

# GENOTYPING 101

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# Objectives

- Describe overall purpose of genotyping in a TB program
- Demonstrate examples of GENType results
- Communicate “Best Practices” per CDC guidelines

## TB Program Genotyping Objective

To reduce TB in Texas by identifying recent TB transmission among cases and contacts using genotyping.

# Overview

- Genotyping: Lab approach used to analyze genetic material of *M. tuberculosis*
- Genotyping uses portions of the genome to identify different strains of *M. tuberculosis*
- Tool to understand transmission of tuberculosis
- When viewing initial genotyping results focus on GENType

# TB Genotyping Results

- When combined with epidemiological data, can identify persons with TB disease involved in same chain of recent transmission
- Do not function as a diagnostic measure
- Once linked to patient data by State Coordinator (Laura Lane), results are found in the CDC database called Tuberculosis Genotyping Information Management System (TB GIMS)

# Uses of genotyping

- Detect false-positive culture results
- Enhance investigations
- Distinguish relapse from new infection
- Monitor trends and evaluate TB control program

# Universal Genotyping

Submitting one isolate from every patient with a culture positive specimen in a TB program's jurisdiction.

# **Essential Components for Genotyping**

# What is the difference between a specimen and an isolate?

- A specimen is a clinical sample
  - Sputum, bronchial wash, urine, blood, cerebrospinal fluid; tissues from organs or gastric aspirates
  - Collected from patients suspected of having TB
  - Specimens may or may not contain *M. tuberculosis*
- If *M. tuberculosis* grows in culture media from a specimen, it is called an isolate
  - Only isolates identified as *M. tuberculosis* can be genotyped

# Laboratory

- It takes approximately 6-8 weeks for a *M. tuberculosis* culture to grow
- Cultures/isolates must flow through DSHS lab
- DSHS ships weekly batches for genotyping
- In total, it can take a minimum of 2 months to obtain genotyping results

# Laboratory

- If no culture or isolate is sent to DSHS, there will be no GENType
  - Only positive cultures are submitted for genotyping
  - True clinical cases will not have a culture to submit
- Private providers may not submit initial specimen
  - Provide education and follow-up with private providers/labs when needed

# Surveillance

- Cases must be reported to DSHS Surveillance
- RVCT forms must contain the following minimum data elements:
  - Name
  - Date of birth
  - Race and ethnicity
  - Country of origin
  - If non U.S., date of entry into the U.S.
  - Address, city, county, zip-code with 4 digit code, and if in or outside the city limits
  - If diagnosed while in a facility or shelter, the name of the facility or shelter

# Best Practices

## Practices All Programs Should Implement

Best Practice #1	Ensure each patient with a positive Mycobacterium tuberculosis culture result has a genotyped isolate
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Best Practice #2	Link genotyping results to surveillance data promptly
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## Practices Programs Should Implement as Resources Allow

Best Practice #3	Integrate genotyping information into routine case management, contact investigation, and cohort review activities
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Best Practice #4	Examine concerning genotyping clusters
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Best Practice #5	Communicate with other jurisdictions and CDC
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Best Practice #6	Develop and maintain capacity for using genotyping information in routine TB control
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# GENType: Spoligotype and MIRU Analysis

Two different types of analytic methods:

- Mycobacterial Interspersed Repetitive Units (MIRU)
- Spaceroligonucleotide (Spoligotype)

# GENType Results

- Each unique combination of spoligotype + MIRU + MIRU2 is assigned a GENType
- Indicated as a “G” followed by 5 digits,  
i.e. G00010
- No GENTypes were automatically assigned prior to 2009



