Identification of novel mutations associated with bedaquiline resistance in Mycobacterium marinum

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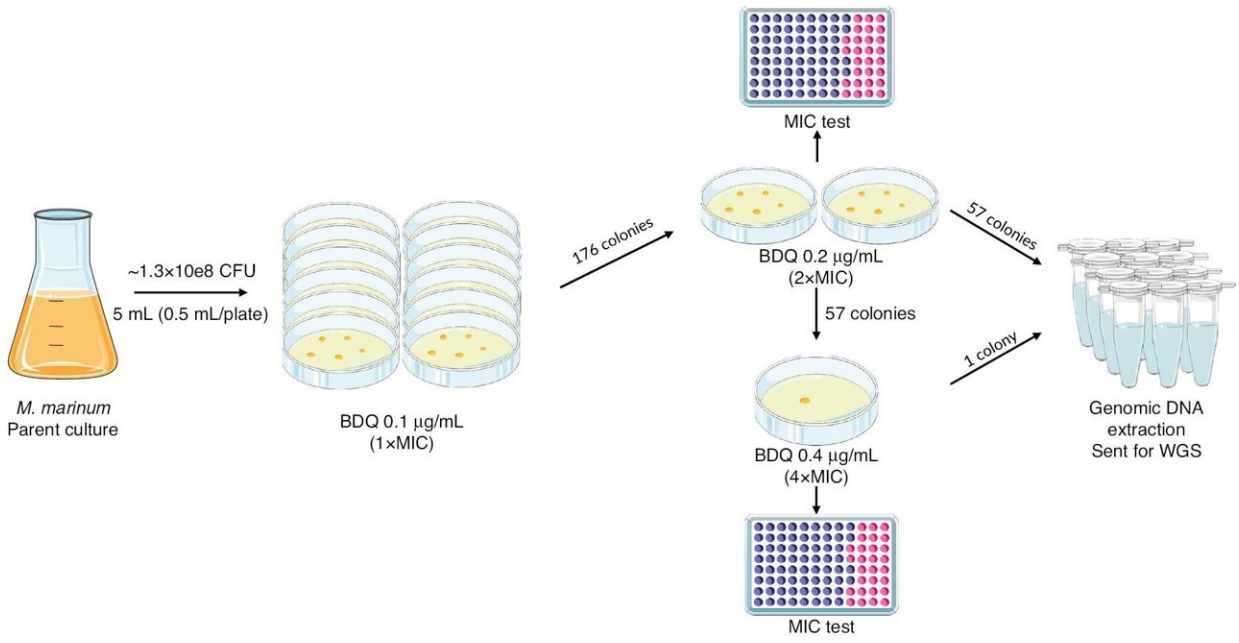

In vitro selection of bedaquiline-resistant isolates in M. marinum. Credit: *Zoonoses* (2023). DOI: 10.15212/ZOONOSES-2022-0042

As infections caused by nontuberculous mycobacteria (NTM) are rapidly increasing globally, a need exists for developing novel antibiotics and discovering the mechanism of resistance. New research reported in *Zoonoses* is aimed at understanding the mechanism of bedaquiline

resistance in the model NTM species Mycobacterium marinum (M. marinum).

The Mycobacterium marinum strain was subjected to mutant selection with different concentrations of BDQ. After three rounds of evolution, 58 BDQ-resistant mutants were isolated and subjected to WGS. The results were confirmed through PCR and Sanger sequencing.

Seven genetic mutations among these mutants were identified. The highest drug resistance (6–10× MIC) was associated with a mutation in AtpB, the primary biochemical target of BDQ in Mtb. Numerous mutations and insertions mapped to the gene MMAR_1007(46/58), which encodes the homolog of Rv0678 (MmpR) in Mtb. More than 93% of mutants (54/58) contained a single mutation (G563A) in MMAR_4049, which encodes the integral membrane protein YrbE3A-1.

Both target-based and efflux-based actions contribute to BDQ resistance in M. marinum. These findings may aid in developing novel potent anti-NTM (BDQ-based) drug regimens and diagnostic assays for the detection of BDQ-resistant M. marinum.

More information: Longlong Wang et al, Identification of Novel Mutations Associated with Bedaquiline Resistance in Mycobacterium Marinum, *Zoonoses* (2023). DOI: 10.15212/ZOONOSES-2022-0042