Global Health Partners Accelerate Uptake of Genetic Sequencing for Surveillance And Diagnosis Of Drug-Resistant Tuberculosis

- **WHO adopts ReSeqTB as bioinformatics platform for TB surveillance, enabling the global scale-up of culture-free, drug-resistant *Mycobacterium tuberculosis* surveillance programs based on sequencing technologies**
- **Renewed funding from the Bill & Melinda Gates Foundation has been applied for to support FIND, C-Path, and WHO to take ReSeqTB to the next level as part of the WHO Sequencing-based TB Drug-Resistance Surveillance Programme**

Geneva, Switzerland; Tucson, AZ; Seattle, WA – 24 March 2018 – The World Health Organization (WHO), the Foundation for Innovative New Diagnostics (FIND), and the Critical Path Institute (C-Path), announced today that the Relational Sequencing TB Data Platform (ReSeqTB), a global TB knowledge base for predicting TB drug resistance, will be adopted as the WHO bioinformatics platform for surveillance of drug-resistant TB (DR-TB). The development of ReSeqTB has been supported by the Bill & Melinda Gates Foundation, and renewed funding has been applied for to support integration into the WHO Sequencing-based TB Drug Resistance Surveillance Programme[1]. The platform will also serve as a resource for the development of global policies on new TB diagnostics and will ultimately support clinical management of DR-TB.

TB is the world's deadliest infectious disease. In 2016 alone, 10.4 million people fell ill with TB, and 1.7 million died from the disease.[2] TB is the major cause of deaths related to antimicrobial resistance, claiming 240,000 lives in 2016. Furthermore, of the 600,000 new DR-TB cases, 74% went undiagnosed. The spread of DR-TB is a major public health crisis, exacerbated by the lack of rapid, accurate diagnostic tests for comprehensive drug resistance testing.

ReSeqTB serves a diverse TB community to rapidly evaluate phenotypic antimicrobial resistance from raw sequence data from *Mycobacterium tuberculosis* (Mtb) in clinical samples – enabling large-scale, culture-free surveillance of TB drug resistance and informing development of new diagnostics and treatment regimens. It is designed to capture, analyze, and report in-country data on mutations associated with TB drug resistance based on an expert-graded mutations list.[3] In addition, the new ReSeqTB website (www.reseqtb.org) now offers open access to the public data stored in the platform.

In this new project phase, ReSeqTB will support surveillance and global policy development for sequencing-

based clinical diagnosis of DR-TB. It could also serve as a model for the broader goals of establishing global antimicrobial resistance surveillance and clinical diagnosis networks for WHO high-priority pathogens.

“Genetic sequencing is the future of surveillance and diagnosis of DR-TB,” said Dr Tereza Kasaeva, Director of the WHO Global TB Programme. “With ReSeqTB, sequencing can be used to rapidly and accurately estimate prevalence of resistance to anti-TB drugs. This platform has the potential to expand our understanding of the genetic basis of drug resistance and open the way for the use of sequencing for effective clinical management of patients with DR-TB, saving millions of lives.”

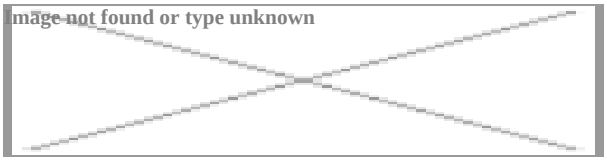
“ReSeqTB is actively collecting, standardizing, and aggregating genomic, phenotypic and, when available, clinical data to support the development of global policy for use of sequencing-based diagnostics in high-burden settings” said Dr. Debra Hanna, Executive Director of C-Path’s Critical Path to TB Drug Regimens (CPTR) initiative. “Together with our partners, we are working with the US FDA to pursue regulatory clearance of ReSeqTB to support patient management decisions.”

ReSeqTB is changing the DR-TB landscape. “ReSeqTB is already informing the development of commercial TB molecular diagnostic solutions, and the confidence-graded mutations list is becoming a standard for interpretation of existing and future molecular diagnostics,” said Dr Catharina Boehme, CEO of FIND. “Building genetic sequencing into global diagnostics policy is an exciting advance. Enhanced diagnostics mean that patients can get a diagnosis earlier, which means they can access the right treatment more quickly – and the transmission of DR-TB is curtailed.”

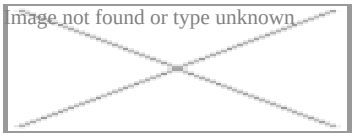
Future funding sources are being sought for the continued evolution of the ReSeqTB knowledge base, in line with the needs of patients, global policy makers, National TB Programme implementers, laboratories, TB practitioners, researchers, and diagnostics and pharmaceutical industry developers.