# How to make a GENType



Spoligotype  
70036777760731



MIRU  
222325143223



MIRU2  
434534412334



PCRTType  
PCR00016



GENType  
G00013

# GENType vs PCRType

## Comparative Examples for GENType and PCRType

Line#	GENType <sup>†</sup>	PCRType	Spoligotype	24-locus MIRU-VNTR	
1	G00010	PCR00002	000000000003771	223325173533	444534423428
2	G00011	PCR00015	777776777760601	224325153323	444234423337
3	G00012	PCR00002	000000000003771	223325173533	445644423328
4	G00013	PCR00016	700036777760731	222325143223	434534412334
5	G00014	PCR00051	776037777760771	223125163324	242434223525

† Unique combination of spoligotype and 24-locus MIRU-VNTR

**One PCRType = Many GENTypes**

**One GENType = One PCRType**

- Common PCRType
- 107 different GENTypes for this PCRType!
- GENType = greater distinction between the results

PCRType	GENType	MIRU	MIRU2
PCR00002	G00010	223325173533	444534423428
PCR00002	G00012	223325173533	445644423328
PCR00002	G01045	223325173533	--36-442312-
PCR00002	G01046	223325173533	--4--4423428
PCR00002	G01048	223325173533	--45-4423428
PCR00002	G01049	223325173533	--53-4423228
PCR00002	G01050	223325173533	--56-4422327
PCR00002	G01053	223325173533	--56-4423328
PCR00002	G01055	223325173533	-44534423428
PCR00002	G01061	223325173533	244242223337
PCR00002	G01063	223325173533	244342223337
PCR00002	G01066	223325173533	244444423238
PCR00002	G01083	223325173533	245544423328
PCR00002	G01106	223325173533	344544433327

# MIRU-VNTR

What is meant by a dash(-) or percent sign (%) in a MIRU-VNTR result?

- A dash (-) at a particular locus means that the result is unknown or cannot be determined (e.g., the MIRU-VNTR result would be: 44332-423261).
- A percent sign (%) at a particular locus means that there are two valid results for a particular loci (both are accurate) and this indicates mixed infection.

# MIRU-VNTR Examples

GENType	Spoligotype	MIRU	MIRU2
G10508	777776777760601	224325153323	43-234422333
G22227	0000000000003771	223325173534	24454442323%
G12705	777777776720771	2x-313153323	233532423337
G03720	676773777777600	2y2324253322	051352253205

# Genotyping and Contact Investigations

Genotyping serves in a supportive capacity and can help:

- Identify persons involved in same chain of transmission
- Confirm links
- Refute Links
- Identify unknown contacts

# Genotyping and You

Expectations for using genotyping in your role?

- Speak to your TB Manager to determine if this will be a portion of your job responsibilities
  - IF yes THEN
    - Contact [Laura.Lane@dshs.state.tx.us](mailto:Laura.Lane@dshs.state.tx.us) to obtain TBGIMS account and to receive technical assistance
- Registrars: please report cases promptly
- Laboratory: please ensure confirmed cultures are sent to our DSHS laboratory in Austin

# **National Tuberculosis Indicators Project**

**(NTIP)**



### Welcome to the National Tuberculosis Indicators Project

The National Tuberculosis Indicators Project (NTIP) is a monitoring system for tracking the progress of U.S. tuberculosis (TB) control programs toward achieving the national TB program objectives. This system will provide TB programs with reports to describe their progress, based on data already reported to the Centers for Disease Control and Prevention (CDC). In addition, these reports will help programs prioritize prevention and control activities, as well as program evaluation efforts.

#### Announcements

June 16, 2014

The Frozen 2013 dataset is now available in NTIP.

Please contact the NTIP Helpdesk at (404) 639-8444 if you have any questions.

Thank you!



