

Study casts doubt on provocative tuberculosis theory

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The tuberculosis bacterium is an insidious germ that can lie dormant for many years, then suddenly emerge and cause potentially fatal disease.

Earlier this year, researchers in Sweden proposed a provocative explanation: TB bacteria have the ability to turn into dormant, armorplated spores. If true, the findings would provide promising new avenues of research in the worldwide fight against TB.

But a new study by researchers at Loyola University Health System and other centers casts doubt on the TB spore theory. Researchers were unable to detect spores in TB cultures and demonstrated that the <u>TB</u> <u>bacterium</u> doesn't even contain genes related to those needed to produce spores. Researchers also failed to find any spores in frogs infected with TB bacteria, which would have been expected if TB bacteria produced spores in the course of infection.

Results are published in the <u>Proceedings of the National Academy of</u> <u>Sciences</u> (*PNAS*).

The new findings could save TB researchers from pursuing strategies that likely would prove to be fruitless, said Loyola microbiologist Adam Driks, Ph.D., second author of the new study. Driks is an associate professor in the Department of Microbiology and Immunology at Loyola University Chicago Stritch School of Medicine. The new study was directed by Richard Losick, Ph.D, and the first author is Bjorn Traag, Ph.D., both of Harvard University.



"Our study illustrates the essential contributions that basic science makes to translational and clinical research," Driks said. "It can help ensure that efforts to improve therapeutics and treatment are focused in the most productive directions."

Tuberculosis, caused by the bacterium Mycobacterium tuberculosis, is the leading cause of death worldwide by a single bacterial germ. The World Health Organization estimates there were 9.3 million new TB cases and 1.3 million TB deaths worldwide in 2007.

One of the mysteries of tuberculosis is its ability to go latent. A person can be infected at a young age and remain healthy for decades. But the disease can later emerge under certain conditions, such as AIDS, cancer, old age or chronic ill health.

In a study published June 30 in PNAS, researchers from Uppsala University in Sweden reported "clear evidence" the TB bacterium can form a type of cell called a spore. Bacterial spores are extremely hardy. During tough times, they lie dormant and form thick walls that ensure their survival. When conditions improve, they revive, shed their armor and start growing again. Some bacteria, notably the Bacilli, make spores when starved. Prior to the June 30 study, the bacteria that cause tuberculosis had never been shown to make these resistant, dormant cells.

Authors of the June 30 study said their finding "might provide new tools to combat mycobacterial diseases such as tuberculosis by preventing the disease itself and/or its transmission by spores."

But the new study casts doubts on this earlier finding. For example, the Swedish researchers reported that spore-related genes are present in the TB bacterium genome. But the new study argues that the TB bacterium lacks the genes known to be needed for spore formation.



In the earlier study, researchers reported finding endospores in a culture of TB cells. In the new study, researchers tried to replicate that experiment, but found no endospores in their culture of TB cells. Driks said it appears that the endospores found in the earlier experiment might be the result of inadvertent contamination by other bacteria.

Provided by Loyola University

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