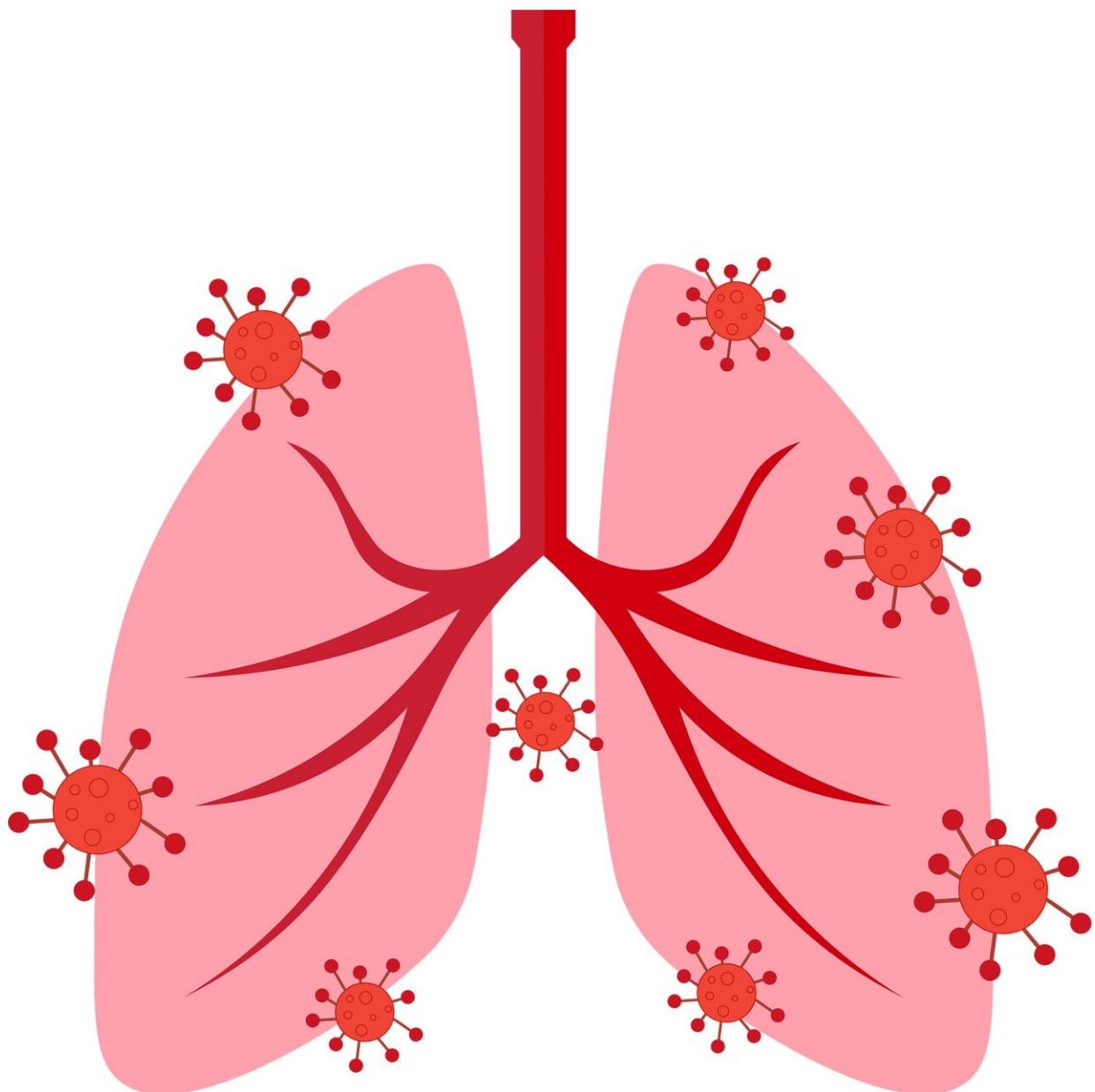


# Novel combination therapy to counter antibiotic-resistant *Mycobacterium abscessus* infections

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Researchers from the Antimicrobial Resistance (AMR) Interdisciplinary Research Group (IRG) at Singapore-MIT Alliance for Research and Technology (SMART), MIT's research enterprise in Singapore, in collaboration with Nanyang Technological University Singapore (NTU Singapore) and National University Hospital (NUH), have discovered a novel therapy by combining two antibiotics, rifaximin and clarithromycin, to treat *Mycobacterium abscessus*, a non-tuberculous mycobacterium that causes chronic lung-related infections.

