TB Bacterium Uses Its Sugar Coat To Sweeten Its Chances Of Living In Lungs

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(PhysOrg.com) -- Common strains of tuberculosis-causing bacteria have hijacked the human body's immune response to play tricks on cells in the lungs, scientists say.

The results of this takeover are mixed. The cells essentially welcome the bacteria into the lungs and invite them to stay a while, meaning the human host becomes infected with the TB bacterium. But in about 90 percent of these cases, the infection remains latent and the infected person never has any symptoms of illness.

The secret weapon in this stealth attack is sugar.

Ohio State University researchers have determined that Mycobacterium tuberculosis has learned through evolution to coat itself with a sugar called mannose, which makes the bacterium attractive to cells in the lungs that are looking to clean up and discard unwanted sugar in the body. Those lung cells absorb the TB bacteria, giving the infecting bacteria a place to live for the long term.

"The bug sugarcoats itself and creates this magical interaction that allows it to slip by the immune system. We think that this is a beautiful example of the concept of host adaptation," said Larry Schlesinger, professor of internal medicine and director of the division of infectious diseases at Ohio State. "TB has evolved in humans. We're the reservoir. It has had centuries to develop a sophisticated way to deal with its encounter with the human, and the lung is the special portal of entry."

Schlesinger, also director of Ohio State's Center for Microbial Interface Biology, reported on TB's adaptation to the human respiratory system Friday (9/26) at the First International Congress "Mycobacteria: A Challenge for the 21st Century" in Bogotà, Colombia.

Part of his presentation in Colombia touched on the most recent discovery in his lab – two strains of TB bacteria that do not show these signs of adaptation. The existence of these other strains suggests that some strains of TB bacteria can be tied to specific regions of the world based on specific ways in which they interact with the human immune system.

This newest research appears online in the *Journal of Biological Chemistry*.

To maintain ideal breathing conditions, the lungs avoid inflammation. They do this by trying to minimize immune responses to various particles humans inhale because the more the immune system responds, the higher the level of inflammation that results.

Too much inflammation can interfere with the ability to breathe.

"Then here comes TB, an organism that gets into an environment that is not very primed to respond to a foreign invader, and the TB fundamentally takes advantage of that environment," Schlesinger said.

About 2 billion people worldwide are thought to be infected with TB bacteria. People who are infected can harbor the bacterium without symptoms for decades, but an estimated one in 10 will develop active disease characterized by a chronic cough and chest pain. An active infection is treated with a combination of antibiotics that patients take for at least six months.

At the point of infection in the lung, TB bacteria are eaten by a macrophage, also called an antigen-presenting cell. As part of what is called the innate immune response, the macrophage activates specific molecules that make pieces of the bacteria visible to infection-fighting T cell warriors, which triggers an eventual T-cell response to come to the macrophage's aid.

The innate response kicks in to fight any pathogen, but an acquired immune response is required to activate T cells that are specifically designed to help macrophages kill TB bacteria. The sugarcoating delays activation of that acquired response, so the bacteria then find comfort in the macrophages, causing a latent infection.

If the immune response is defective and fails to prompt macrophages to kill the TB bacteria, the bacteria eventually multiply so much that the infected cells burst and release the bugs into the lungs, leading to active infection.

Schlesinger's lab has discovered that the most common strain of TB bacteria has evolved over time to make itself particularly attractive to the macrophages in the lungs. The mannose, or sugar, on the surface of these bacteria is the same mannose that the human body produces when it makes new proteins.

"When we make new proteins and they get into circulation and end up where they don't belong, we have mannose receptors that exist primarily to scavenge unwanted mannose proteins that we make without activating the innate immune system. It's a receptor to keep humans healthy," Schlesinger said.

It turns out that macrophages in the lungs have high activity of this mannose receptor.

“So the TB coats itself with sugars like decorating the branches of a Christmas tree, and that allows it to avoid an inflammatory response by slipping into the macrophage through this scavenger receptor,” Schlesinger said.

During his presentation in Colombia, Schlesinger also described the related work that he and colleagues recently reported in the Journal of Biological Chemistry. The research team has identified two different strains of TB from ill patients that interact completely differently with macrophages. These strains do not coat themselves with sugar, so they have a harder time finding their way into macrophages in the lungs, where they could cause latent infection. Instead, they use a more primitive pathway to enter the macrophages, so fewer bacteria enter the lungs.

“We believe that these strains haven’t been living in humans for very long, so they don’t know how to get into their niche and sleep into latency, which is the most commonly seen TB behavior,” Schlesinger said. “But the few bacteria that do get into the lung macrophages grow like gangbusters, and we speculate that this is one reason for why they are a cause of TB outbreaks.”

Schlesinger said that the discovery of these strains of TB that behave so differently – and which are associated with outbreaks of active disease – is another indication that the TB bacterium has evolved in relative isolation in different regions of the world.

“We feel that these isolates in different areas of the world interact with humans in a special way, and if these bugs then travel to a different part of the world and an abnormal encounter occurs, there can be outbreaks of TB as a result of the migration patterns of these strains,” he said.

Provided by Ohio State University

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