Novel mechanism allows Legionella to hide in body

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(Medical Xpress)—The feared Legionella pneumophila is responsible for legionellosis, an infectious disease that can lead to pneumonia. To infect humans, this pathogen has developed a complex method that allows it to camouflage itself and pass unnoticed inside our cells, thus preventing them from fighting against it.

A study led by the Basque bioscience research centre CIC bioGUNE, together with groups from the US National Institutes of Health (NIH) and the Barcelona Supercomputing Centre (BSC), has described a mechanism that helps this bacterium camouflage itself inside human cells for the first time. This study, published recently in the prestigious journal *PLOS Pathogens*, has solved the structure of the Legionella pneumophila protein SidD, which interferes with cell-based processes during infection.

Legionella, which lives in stagnant water, enters our body via the airways when we inhale microscopic drops of contaminated water. Once there, it is phagocytosed (in other words "swallowed") by immune system cells but not destroyed. This occurs because the bacterium manages to manipulate the host cell in order to establish a replicative niche in its interior, where it can hide and multiply without being destroyed.

The strategy employed by the microorganism involves releasing up to 300 proteins inside the cell. These proteins hijack many host's own proteins to modulate cellular processes that prevent the bacterium from being destroyed, thus allowing it to pass unnoticed for long enough to

allow it multiply.

One such protein, known as SidD, regulates a chemical modification involved in the intracellular camouflage process. The role of this protein has been described in the study by CIC bioGUNE, the NIH and the BSC. Once Legionella has managed to multiply itself, SidD unblocks cell-based processes that allow the infection to progress.

New targets

"Legionella pneumophila is an organism which, over millions of years of evolution, has learned to manipulate host proteins for its own benefit and thus favour infection", explains the CIC bioGUNE researcher Aitor Hierro. "Understanding how it does so", he adds, "may help us to manipulate our own proteins for our benefit".

The discovery of the mechanism that allows the bacterium to survive and grow in our cells may lead to new strategies. According to Hierro, "this discovery not only suggests new targets that may be used to design inhibitors but also reveals molecular mechanisms that could be readapted and used, for example, in the selective transport of molecules of therapeutic utility".

About legionellosis

Legionellosis was given its name in 1976, when an epidemic outbreak of pneumonia was reported amongst the participants at an American Legion convention in Philadelphia (USA). This disease is caused by the bacterium Legionella pneumophila , which lives in stagnant water and is transmitted in the air when we inhale microdrops of contaminated water in suspension.

The most important sources of infection are water systems or cooling towers in large buildings, such as hotels, hospitals or spas. Contamination in one of these installations may cause an outbreak of legionellosis in people living and working nearby.

Infection by this pathogen can cause two diseases with very different prognoses. The most well known is Legionnaire's disease, a severe respiratory infection that may lead to pneumonia and high mortality if a suitable antibiotic-based treatment is not used.

The other disease is known as Pontiac fever, a much less severe disease that progresses with short episodes of high fever and usually cures itself.

More information: Chen, Y. et al. Structural Basis for Rab1 De-AMPylation by the Legionella pneumophila Effector SidD, *PLOS Pathogens*. www.plospathogens.org/article/ … journal.ppat.1003382

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