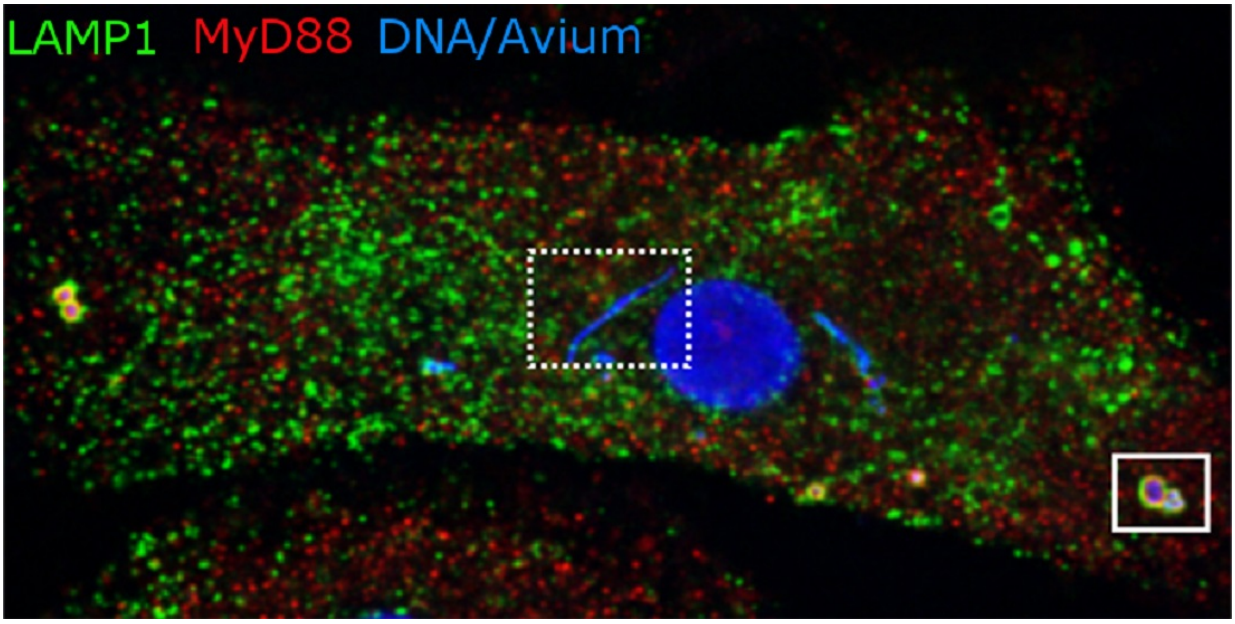
How tuberculosis bacteria hide in the body

September 28 2017



A macrophage with the mycobacterium *M. avium*. Bacteria like the one on the right are about to be broken down by lysosomes. But the blue strip in the middle contains bacteria that reside in phagosomes, which for some reason are not being transformed into the degrading lysosomes. Credit: Illustration: Alexandre Gidon, CEMIR and Department of Clinical and Molecular Medicine, NTNU

Tuberculosis bacteria hide in the very cells that would normally kill them. Now we know more about how they evade recognition. Tuberculosis affects millions of people worldwide. Treatment is often prolonged, from six months to two years. Therefore, researchers seek better treatment methods by understanding how the bacterium works.

"Tuberculosis has been around as long as human beings have existed," says Professor Trude Helen Flo, co-director of the Centre of Molecular Inflammation Research (CEMIR) at the Norwegian University of Science and Technology (NTNU). This long history has made the bacterium very widespread. One in every three individuals may be hosting tuberculosis, and even if only 10 percent develop the illness, it poses a significant public health problem.

One reason the bacterium has survived for so long is that it has developed a sophisticated mechanism for hiding in the body: it resides in white blood cells called macrophages, the very cells that would normally kill it.

