

Scientists identify protein central to immune response against tuberculosis bacteria

January 12 2017



This photomicrograph reveals *Mycobacterium tuberculosis* bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000 X. The acid-fast stains depend on the ability of mycobacteria to retain dye when treated with mineral acid or an acid-alcohol solution such as the Ziehl-Neelsen, or the Kinyoun stains that are carbolfuchsin methods specific for *M. tuberculosis*. Credit: public domain

UT Southwestern Medical Center researchers have identified a protein that is central to the immune system's ability to recognize and destroy the bacterium responsible for the global tuberculosis (TB) epidemic. The

new finding, reported recently in *Cell Host & Microbe*, could someday lead to the development of immunity-based therapies to treat tuberculosis—which typically takes months to eradicate and has become increasingly resistant to antibiotics—by strengthening this immune pathway, said Dr. Michael Shiloh, Assistant Professor of Internal Medicine and Microbiology.

According to the World Health Organization, TB is a top infectious disease killer worldwide and is estimated to have infected 9.5 million people and caused 1.5 million deaths in 2014. That year, [tuberculosis](#) surpassed HIV as the world's most lethal infection.

"The protein Smurf1 functions in specialized white blood cells called macrophages in both mice and humans, thereby suggesting a conserved evolutionary pathway," said Dr. Shiloh, co-senior author of the study along with Dr. Beth Levine, Director of the University's Center for Autophagy Research.

In 2011, UT Southwestern researchers in Dr. Levine's laboratory identified the protein Smurf1 as important for the elimination of viruses and damaged mitochondria from cells via a cellular housekeeping process called autophagy. Dr. Levine is also a Professor of Internal Medicine and Microbiology; a Howard Hughes Medical Institute Investigator; and holder of the Charles Cameron Sprague Distinguished Chair in Biomedical Science.

That result led to the current study, a collaboration between the Shiloh and Levine laboratories to determine if Smurf1 plays a similar role in the autophagy of bacteria like *M. tuberculosis* inside cells.

In addition to recycling components of the cell to provide nutrients during starvation and acting as quality control for the organelles and proteins inside cells, autophagy helps eliminate pathogens such as

viruses, parasites, and bacteria that get inside the cell. During antibacterial autophagy, the bacteria get tagged with the protein ubiquitin, marking them for destruction by an organelle called the lysosome. The role of Smurf1—one of hundreds of E3 ubiquitin ligases in mammals—was unknown in this process.

In this study, the researchers found that macrophages from mice lacking Smurf1 were unable to attach the death-tagging protein ubiquitin to [intracellular bacteria](#), resulting in a failure of the autophagy pathway and runaway growth of the bacteria inside the cells. When infected with TB, mice lacking Smurf1 had higher bacterial loads, increased lung inflammation, and accelerated mortality compared to mice with normal Smurf1 activity, Dr. Shiloh said.

The researchers next showed that the Smurf1 gene controls *M. tuberculosis* growth in human macrophages and that the Smurf1 protein was found in association with bacteria in the lungs of patients with tuberculosis infections.

"Even though humans mount a defense against *M. tuberculosis* that can contain its growth, in general that defense is insufficient to kill the bacteria," Dr. Shiloh explained. "Finding ways to harness or enhance the [autophagy](#) pathway and Smurf1 could lead to new strategies to kill intracellular [bacteria](#) like those that cause TB," he added.

More information: Luis H. Franco et al, The Ubiquitin Ligase Smurf1 Functions in Selective Autophagy of Mycobacterium tuberculosis and Anti-tuberculous Host Defense, *Cell Host & Microbe* (2017). [DOI: 10.1016/j.chom.2016.11.002](https://doi.org/10.1016/j.chom.2016.11.002)

Provided by UT Southwestern Medical Center

Citation: Scientists identify protein central to immune response against tuberculosis bacteria (2017, January 12) retrieved 10 April 2024 from <https://medicalxpress.com/news/2017-01-scientists-protein-central-immune-response.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.