National Tuberculosis Indicators Project Version 3.2.1

**Report Settings** ✕

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**Data Source** Current Data [\(change\)](#)

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**Program Area**

- Texas
- Bexar [TX]
- Cameron [TX]
- Collin [TX]
- Dallas [TX]
- Denton [TX]
- El Paso [TX]

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**Indicator**

<ul style="list-style-type: none"> <li>Completion of Therapy</li> <li>Contact Investigation</li> <li>Data Reporting - ARPEs</li> <li>Data Reporting - EDN</li> <li>Data Reporting - RVCT</li> <li>Drug-susceptibility Result</li> <li>Eval of Immigrants and Refugees</li> <li>Indicator Summary</li> <li>Known HIV Status</li> </ul>	<ul style="list-style-type: none"> <li>Laboratory Turnaround Time</li> <li>Performance Snapshot</li> <li>Recommended Initial Therapy</li> <li>Sputum Culture Conversion</li> <li>Sputum-culture Reported</li> <li>TB Case Rates</li> <li>Treatment Initiation</li> <li>Universal Genotyping</li> </ul>
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**Case Year** 2000 2002 2004 2006 2008 2010 2012 2014  
**or** 2001 2003 2005 2007 2009 2011 2013

**Quarter**  Annual  Q1  Q2  Q3  Q4

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**Report List** Print ✕

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NTIP: National Tuberculosis Indicator Project - Windows Internet Explorer

https://webappx.cdc.gov/NTIP/nt/generateReport/generateReport.do

File Edit View Favorites Tools Help

NTIP: National Tuberculosis Indicator Project

Centers for Disease Control and Prevention  
Your Online Source for Credible Health Information

National Tuberculosis Indicators Project Version 3.2.1

Report Settings

Data Source Current Data (change)

Program Area Texas (change)

Indicator Universal Genotyping (change)

Case Year 2014 (change)  
or  
Quarter  Annual  Q1  Q2  Q3  Q4

Reset Cancel Generate Report

Report List

Add a report

Done Internet | Protected Mode: On 100%

**National Tuberculosis Indicators Project**

Data Updated: 10/14/2014

**Universal Genotyping**

**National Objective**

Increase the proportion of culture-confirmed TB cases with a genotyping result reported to 94.0% by 2015.

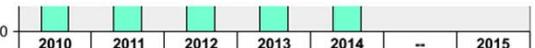
**Culture-confirmed TB Cases with an Isolate Submitted for Genotyping and Linked to the RVCT Record  
 Texas  
 2010 to 2014**



Cohort Period	2010	2011	2012	2013	2014	--	2015
With an Isolate Submitted and Linked to RVCT (%)	91.9	95.7	94.1	95.9	86.4	--	
Program Targets (%)	75.0	77.5	80.0	82.5	85.0	--	N/A
National Average (%)	91.7	94.2	94.7	94.9	77.2	--	
National Target (%)						--	94.0



National Tuberculosis Indicators Project Version 3.2.1



Cohort Period	2010	2011	2012	2013	2014	--	2015
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Program Targets (%)	75.0	77.5	80.0	82.5	85.0	--	N/A
National Average (%)	91.7	94.2	94.7	94.9	77.2	--	
National Target (%)						--	94.0

Cohort Period	2010	2011	2012	2013	2014
Total TB Cases with Positive Culture Result (N)	1,015	1,014	932	921	631
With an Isolate Submitted and Linked to RVCT (n)	933	970	877	883	545
With No Isolate Submitted and Linked to RVCT (n)	82	44	55	38	86

**Objective:** Increase the proportion of culture-confirmed TB cases with a genotyping result reported to 94.0% by 2015

**Indicator:** Percent of culture-confirmed TB cases with an isolate submitted for genotyping and linked to the RVCT record.

**Cohort:** All TB cases with positive culture result, counted in the year of interest. Records with missing or incomplete data where exclusion criteria cannot be assessed are included in the analytic cohort.

**Data Sources:** RVCT fields: Date Counted, Sputum Culture, Culture of Tissue and Other Body Fluids, and TB Genotyping Information Management System (TB GIMS).

