

Tuberculosis researchers find answer to 30-year-old puzzle

February 21 2012

(Medical Xpress) -- After three decades of searching, the random screening of a group of compounds against the bacterium that causes tuberculosis has led scientists to a eureka discovery that breaks through the fortress that protects the bacterium and allows it to survive and persist against treatments.

The two findings, which occurred at Colorado State University, are published today in [Nature Chemical Biology](#). The article describes the [discovery](#) of an important cell function in the bacterium that causes [tuberculosis](#) which allows the bacterium to survive. The researchers also discovered a compound that prevents this cell function.

The bacterium that causes tuberculosis is extremely difficult to kill and current tuberculosis drugs on the market don't do well to treat it. Six months of multiple antibiotics are generally required to treat tuberculosis in most people, and many current drugs no longer work because of resistant strains of the bacterium that causes tuberculosis. Scientists hope that finding new drugs to kill the bacteria in ways different than current drugs will help tackle those strains.

Cell envelopes form a virtually impenetrable bubble around the bacterium cell and protect it. Mycolic acids are key portions of this bacterium's cell envelope. They are made inside the cell, but have to cross the cell membrane – with the help of a transporter -- to reach their final location in the cell envelope.

“Without mycolic acids in the cell envelope, the bacteria die,” said Mary Jackson, one of the leading researchers on the project. Jackson is a professor in the Department of Microbiology, Immunology and Pathology. “While randomly testing a group of compounds against the bacterium in the lab, we found one class of compounds that powerfully stops the growth of the bacterium—a significant finding on its own. When we looked closer, we found that the [compounds](#) stopped a transporter from moving mycolic acids from inside to outside the cell, which also means this discovery identified a new method of killing the bacterium.

Scientists have been trying to find the transporter of mycolic acids for decades, knowing that understanding how to stop mycolic acids from reaching the surface of the cell could lead to new tuberculosis treatments.

“If mycolic acids cannot be transported, the tuberculosis bacterium cannot grow,” said Mike McNeil, co-researcher on the project with Jackson and also a professor in the Department of Microbiology, Immunology and Pathology at CSU. “It is like a factory making bricks and no way to get them to the construction site. It is a long, hard road to develop new, badly-needed tuberculosis drugs. Still, we are optimistic that this research will strongly contribute to the worldwide crusade to diminish suffering and death caused by tuberculosis.”

Jackson, McNeil and partner researchers from CSU and St. Jude Children’s Hospital in Memphis also note that there are other potential transporters in the [bacterium](#) that resemble the one just found.

“We hope that our work also will pave the way to understanding what those transporters do in the cell and finding how to target them to kill the mycobacteria,” Jackson said.

Tuberculosis causes the death of more than 1.5 million people around the globe each year.

Provided by Colorado State University

Citation: Tuberculosis researchers find answer to 30-year-old puzzle (2012, February 21)
retrieved 19 April 2024 from

<https://medicalxpress.com/news/2012-02-tuberculosis-year-old-puzzle.html>

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