

About the specimen bank

FIND has had an established, high-quality biorepository for TB since 2006, with over 80,000 samples from patients in endemic countries. Providing access to these specimens serves to support the development and evaluation of new and existing tools to improve TB diagnosis. Sample types range from sputum to urine, plasma and serum. Specific sample types, such as P800, are available as well. Since 2015, FIND has added strains from MDR-TB and pre-XDR-TB patients.

All specimens are collected at qualified clinics, under a protocol approved by an Institutional Review Board and with informed consent from patients meeting the inclusion criteria for sample collection. FIND follows good clinical and laboratory practice in obtaining and processing samples.

Distribution of specimens

The FIND TB Specimen Bank dispatched 18 shipments to test developers between Q4 2016 and Q3 2017. A total number of 3,355 aliquots were granted. See table below for details.

Summary of requests and aliquots granted

Period	Requests approved	# of requestors	Sputum	Serum	Plasma	Strain DNA	Urine	Total
Q4 2016	4	5	430	160	450		119	1159
Q1-Q3 2017	14	14	846	520	90	400	340	2196
Total	18	19	1276	680	540	400	459	3355

Inventory

The FIND repository currently holds 88,543 aliquots from collection sites in Bangladesh, Brazil, Georgia, Moldova, Peru, South Africa, Uganda, Viet Nam and Zimbabwe. FIND also manages the WHO-TDR TB collection, which includes 27,570 aliquots from Spain, Gambia, El Salvador, Peru, South Africa, Tanzania, Uganda, Viet Nam, Canada, Bangladesh, Brazil, Colombia and Kenya.

New collections

Specimens in the **monitoring collection** are collected over a 12-month period, and must fulfill a very stringent set of inclusion criteria. A total of 389 patients have enrolled from five sites in South America, Sub-Saharan Africa, East Asia and Eastern Europe. By the end of 2018, all patients will have completed follow up.

In response to multiple requests from TB test developers, FIND has started a collection of **peripheral blood mononuclear cells (PBMC)** at our collaborating site in Peru. In 2017, we collected 173 aliquots from 97 subjects suspected of having TB.

Virtual Strain Bank

The Virtual Strain Bank (VSB) is an online database that allows researchers and test developers to have an overview of globally accessible TB strains. The VSB aims to support and facilitate collaboration between researchers and developers to further TB diagnostic development. Registration for the VSB is free of charge and the database is easily searchable. Strains can be filtered and selected based on criteria such as country, clade, drug resistance, drug sensitivity, mutations and sequencing data availability. Currently, the VSB contains the relevant meta-data for 409 strains in the FIND specimen bank, and by the end of 2018, 800 strains will be available. Users are encouraged to examine the existing strain data from FIND and partners, upload their own strain data and connect with FIND or partners through the VSB to request strains.

Summary of activities

FIND collection at ZeptoMetrix, USA

Diagnostic category	Patients	Sputum	Serum	Plasma	P800	Urine	Total
Non TB	757	1,806	1,790	1,779	2,067	1,683	9,882
Smear-neg, cult-neg, CXR-pos	446	515	1,895	454	176	243	3,729
Smear-neg, cult-pos	739	1,401	5,547	1,215	925	2,349	12,176
Smear-pos, cult-pos	2,543	5,997	15,843	2,633	2,088	5,044	34,148
Undefined	2,694	4,258	9,478	7,627	2,239	2,312	28,608
Total	7,179	13,977	34,553	13,708	7,495	11,631	88,543

WHO-TDR collection at Biobanque de Picardie, FR

Diagnostic category	Patients	Sputum	Serum	Urine	Total
Smear-pos, cult-pos (WHO Cat. 1)	690	748	10,318	688	11,754
Smear-neg, cult-pos (WHO Cat. 2)	92	190	1,410	203	1,803
Smear-neg, cult-neg, CXR-pos (WHO Cat. 3)	66	163	1,124	163	1,450
Non-TB (WHO Cat. 4)	148	8	1,920	166	2,094
Total	996	1,109	14,772	1,220	17,101

WHO-TDR collection at ZeptoMetrix, USA

Diagnostic category	Patients	Sputum	Serum	Urine	Saliva	Total
Smear-pos, cult-pos (WHO Cat. 1)	602	671	3,359	439	677	5,146
Smear-neg, cult-pos (WHO Cat. 2)	62	9	387	78	66	540
Smear-neg, cult-neg, CXR-pos (WHO Cat. 3)	24	13	55	29	24	121
Non-TB (WHO Cat. 4)	498	1,337	1,487	1,734	104	4,662
Total	1,186	2,030	5,288	2,280	871	10,469

