



Network for the Application of Sequencing Technologies for the Fight Against Resistant Tuberculosis in High Incidence Settings

SeqMDRTB_NET

Duration 2019 – 2021

Budget/year approx. 300,000 EUR

Partner countries

Eswatini Kyrgyzstan Moldova Mozambique Namibia



Challenges addressed by the project

Resistant, multi-resistant and extremely resistant tuberculosis (M/XDR-TB) represent an increasing threat to global TB control. The difficult-to-treat Tuberculosis (TB) forms are caused by bacteria from the Mycobacterium tuberculosis complex (Mtbc), which carry DNA mutations that mediate resistance against standard drugs. Successful treatment requires early diagnosis and resistance testing. However, due to lacking infrastructure, this is often not available in countries with a medium to high TB incidence. As a result, patients receive largely empirical treatment regimens with frequently low cure rates. New molecular methods such as Whole Genome Sequencing (WGS) or Targeted Sequencing can provide accurate and rapid information on the mutations that mediate drug-resistance in the bacterial genome.

SeqMDRTB_NET supports Kyrgyzstan in Central Asia, Moldova in Eastern Europe, and Eswatini, Mozambique and Namibia in Southern Africa in establishing DNA sequencing technology. Based on the results of molecular resistance testing, patients can be effectively treated at an early stage, increasing cure rates and minimizing the risk of (i) additional resistance development and (ii) transmission of M/XDR strains.

Objectives

- » Technology transfer
- » Personnel and organizational development through further training measures
- » Establishment of a competence network
- » Integration of new technologies into the local health system

Overview of activities

To begin with, DNA sequencing technology is established in the partner country and employees are trained on-site. This technology transfer is made possible by an expert team assembled at the Research Center Borstel – Leibniz Lung Center (FZB) to conduct method-specific training courses in the partner countries. It enables the local staff to carry out molecular biological analyses independently and to evaluate the results obtained. The performance of these established methods is evaluated through targeted studies. The knowledge gained through this technology transfer ultimately helps to optimize the established DNA sequencing methods and to integrate them into the national TB strategy. Besides, competence networks are established to provide a platform for discussing results and exchanging individual challenges.

The overriding goal is to integrate modern sequencing technology into the standard diagnostic procedures of the partner countries in the long term and, thus to improve the diagnosis and treatment of M/XDR-TB patients.

on the basis of a decision by the German Bundestag



Development of the project activities by lab technicians, microbiologists, and researchers from the "National Institute of Health", Mozambique



Development of the project activities by lab technicians, microbiologists, and researchers from the University of Namibia, Namibia



Development of the project activities by lab technicians, microbiologists, and researchers from the National Reference Laboratory of Tuberculosis, Kyrgyzstan



Preparation of a sample for SARS-CoV-2 diagnostics, Kyrgyzstan

The ongoing global pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had an unfavorable impact on the development of this project: travel restrictions preclude in-person workshops, local partners have been deployed to support their national COVID management, and disrupted supply chains have led to shortages of laboratory consumables. These impacts may be exacerbated if the emergence of new variants of SARS-CoV-2 are not detected and controlled in a timely manner. Therefore, we have expanded the SeqMDRTB_NET project beyond the original goal of implementing next-generation sequencing (NGS) for MTB complex strains in partner countries, by also supporting the use of these technologies for the elucidation of SARS-CoV-2 variants. Viral RNA can be isolated from patient samples, and NGS can be used to sequence the SARS-CoV-2 genome, then identify potential variants. Our objective is to enable our partners to quickly and easily identify the so-called "variants of concern" (voc) of SARS-CoV-2. We are supporting our partners in Kyrgyzstan, Mozambique, and Namibia to conduct SARS-CoV-2 WGS.

Partner institutions

- » Eswatini Ministry of Health, Eswatini
- » Baylor Children's Foundation, Eswatini
- » The Ospedale San Raffaele: The San Raffaele Hospital (OSR), Italy¹
- » The National Tuberculosis Center under the Ministry of Health of the Kyrgyz Republic, Kyrgyzstan²
- » The National Institute of Health, Mozambique³
- » Institute of Phthisiopneumology "Chiril Draganiuc", Republic of Moldova⁴
- » School of Medicine University of Namibia, Namibia⁵
- » Institute for Microbiology and Laboratory Diagnostics (IML), Germany⁶
- » The National Reference Laboratory for Mycobacteria and the WHO Supranational TB Reference Laboratory, Germany⁷

Supporting institution in Germany/Contact

Research Center Borstel – Leibniz Lung Center Research Group Molecular and Experimental Mycobacteriology Prof Stefan Niemann <u>sniemann@fz-borstel.de</u> www.fz-borstel.de

- 1 OSR is a university hospital in Milan. The WHO "Collaborating Centre ITA98 for laboratory strengthening for tuberculosis diagnosis" and the WHO Supranational TB Laboratory are located here. OSR has many years of experience in setting up laboratory capacities in Africa.
- 2 The National TB Center is the central coordinating and controlling body of the National TB Programme in Kyrgyzstan. A modern TB laboratory is located here, which was built with funding from the Federal Republic of Germany and planned by the SeqMDRTB_NET project partner IML-Gauting.
- 3 The institute is a technical and scientific institution of the Ministry of Health of Mozambique. It has a mandate to carry out health-related research and set up national management programmes.
- 4 The institute is the central institute for the fight against TB in the Republic of Moldova.
- 5 The School of Medicine was founded in 2009. For several years the University of Namibia (UNAM) and FZB have been successfully cooperating in the field of TB. A sequencing laboratory was set up here with German support.
- 6 The institute is a WHO supranational TB reference laboratory and is responsible for establishing TB laboratory capacities in Central Asian countries.
- 7 These laboratories are located at the Research Center Borstel Leibniz Lung Center in Borstel (FZB). Here, the research group for Molecular and Experimental Mycobacteriology and the Medical Clinic hold many years of experience in the field of molecular genotyping (WGS) and clinical implementation of next generation sequencing (NGS) -based resistance testing.