Tuberculosis bacteria belong to the mycobacterial pathogens that can cause chronic infectious diseases. The bacterium can be dangerous and difficult to study, but CEMIR's new high-risk laboratory now makes such research possible. However, a lot of tuberculosis research is undertaken using the closely related Mycobacterium avium. This bacterium is far less aggressive and usually only causes problems in birds. It doesn't kill the cells that it hides in, but is dangerous enough that it can cause infections in individuals with impaired immune systems, such as patients who are receiving cancer treatment, who have pre-existing lung problems or whose immune systems are otherwise compromised.

This makes it interesting to study M. avium directly, but the results can also be transferred to tuberculosis research. So how do tuberculosis bacteria hide?

The mycobacteria are essentially stowaways. They live in macrophages, the major cells whose task is to gobble up enemies, useless cells and other particles. Macrophages are a kind of brutal guard in the service of our bodies. Most dangerous bacteria are attacked by macrophages. The

macrophage engulfs bacteria and immediately traps them in a separate cell compartment, or vesicle. This vesicle is called a phagosome and is the actual "executioner" in the cell.

The phagosome fuses with other vesicles that contain decomposing substances. It matures and turns into a lysosome. In the lysosome, bacteria are broken into their individual constituents, which can be reused by the body. However, some of the mycobacteria go undetected. A new study from CEMIR provides new insight into why. The study, led by Professor Flo, has just been published in *PLOS Pathogens*.

Postdoctoral fellow Alexandre Gidon at CEMIR specializes in the use of advanced microscopes. He and his colleagues have studied mycobacteria and macrophages directly through a confocal microscope. Gidon is the first author of the new study. Their research shows that M. avium not only avoids being killed by macrophages, but even avoids being discovered by them. It is this recognition phase that the CEMIR researchers are now able to shed more light on.

In the beginning, macrophages bind to and sense M. avium, which initiates an inflammatory response, which is key to limiting an infection. But then, the bacterium prevents the phagosome from being converted to a lysosome. "After M. avium is engulfed by the macrophage, it avoids getting degraded and hides in a separate compartment inside the macrophage, a vesicle, where it is no longer recognized—the sensors are either not present or else don't react to the presence of the bacteria. This way they can thrive and divide," Flo says.

"How this happens, we don't yet know. But if we could prevent mycobacteria from hiding in this compartment, or force the bacteria out of it, they would have a hard time surviving. Then they would have trouble causing a chronic infection," she said.

An important lead may be that not all mycobacteria manage to avoid being detected. The macrophages engulf all the bacteria, but only the most well-adapted ones are not discovered and manage to hide and survive. The researchers envision future research where they would try to find out how the mycobacteria manage to establish and sustain the vesicle hideouts as they evade discovery. That would enable something to be done about these chronic troublemakers.

The treatment for common tuberculosis usually involves four different antibiotics to start, and gradually decreases to two. The whole process takes about six months. But if the tuberculosis bacterium is resistant to antibiotics, recovery can take up to two years. "Unlike a number of other infectious diseases, you don't become immune even if you've had tuberculosis. You can become infected and sick again, so it's important to find solutions that can provide milder, shorter-term treatment," says Flo.

CEMIR's basic research is part of this work. Antibiotics are designed to kill bacteria. Antibiotic resistance is an increasing problem. An effective solution may be to combine antibiotics with substances that stimulate our own immune system. In this way, the bacteria would be attacked from two sides and would therefore have a harder time finding places to hide.

More information: Alexandre Gidon et al, Persistent mycobacteria evade an antibacterial program mediated by phagolysosomal TLR7/8/MyD88 in human primary macrophages, *PLOS Pathogens* (2017). DOI: 10.1371/journal.ppat.1006551

Provided by Norwegian University of Science and Technology

Citation: How tuberculosis bacteria hide in the body (2017, September 28) retrieved 27 April

2024 from https://medicalxpress.com/news/2017-09-tuberculosis-bacteria-body.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.