Summary inventory by selected countries/Aliquot types

Country	Patients	Total aliquots	Serum	Sputum	Plasma (EDTA)	Plasma (P800)	Saliva	Urine
Bangladesh	282	4,666	0.5 ml	0.5 ml	0.5 ml	0.5 ml	0.5 ml	1.5 ml or 3.5 ml
Brazil	322	4,028						
Peru	2,122	19,480						
South Africa	1,534	19,719						
Uganda	426	2,465						
Viet Nam	3,418	45,208						

Strains/DNA isolates and matching specimens

Specimens from MDR/XDR-TB patients are collected from globally representative sites in South America, South East Asia, Africa and Eastern Europe. These include sputum, plasma, serum and PAXgene tubes. Strains are characterized by whole genome sequencing and phenotypic testing against first- and second-line drugs and the minimum inhibitory concentration. Approximately 800 strains and DNA isolates are currently available in FIND's specimen bank.

Quality control

FIND has developed and implemented a quality assurance programme to ensure the highest quality of collected specimens. Starting in 2016, FIND has captured and analyzed pre-analytical parameters related to the collection, processing, handling and storage of specimens to minimize their impact on the results of validation studies. FIND conducts quality checks regularly and continues to re-test the representative number of specimens from each site at the independent partner laboratory.

The Developers' Toolset

In collaboration with ZeptoMetrix, FIND is developing a toolset for developers to support the evaluation of new diagnostic tests for TB. As the first component in this toolset, five inactivated, well-characterized strains of MTBC are now available as reference materials. Individual panel strains are inactivated and stable at 2-8°C, allowing developers to use biosafety level II facilities. Each panel comes with homogenized sputa collected from non-TB patients that can be used as a matrix.

FINDings

FINDings is a support service that provides an independent report based on the data that is generated through the use of specimens distributed by FIND. The data is submitted to FIND through a standardized reporting spreadsheet submitted by developers, and FIND performs an independent analysis to show the diagnostic accuracy of a new test or biomarker. This analysis is based on the performance targets set by target product profiles (TPPs). The FINDings report that is produced allows innovators to better understand the performance and development status of their technology. This service enables data-driven decision-making, optimizing R&D efforts and maximizing the impact of funding.

Q4 2016 - Q3 2017 requests approved and specimens distributed

Organization	Aliquots requested	Purpose	Aliquots granted
Cornell University	450 plasma	Cross-cutting evaluation of cell-free DNA	450 plasma
Wayne State University	200 serum	Classifiers to discriminate active and latent TB using T7 phage display library	160 serum
FIND	120 sputum	Truenat MTB and RIF-RCA	120 sputum
McGill University Health Centre	150 serum	A novel serum panel to rule out active tuberculosis	150 serum
Beth Israel Deaconess Medical Center	210 urine	Glycan microarray from <i>Mtb</i> urine LAM fraction	pending 210 urine
Quanterix	50 serum	LAM as a biomarker in blood	50 serum
Aiken Biosciences, Inc.	100 sputum	Ultrasensitive and Rapid Detection of <i>Mtb</i>	30 sputum
Stanford University	500 plasma	Evaluation of a novel blood test for diagnosis of TB	90 plasma
QuantuMDx	40 sputum	A low-cost molecular disposable device for TB diagnostics	50 sputum
Cepheid	90 sputum	Xpert MTB/RIF Enzyme Vendor Evaluation	90 sputum
The Biodesign Institute, ASU	430 serum and urine	Quantification of circulation MTB antigen peptides for rapid diagnosis	220 serum
ViaPath, King's College Hosp.	4 culture isolates	Development of a sensitive molecular test to detect MTB resistant strains	0
Genoscreen	400 strain DNA	Evaluation of the Deeplex-MycTB assay	400 strain DNA
QuantuMDx	400 sputum	A low-cost molecular disposable device for TB diagnostics	400 sputum
University of Washington	150 sputum	Ultra-sensitive diagnosis of paucibacillary TB	186 sputum
Omunis	320 serum	Evaluation of an innovative transportable serologic test for tuberculosis	100 serum
Fujifilm Corporation	119 urine	GHIT-Fujifilm-FIND LAM Project	119 urine
Salus Discovery	120 urine	Rapid diagnostic test for LAM in urine from patients with active TB disease	130 urine
Bigtec Private Limited	100 sputum	Demonstration of equivalent of RIF assay on two platforms	400 sputum