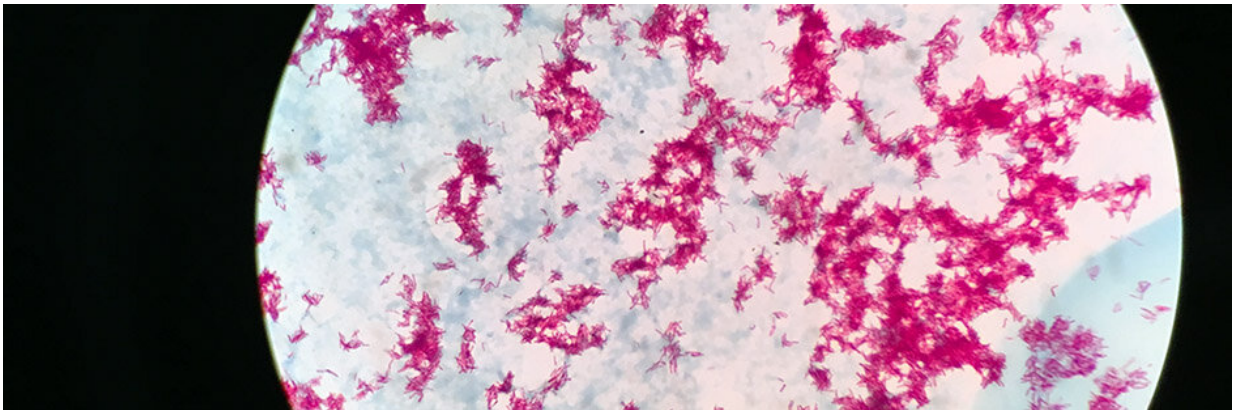# Researchers study resistance to 'protect' anti-TB drug

May 30 2019

Credit: Stellenbosch University

In July last year, South Africa became the first country to roll out a new anti-tuberculosis drug in its national programme.

This new drug, called bedaquiline, is the first new anti-tuberculosis drug to be developed in four decades. It improves the survival of patients with multidrug resistant TB, potentially offering a shorter treatment time with fewer side effects.

Scientists from Stellenbosch University (SU), in collaboration with a multidisciplinary team of researchers and clinicians, are now trying to conserve this life-saving treatment by studying how Mycobacterium

tuberculosis, the bacterium that causes TB, can develop resistance to this drug. Their findings will be used to inform tuberculosis treatment guidelines to ensure that the right combination of anti-tuberculosis drugs are used along with bedaquiline in order to optimise patient treatment outcomes, while minimising the risk of developing resistance to the drug.

"We need to protect bedaquiline from the development of resistance and therefore it is crucial to understand how quickly and through which mechanisms bedaquiline resistance develops," says Dr. Margaretha de Vos, one of the lead authors of a scientific commentary article recently published in the *New England Journal of Medicine*. The article is based on research by De Vos and colleagues at the Division of Molecular Biology and Human Genetics at SU's Faculty of Medicine and Health Sciences (FMHS).

SU researchers studied the development of bedaquiline resistance in TB bacteria in a 65-year-old patient from Cape Town using a combination of novel techniques. These included (1) whole-genome sequencing of the bacteria in patient samples taken throughout various stages of the disease, (2) targeted deep sequencing of Rv0678, a gene of the bacteria that is associated with bedaquiline resistance, and (3) culture-based drug susceptibility testing.

The study showed that resistance to bedaquiline emerged despite the patient adhering to the standard treatment regimen, which requires bedaquiline to be taken along with at least five antibiotic drugs which the bacterium does not resist.

"These results show that it is crucial to increase our efforts to monitor patients receiving bedaquiline and to develop new diagnostic tools to rapidly identify bedaquiline resistance. By rapidly identifying bedaquiline resistance, we will be able change treatment and thereby

prevent spread," says Rob Warren, distinguished professor in microbiology and co-author of the article.

Helen Cox, one of the senior co-authors of the study, suggests that "while it is important to monitor the emergence of resistance to new drugs such as bedaquiline, these data should not suggest that we restrict access to bedaquiline for the thousands of patients in South Africa who are in dire need of improved treatment for drug-resistant tuberculosis".

More information: Margaretha de Vos et al, Bedaquiline Microheteroresistance after Cessation of Tuberculosis Treatment, *New England Journal of Medicine* (2019). DOI: 10.1056/NEJMc1815121

Provided by Stellenbosch University South Africa