Extensive contributions to ReSeqTB have been made by several partner organizations, including the Stop TB Partnership’s New Diagnostics Working Group, the US National Institute of Allergy and Infectious Diseases, and the US Centers for Disease Control and Prevention. ReSeqTB is supported by funding from the Bill & Melinda Gates Foundation.

About the organizations:

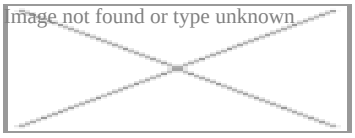


The Relational Sequencing TB Data Platform (ReSeqTB) is a joint initiative of the Critical Path Institute’s Critical Path to TB Drug Regimens (CPTR) initiative, FIND, the World Health Organization, the Stop TB Partnership’s New Diagnostics Working Group, and the US Centers for Disease Control and Prevention, with contributions from several partner organizations and funding from the Bill & Melinda Gates Foundation. As a data-sharing platform and analytic visualization tool, ReSeqTB can be used to discover, grade, and track key bacterial drug resistance mutations. The resource facilitates the development of new diagnostics capable of rapidly testing drug susceptibility, which could be used to identify effective treatment regimens for better managing patients with drug-resistant TB.



The World Health Organization (WHO) is the directing and coordinating authority for health within the United Nations system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries, and monitoring and assessing health trends.

The Global TB Programme at WHO guides global action for a world free of TB by advancing universal access to TB prevention, care, and control; framing the response to threats through norms, standards, and strategy; technically supporting Member States; monitoring the burden and response; and promoting innovation.



FIND was established in 2003 as a global nonprofit dedicated to accelerating the development, evaluation, and delivery of high-quality, affordable diagnostic tests for poverty-related diseases, now including malaria, tuberculosis, HIV/AIDS, sleeping sickness, hepatitis C, leishmaniasis, Chagas disease, Buruli ulcer, non-malarial fever, and diseases with outbreak potential, such as Ebola. FIND has partnered in the delivery of 20 new diagnostic tools and created an enabling environment for numerous others through the provision of specimen banks, reagent development, and better market visibility. FIND also supports better access to new diagnostics through implementation, quality assurance, and lab strengthening work. FIND has nearly 200 partners globally, including research institutes and laboratories, health ministries and national disease control programmes, commercial partners, bilateral and multilateral organizations, especially WHO, and clinical trial sites. For further information, please visit www.finddx.org

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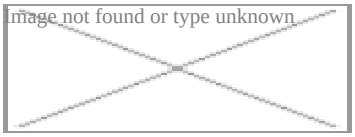
CRITICAL PATH INSTITUTE

Critical Path Institute (C-Path) is an independent, nonprofit organization established in 2005 with public and private philanthropic support from the Arizona community, Science Foundation Arizona, and the US Food and Drug Administration (FDA). C-Path's mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world. An international leader in forming collaborations, C-Path has established numerous global, public-private partnerships that currently include over 1,450 scientists from government and regulatory agencies, academia,

patient advocacy organizations, and dozens of major pharmaceutical companies. C-Path is headquartered in Tucson, Arizona. For more information, visit www.c-path.org.

CPTR (Critical Path to TB Drug Regimens) is an initiative that aims to speed the development of new and markedly improved drug regimens for tuberculosis (TB). This partnership brings together the world's leading pharmaceutical and other drug developers, global regulatory agencies, and civil society organizations to support advances in regulatory science, the development of infrastructure, and other progress needed to facilitate the development and availability of new TB drug treatments. Co-founded by the Bill & Melinda Gates Foundation, the Critical Path Institute, and the TB Alliance, and launched in March 2010, CPTR is working with stakeholders around the world to advance a new paradigm that dramatically speeds new TB drug regimens to patients.



Guided by the belief that every life has equal value, the **Bill & Melinda Gates Foundation** works to help all people lead healthy, productive lives. In developing countries, it focuses on improving people's health and giving them the chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people—especially those with the fewest resources—have access to the opportunities they need to succeed in school and life. Based in Seattle, Washington, the foundation is led by CEO Sue Desmond-Hellmann and Co-chair William H. Gates Sr., under the direction of Bill and Melinda Gates and Warren Buffett. www.gatesfoundation.org

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[1] Zignol M, *et al*. Genetic sequencing for surveillance of drug resistance in tuberculosis in highly endemic countries: a multi-country population-based

study. *Lancet Infect Dis* 2018; Published online March 21. Available at: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30073-2/fulltext
[2] *WHO Global Tuberculosis Report 2017*. Available at: http://apps.who.int/iris/bitstream/10665/259366/1/9789241565516-eng.pdf?ua=1
[3] Miotto P, *et al*. A standardised method for interpreting the association between mutations and phenotypic drug resistance in Mycobacterium tuberculosis. *Eur Resp J* 2017;50:1701354. Available at: http://erj.ersjournals.com/content/50/6/1701354