How Legionella subverts to survive

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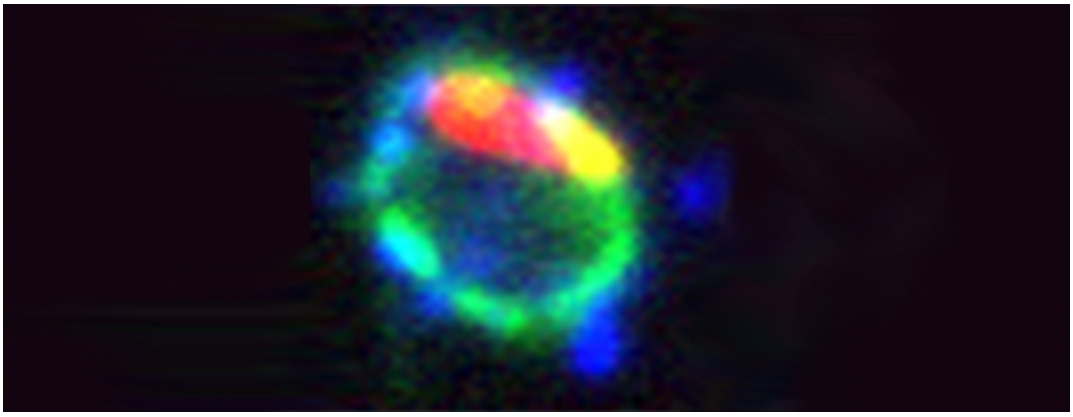

The picture shows a Legionella-containing vacuole (0.002 mm in diameter) isolated from an infected Dictyostelium amoeba. The vacuole is fluorescently labeled with the Dictyostelium protein calnexin (green) and the membrane lipid phosphatidylinositol-4-phosphate (blue), and encloses a single Legionella bacterium (red).

(Medical Xpress)—Bacteria of the genus Legionella have evolved a sophisticated system to replicate in the phagocytic cells of their hosts. LMU researchers have now identified a novel component of this system.

In humans, Legionella is responsible for the so-called Legionnaires' disease, a form of bacterial pneumonia that is often lethal. The bacteria can also cause Pontiac fever, a flu-like condition characterized by coughing and vomiting. Most Legionella-associated illnesses in humans are caused by Legionella pneumophila.

These microorganisms are found in soil, lakes and rivers, and can enter our water supply via the groundwater. The greatest risk of human infection arises when the bacteria colonize air-conditioning ducts or piping used to transport warm water. Persons can be infected when they inhale contaminated aerosols – in the shower, for instance.

The research group led by Hubert Hilbi, Professor of Medical Microbiology at LMU, studies how these intracellular parasites survive and replicate in phagocytic cells of their eukaryotic hosts or in the environment. For instance, the pathogen can grow and proliferate in the amoeba Dictyostelium, which normally preys on soil bacteria, engulfing and digesting them. But Legionella turns the tables, resists degradation and continues to grow in the amoeba until it is so full of bacteria that it bursts.

Legionella sabotages the immune system

When L. pneumophila cells infect the human lung, essentially the same thing happens. The bacteria are taken up by white blood cells called macrophages, which normally clear bacterial pathogens from the circulation. But instead of being consumed, the bacteria replicate in the macrophages and ultimately destroy them. Robbed of its first line of defense, the immune system has difficulty coping with the infection, and a life-threatening pneumonia may develop.

The biochemical processes that enable the parasites to outwit their temporary hosts are highly complex. Thus, L. pneumophila secretes around 300 proteins into the infected cell, which is forced to redirect its resources for the bacterium's benefit.

Hilbi and his colleagues have now characterized one of these proteins and describe its mode of action for the first time. This factor, called RidL, disrupts an intracellular transport system that is necessary for the

elimination of ingested bacteria. RidL binds to the so-called retromer complex, which is needed for the continued recycling of receptors, which deliver degradative enzymes to phagosomes containing bacteria destined for digestion. "We demonstrate that Legionella blocks the retromer-dependent transport route, thus promoting its own survival in the cell," Hilbi explains. This function is unique. "Proteins that act in this way are otherwise unknown in the bacterial world, and are not found in higher organisms either," he adds.

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