

Genomic insights into the mechanisms of drug resistance, virulence and transmission of *Mycobacterium tuberculosis* strains from Lithuania and Poland

POPULAR SCIENCE ABSTRACT

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* bacteria, persists as a significant health problem for the entire human population. Every year, about 10 million people develop TB, and nearly 2 million die from the disease. In fact, TB ranks first as the leading cause of mortality due to infectious diseases. The burden of TB has been exacerbated by the emergence and spread of drug-resistant (DR), and more importantly multidrug-resistant (MDR), extensively drug-resistant (XDR), and totally drug-resistant (TDR) *M. tuberculosis* strains, unresponsive to most or virtually all anti-TB drugs available. Eastern Europe, including Russia, Belarus, and the Baltic states have been reported as 'hot spots' of DR-TB. Poland and Lithuania are two neighboring countries, which together with Latvia and Estonia form an eastern flank of the European Union, and thus are particularly exposed to migration and refugee flows from outside the Union, posing a potential epidemiological hazard. The geographical context which locates Lithuania and Poland at the frontline for intercepting the transmission of DR-TB from the East urge for installation of more stringent control measures in the two countries. This in turn requires more reliable, efficient, and faster diagnostic and therapeutic modalities.

With the advent of molecular biology tools, a wide array of genotyping methods have been developed, facilitating the identification of tubercle bacilli, detection of drug resistance, and delineation of TB transmission routes and sources. However, large-scale, nation-wide molecular epidemiological studies, using robust and sound methodologies, have only sporadically been performed in central or eastern European countries. Even fewer studies have investigated TB transmission using whole genome sequencing (WGS), which has recently emerged as a powerful tool to map, most thoroughly and accurately, genetic diversities among bacterial pathogens, including *M. tuberculosis*. Such studies are importantly missing in Central and Eastern Europe.

This project was conceived with the aim of providing a comprehensive picture of the genetic structure of *M. tuberculosis* populations circulating in Lithuania and Poland. For the first time, phylogenetic and evolutionary links between the *M. tuberculosis* genotypes found in the two countries will be disclosed, domestic and cross-border TB transmission events will be ascertained, and the usefulness of WGS for carrying out epidemiological investigations and for rapid diagnosis of drug resistance (and other phenotypic traits) will be evaluated.

The project will operate on prospectively and retrospectively collected *M. tuberculosis* strains isolated from Lithuanian and Polish pulmonary TB patients. The strains will be subjected to extensive molecular typing, including high-throughput WGS approach, and the results will be interpreted in the context of the clinical and epidemiological data.

The completion of the project not only will expand the knowledge on the diversity and complexity of *M. tuberculosis* genomes, but will also guide the refinement of the existing diagnostic tools or the development of alternative algorithms allowing for faster and more accurate detection of drug resistance, and other clinically-related characteristics (virulence, infectivity, transmissibility, etc.). All this will make a valuable contribution to the global fight against TB.