Mycobacterium abscessus is a non-tuberculous mycobacterium (NTM) that causes lung-related infections and is becoming increasingly resistant to clarithromycin, a key antibiotic for NTM treatments. SMART researchers from the Antimicrobial Resistance (AMR) Interdisciplinary Research Group (IRG) have discovered rifaximin as a clarithromycin potentiator that can increase clarithromycin sensitivity and improve bacterial killing against Mycobacterium abscessus.

This combination of rifaximin and clarithromycin showed efficacy both in vitro and in a zebrafish embryo infection model, and is promising to effectively treat lung-related infections caused by NTMs.

In collaboration with:

As clarithromycin is the only highly effective oral antibiotic for treating M. abscessus infections, the identification of compounds that are clarithromycin potentiators, such as rifaximin, can help address existing challenges faced in treating NTM infections.

The researchers are now preparing for preclinical studies to evaluate this drug combination against M. abscessus, and are 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.

Researchers performed cell-based phenotypic screening of a compound library (see figure above) against clarithromycin-resistant M. abscessus, and evaluated the toxicity and efficacy of the top compound in a zebrafish embryo infection model.

The study showed that rifaximin synergises with clarithromycin to reduce the load of M. abscessus in infected zebrafish. This builds on the strong synergy already observed in vitro between the two drugs, with clarithromycin's minimum inhibitory concentration (MIC) significantly lowered in the presence of rifaximin - meaning that rifaximin significantly reduces the amount of clarithromycin needed to inhibit and kill M. abscessus.