

# RESEARCH AREA I

# HIGHLIGHT

## 01 TITLE OF THE WORK

Compensatory evolution drives multidrug-resistant tuberculosis in Central Asia

## 02 SOME BACKGROUND

Multidrug-resistant tuberculosis (MDR-TB) is considered as public health crisis and entails a long-term treatment up to two years with severe side effects and low cure rates globally. Usually drug resistance goes along with a reduced bacterial fitness, e.g. lower growth rate and/or less tissue damage, thus the ability of MDR strains to cause outbreaks has been ignored for several decades.

## 03 WHAT DID SCIENTISTS DISCOVER?

By investigating whole bacterial genomes ("whole genome sequencing") from a Central Asian setting we traced the evolutionary history of a MDR outbreak in Central Asia. The clonal expansion started already in former Soviet times in the mid-1970s followed by acquisition of additional resistance mediating mutations and mutations that compensate a potential fitness loss. Importantly, we demonstrated that the recent success of these MDR outbreak strains coincided with the implementation of a new treatment program in 1998 (named DOTS) most likely in conjunction with the absence of appropriate drug resistance diagnostics during that time.

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**WHY IS IT IMPORTANT?**

The conditions leading to such a scenario, including inappropriate and delayed TB diagnosis, absence of comprehensive drug susceptibility testing, and interrupted drug supply are common to many high burden settings globally. Our findings emphasize the need for universal access to drug susceptibility testing, individualized patient-tailored therapies including also new and repurposed drugs in order to reduce the risk of resistance amplification and extended transmission of MDR strains.

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**WHO DID THE RESEARCH?**

Matthias Merker and Stefan Niemann from the EvoLung science campus in cooperation with 13 international scientists, please see details below

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**WHY DID THEY CHOOSE THE DESCRIBED METHODS?**

The combination of whole genome sequencing data and Bayesian statistics allows an unprecedented view on the pathogens' resistance and virulence traits and timing of past bacterial population expansions. Thus, historic events such as war, economic crisis or programmatic treatment changes can be interpreted with regard to their effect on an endemic pathogen population and the selection of antibiotic resistances.

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**DETAILS FOR SCIENTISTS – PUBLICATION**

Matthias Merker\*, Maxime Barbier\*, Helen Cox, Jean-Philippe Rasigade, Silke Feuerriegel, Thomas A. Kohl, Roland Diel, Sonia Borrell, Sebastien Gagneux, Vladyslav Nikolayevskyy, Sönke Andres, Ulrich Nübel, Philip Supply, Thierry Wirth, Stefan Niemann (2018)

Compensatory evolution drives multidrug-resistant tuberculosis in Central Asia

Elife, doi: 10.7554/eLife.38200

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