# Global team aim for faster, more effective TB diagnosis

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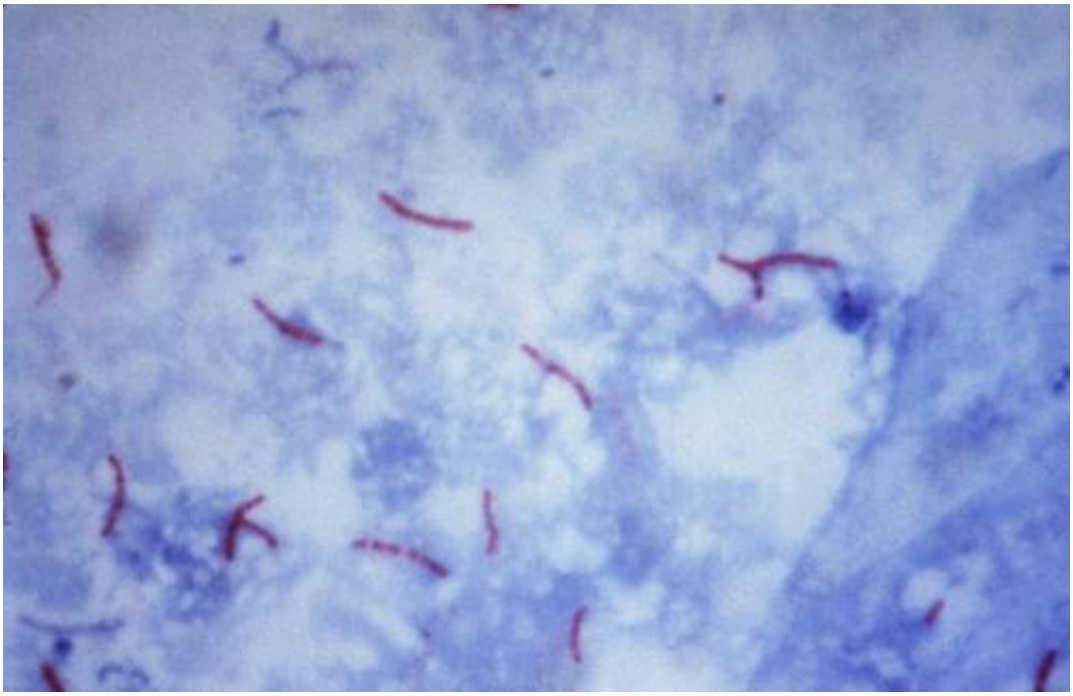

This photomicrograph reveals Mycobacterium tuberculosis bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000 X. The acid-fast stains depend on the ability of mycobacteria to retain dye when treated with mineral acid or an acid-alcohol solution such as the Ziehl-Neelsen, or the Kinyoun stains that are carbolfuchsin methods specific for M. tuberculosis. Credit: public domain

As World TB day (24 March) marks global efforts to eliminate tuberculosis as a public health problem by 2035, Oxford University researchers, in partnership with Public Health England (PHE), will lead a

new worldwide collaboration called CRyPTIC to speed up diagnosis of the disease.

TB infects nearly 10 million people each year and kills 1.5 million, making it one of the leading causes of death worldwide. Almost half a million people each year develop multidrug-resistant TB (MDR-TB), which defies common TB treatments. Time consuming tests must be run to determine whether a patient has MDR-TB, and if so, which drugs will work or fail. This delays diagnosis and creates uncertainty about the best drugs to prescribe to individual patients.

A potential alternative to help with faster identification of drug-resistant TB is to use whole genome sequencing (WGS) to determine the genetic code of the TB bacterium. This genetic code can be compared against a library of other TB bacteria with known drug-resistance. Identifying whether the genes that give resistance to particular drugs in the library are also present in the samples allows clinicians to make the correct treatment choice in the most complex cases.

Professor Derrick Crook leads Oxford's Modernising Medical Microbiology team and is also the Director of National Infection Service at PHE. He said: 'We have carried out a range of studies using thousands of clinical samples, that show WGS could work for diagnosing drug-resistant TB, ranging from pure research to the practicalities of implementing tests in a public health laboratory. The key is that you need to know which genetic mutations cause drug resistance - it turns out there are a host of rare mutations which are the culprits, and so we have assembled a consortium to collect a large number samples from across the world, and both measure their drug resistance and decode their genomes.'

Now, with a $2.2m (£1.53m) grant from the Bill & Melinda Gates Foundation and a £4m ($5.75m) grant from the Wellcome Trust and

MRC Newton Fund, the Oxford team aims to build that library of TB genes. Their initial study, in partnership with University of Leeds, Brighton and Sussex University Hospitals NHS Trust and PHE Birmingham, sequenced 3651 TB genomes. The CRyPTIC study aims to collect and analyse a further 100,000 samples from across the world, providing a database of MDR-TB that will underpin diagnosis using WGS.

Samples from across Africa, Asia, Europe and the Americas will be collected by teams at more than a dozen centres They will conduct drug resistance testing and much of the genome sequencing. The Oxford team will then assemble these results into a single open-access database, which will be used to identify genes associated with resistance to certain treatments. The team will also work on developing artificial intelligence that can predict drug resistance.

Ana Gibertoni Cruz, a Clinical Research Fellow working on the project said: 'The programme will take around five years but when complete it will give us the baseline we need for quick effective TB diagnosis using whole genome sequencing. Faster results will mean not just faster treatment, but the right treatment, potentially saving lives and avoiding further transmission.'

Provided by University of Oxford