legionella*, must contend with vesicular trafficking and membrane fusion in the host cell. But they manage to bypass the lysosome, where other pathogens would normally be destroyed.

The researchers tested the hypothesis that SNARE-like proteins expressed by the bacteria themselves were capable to interact with the eukaryotic SNAREs and alter membrane fusion to their advantage. The *Chlamydia* bacteria expressed a SNARE-like protein called IncA and the *Legionella* expressed a SNARE-like protein called IcmG/DotF, both of which inhibit SNARE-protein-mediated fusion.

"Based on our results, it seems that intracellular bacteria are able to express 'inhibitory SNAREs' to block fusion between the lysosome and the compartment containing the bacteria," Dr. Paumet said. "The SNARE proteins function like a zipper, and without each half, they can't fuse."

SNARE-like bacterial proteins would appear to be a viable therapeutic target, since disruption of their protective function should render intracellular bacteria more susceptible to clearance from the phagosome.

"Thorough understanding of the bacterial SNARE-like protein system will give us the necessary tools to design such therapeutics," Dr. Paumet said.

Source: Thomas Jefferson University (news : web)