ReSeqTB
Relational Sequencing TB Data Platform

The Need

Rapid drug susceptibility tests (RDSTs) are needed to improve the management of tuberculosis (TB) patients, to facilitate drug development and rational use of new TB drug regimens, and to better understand the global burden of drug-resistant TB. The field has recognized the need for a data-sharing platform that provides a one-stop data source for clinically relevant genotypic and phenotypic information on *Mycobacterium tuberculosis* (MTB). Having such data reviewed and validated, and made accessible in one place, would support the development of new RDSTs that can quickly inform appropriate therapy for TB patients. A comprehensive, curated, and easy-to-use data platform of this scope does not currently exist and is a major barrier to the understanding of the relationship between genetic mutations and drug resistance in MTB. This barrier impacts drug and diagnostic developers, clinicians prescribing therapy, and ultimately patients who should have earlier access to appropriate drug regimens. Successful execution of such an extensive database platform requires substantial collaboration from scientists investigating the genetic basis for drug resistance worldwide, and from developers with expertise in database design and implementation. This would ensure quality security, while providing assurance that all relevant legal, patient data privacy, and intellectual property standards are met.
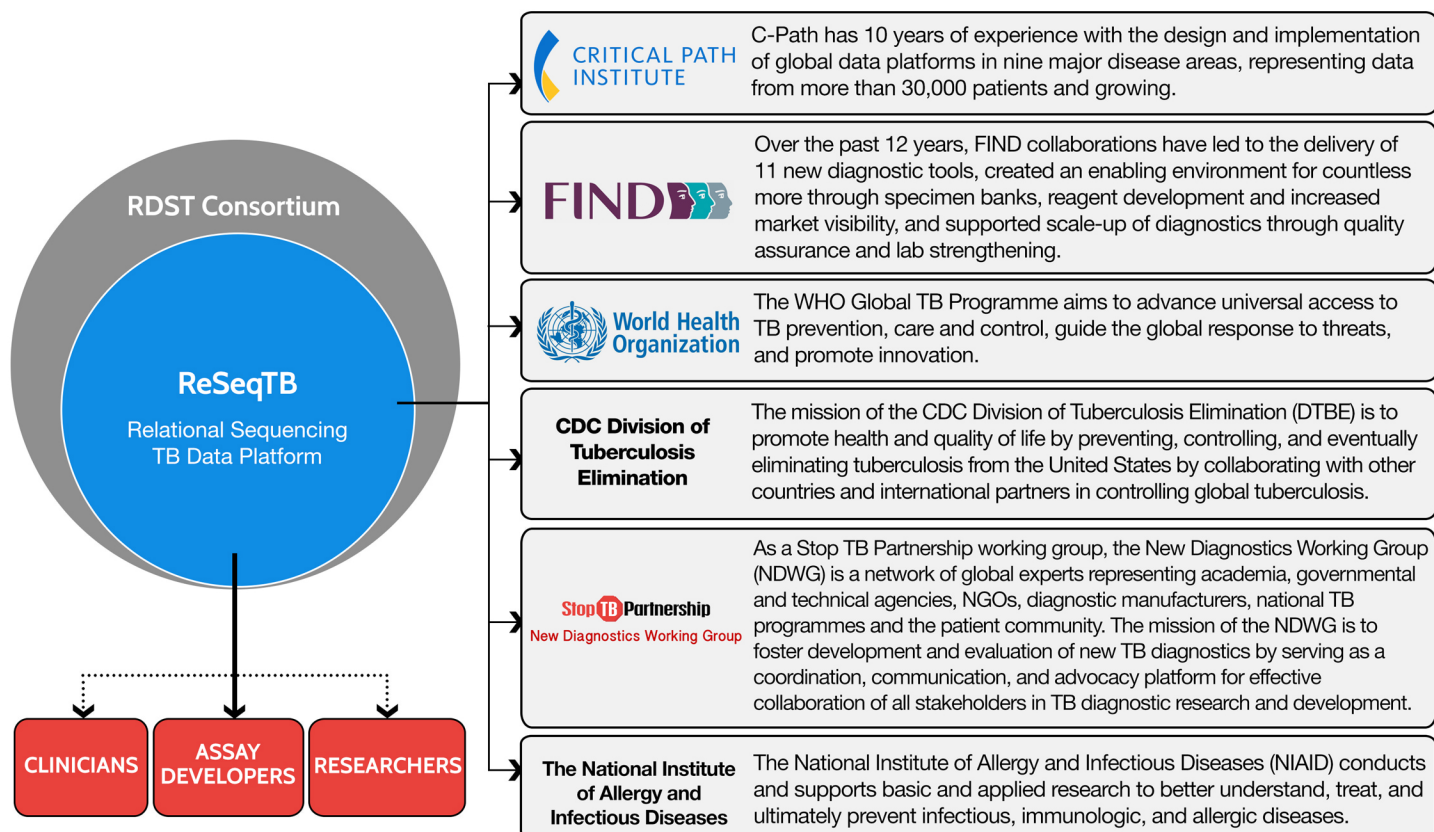
The Opportunity

