

# How mycobacteria avoid destruction inside human cells

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Tuberculosis, or TB, is a dreaded contagious disease of the lungs and other organs. The causative agent, *Mycobacterium tuberculosis* (or *M. tuberculosis*), infects roughly a third of the world's population and one-in-ten to one-in-twenty of the infected population becomes sick or infectious at some point during their lifetime.

The [mycobacteria](#) survive, and even thrive, inside host macrophages - cells that are part of the human immune system and that usually engulf and destroy bacteria in structures called phagosomes. *M. tuberculosis* is taken into phagosomes but it somehow blocks phagosome maturation, and hence survives. Figuring out how could open up new therapeutic targets for the treatment of TB as well as shedding light on the mechanism of intracellular parasitism.

Researchers at the Pasteur Institutes in Seoul and Paris and Institute of Pharmacology and [Structural Biology](#) (IPBS) in Toulouse joined forces to systematically search for mycobacterial genes that block phagosome maturation. To do this, they generated 11,000 different mutants of the *M. tuberculosis* Beijing strain, which has been associated with large outbreaks of TB, increased virulence, and multidrug resistance.

Using a high-throughput visual assay, the researchers screened for mutant mycobacteria that had lost the ability to arrest phagosomal maturation. Lead author Dr. Priscille Brodin, heading the Inserm Avenir Unit at Institut Pasteur Korea describes the screen as "enabling stringent selection of mutants that have the most pronounced subcellular localization within intracellular acidic compartments through the use of automated confocal quantitative imaging. Our approach", she adds, "may be useful to identify virulence genes in other [intracellular pathogens](#)".

The team identified ten distinct mutants, only one of which had previously been shown to play a part

in phagosome maturation arrest. Finding that two independent mutants mapped to the same region, they studied this locus in more detail. The work revealed that the biosynthesis of particular glycolipids containing acyltrehalose was perturbed, suggesting to the researchers that these glycolipids play a critical role in the early intracellular protection of mycobacteria.

"Our study unravels the role of novel lipid molecules in mycobacterial intracellular parasitism" says Dr. Olivier Neyrolles leading a CNRS Unit at IPBS in Toulouse France. "This establishes potential new drug targets", especially important given the emergence of multidrug-resistant and extensively drug-resistant TB. "In addition", Dr Brodin points out, "the assay that have we developed can be readily adapted for the screening of novel antimicrobials".

**More information:** P. Brodin<sup>1</sup>, Y. Poquet et al., "High content phenotypic cell-based visual screen identifies *Mycobacterium tuberculosis* acyltrehalose-containing glycolipids involved in phagosome remodeling", *PLoS Pathogens*

Provided by Institut Pasteur Korea

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