Infections caused by NTM are a fast-growing health concern worldwide, particularly in the context of lung-related infections. Among NTMs, *M. abscessus* is one of the most prevalent, causing pulmonary infections in humans with immune deficiencies or underlying lung conditions. *M. abscessus* has also been linked to severe infections in various other parts of the body, including the skin, joints, soft tissues, and surgical sites. These infections are difficult to treat due to the bacterium's extensive innate resistance to many commonly used antibiotics.

Currently, *M. abscessus* infections are treated by a multidrug regimen that includes [clarithromycin](#), but some *M. abscessus* subspecies acquire resistance upon repeated exposure to the drug. As a result, available treatment options are limited, leading to prolonged and recurrent infections and even fatalities in some cases. With clarithromycin being the mainstay of NTM treatments and currently the only highly effective oral antibiotic for treating *M. abscessus* infections, there is an urgent medical need for the identification of compounds that are clarithromycin potentiators in order to effectively restore clarithromycin efficacy

against *M. abscessus*.

A recent study by SMART researchers, "Rifaximin potentiates clarithromycin against *Mycobacterium abscessus* in vitro and in zebrafish," published in the journal *JAC-Antimicrobial Resistance*, revealed promising findings on the use of rifaximin (an antibiotic commonly used to treat gastrointestinal bacterial infections) as a clarithromycin potentiator with the ability to increase clarithromycin sensitivity and improve its ability to kill *M. abscessus*.

During the discovery stage of the study, the researchers conducted drug screening campaigns and successfully identified several drug candidates as clarithromycin potentiators. Further preclinical testing of these drug candidates confirmed rifaximin as the most effective clarithromycin potentiator, with the combination of rifaximin and clarithromycin showing efficacy both in vitro and in a zebrafish embryo [infection](#) model.

"We recognize the urgent need to address the growing problem of clarithromycin resistance in *M. abscessus* and are pleased to have discovered rifaximin as a potent clarithromycin potentiator. Despite being primarily used for gastrointestinal infections and having limited activity against drug-resistant *M. abscessus*, our study demonstrated the synergistic effect of rifaximin with clarithromycin in effectively eliminating the bacteria," said Dr. Boon Chong Goh, first author of the paper and principal research scientist at SMART AMR.

"With limited treatments available due to *M. abscessus* innate resistance to most antibiotics, including clarithromycin, the novel discovery of the strong combination between rifaximin and clarithromycin is a significant step towards addressing the challenge of treating NTM infections. As FDA-approved drugs, we will be able to quicken the process and translate the findings into improved treatment outcomes for patients

suffering from *M. abscessus* infections," added Professor Peter C Dedon, corresponding author of the paper, Co-Lead Principal Investigator at SMART AMR and Professor at MIT.

The researchers are furthering their research with animal preclinical studies to prepare for human clinical trials. As both [rifaximin](#) and clarithromycin are approved by the U.S. Food and Drug Administration, the preclinical studies evaluating their combination against *M. abscessus* can be accelerated. The team is also collaborating with a commercial manufacturing partner to create inhalation formulations suitable for delivering the drug combination directly to the lungs for use in human clinical trials.

**More information:** Boon Chong Goh et al, Rifaximin potentiates clarithromycin against *Mycobacterium abscessus* in vitro and in zebrafish, *JAC-Antimicrobial Resistance* (2023). [DOI: 10.1093/jacamr/dlad052](#)

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