With two new drugs recently approved (Bedaquiline and Delamanid), and drugs being used in TB treatment regimens despite having no TB label claims (Linezolid and Clofazamine), clinical trials are underway to test new combinations of these and other existing drugs that may prove more safe and effective, which in return may allow for shorter treatment duration. If these new treatment regimens prove to be superior to the standard of care, they will be widely adopted by global public health care programs and will require improved and novel RDSTs in order to effectively implement them. The inclusion of new drugs could potentially unify treatment for patients with drug-susceptible infections, as well as for an increasing number of patients who are infected with drug-resistant strains of MTB, or who develop drug resistance during therapy. However, treatment without identifying drug susceptibility runs the risk of employing suboptimal drug regimens with fewer effective drugs. As a small number of TB isolates may be naturally resistant, these new drug regimens may exert selection pressure that could promote transmission of drug-resistant strains. Therefore, vigilance is required to quickly identify patients who harbor drug-resistant TB, map the trajectory of drug resistance in the population, and develop alternatives to ensure the new drug armaments remain effective.

Evolution of Project

Currently, the correlation between MTB genotypic data and TB drug resistance is widely dispersed among multiple MTB sequence databases, both private and public. Meta-analysis of these divergent published data sets has highlighted gaps and discrepancies in our knowledge, as well as bias that may be present because geographic strain diversity is not well represented. These findings highlight the need of a universally harmonized database platform that is widely accessible and user-friendly. With sufficient numbers of globally-derived MTB whole genome sequences, such a statistically powered database platform could robustly facilitate the clinical interpretation of different genetic polymorphisms. Test developers could then rely on such clinically validated genome sequence interpretations and confidently accelerate development of RDSTs for both current and newly emerging TB drugs and drug regimens. To get there, however, thousands of genomic sequences subject to robust quality checks will need to be sourced from multiple global researchers to account for strain variation. In addition, data sets will need to be curated to provide the highest possible confidence in clinical interpretation to support assessment and informed decision making. The ReSeqTB database platform will serve as a single globally harmonized repository for the compilation, curation, and validation of existing and newly created data on TB drug resistance correlations.

Our Collaborative Partnership

RDST Consortium

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CLINICIANS   ASSAY DEVELOPERS   RESEARCHERS

CRITICAL PATH INSTITUTE
C-Path has 10 years of experience with the design and implementation of global data platforms in nine major disease areas, representing data from more than 30,000 patients and growing.

FIND
Over the past 12 years, FIND collaborations have led to the delivery of 11 new diagnostic tools, created an enabling environment for countless more through specimen banks, reagent development and increased market visibility, and supported scale-up of diagnostics through quality assurance and lab strengthening.

World Health Organization
The WHO Global TB Programme aims to advance universal access to TB prevention, care and control, guide the global response to threats, and promote innovation.

CDC Division of Tuberculosis Elimination
The mission of the CDC Division of Tuberculosis Elimination (DTBE) is to promote health and quality of life by preventing, controlling, and eventually eliminating tuberculosis from the United States by collaborating with other countries and international partners in controlling global tuberculosis.

Stop TB Partnership
New Diagnostics Working Group
As a Stop TB Partnership working group, the New Diagnostics Working Group (NDWG) is a network of global experts representing academia, governmental and technical agencies, NGOs, diagnostic manufacturers, national TB programmes and the patient community. The mission of the NDWG is to foster development and evaluation of new TB diagnostics by serving as a coordination, communication, and advocacy platform for effective collaboration of all stakeholders in TB diagnostic research and development.

The National Institute of Allergy and Infectious Diseases
The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases.

Critical Path Institute
Dr. Debra Hanna
dhanna@c-path.org
(520) 382-1406

FIND
Dr. Claudia Denkinger
claudia.denkinger@finddx.org
+41 22 749-2931

New Diagnostics Working Group
Dr. Daniela Cirillo
cirillo.daniela@hsr.it
+39 02 2643-794

CRITICAL PATH INSTITUTE   FIND   Critical Path to TB Drug Regimens   World Health Organization   Stop TB Partnership New Diagnostics Working Group