**Calculation:** [Number of culture-confirmed TB cases with an isolate submitted for genotyping and linked to the RVCT record / Cohort] x 100

# TBGIMS and NTIP Access

Please email:  
Laura Lane  
[Laura.Lane@dshs.state.tx.us](mailto:Laura.Lane@dshs.state.tx.us)

# SAMS (secure access management services)

**SAMS**  
secure access management services

>Welcome Laura Lane

My Profile Logout

**Warning:** This is a U.S. Federal Government system and shall be used only by authorized persons for authorized purposes. Users do not have a right to privacy in their use of this government system. System access, activity, and information stored or transmitted may be monitored for adherence to acceptable use policy. Users of this system hereby consent to such monitoring. Improper or illegal use detected may result in further investigation for possible disciplinary action, civil penalties, or referral to law enforcement for criminal prosecution. This system contains non-public information that must be protected from unauthorized access, disclosure, sharing, and transmission, violation of which can result in disciplinary action, fines, and/or criminal prosecution.

**Links**

- SAMS User Guide
- SAMS User FAQ
- Identity Verification Overview

**My Applications**

**The Epidemic Information Exchange (Epi-X)**

- The Epidemic Information Exchange (Epi-X)
- Epi-X Forum

**National Tuberculosis Indicators Project**

- NTIP

**National TB Surveillance System Reports**

- NTSS

**Tuberculosis Genotyping Information Management System**

- TB GIMS

\* Strong credentials required.

# TBGIMS Dashboard

**Centers for Disease Control and Prevention**  
Your Online Source for Credible Health Information

CDC Search:

User: Lane, Laura
Tuberculosis Genotyping Information Management System Version 2.0.0
Role: Super User

[Contact Us](#) | [FAQs](#) | [Help](#) | [Training Resources](#) | [Logout](#)

**TB GIMS Home**

**Search**

Genotype Results

Patient Results

Blank State Case Numbers

Blank Surveillance

**Records**

Edit Isolates

Find Duplicates

Import Data

**Reports and Tools**

Watch List

Cluster Snapshot

Generate Reports

Templates

Export Data

**Additional Testing**

Submit Requests

View Pending Results

**Directory**

View Users

Contact Us

**Tuberculosis Genotyping Information Management System**

**The last TB GIMS Surveillance Upload includes data transmitted to CDC through: 10/19/2014**  
Searches and reports will only include data reported to CDC by the state and included in the latest TB GIMS surveillance upload.

**Announcements:**  
No New Announcements.

**Recent GENType Cluster Alert Changes\***

GENType	County	Change in Alert Level	Alert Date
G05783	BEE	None to Medium	10/15/2014
G03270	BEXAR	Medium to High	10/08/2014
G20366	HARRIS	None to Medium	09/24/2014
G17321	BEXAR	None to Medium	09/03/2014
G10518	DALLAS	None to Medium	08/20/2014

\*Up to five shown-click PDF icon for full list.

**Genotyping Surveillance Coverage**

Year	2011	2012	2013	2014*
TEXAS (%)	95.6	94.0	95.8	83.0
National (%)	94.1	94.6	94.9	79.4

\*Year to date. NA-Not Available. Source: NTIP

**Timeliness of Genotyping - by Isolate**

Time From → To	Median number of days				Goal (days)
	State		National		
	2013	2014*	2013	2014*	
Specimen collection → Isolate shipped to genotyping lab	51	44	62	58	NA
Receipt at genotyping lab → Genotype create date	18	14	13	14	14
Genotype create date → State Case No. entered	41	5	0	0	56
Genotype create date → Isolate Linked	47	6	12	7	90
Specimen collection → Isolate Linked	135	77	107	97	NA

\*Year to date. NA-Not Available.

**Isolate Linking**

Number of Isolates	2013	2014*
Total isolates	1,563	1,253
Linkable isolates <sup>1</sup>	1,486	1,224
Linked isolates	1,486	1,146
Not linked isolates	0	78
Due to blank State Case No. <sup>2</sup>	0	77
Due to blank surveillance <sup>3</sup>	0	1
Not linkable isolates	77	29

**Pending Isolates**

Number of Isolates	2013	2014*
Pending genotype results	0	49
Pending additional results (MIRU2 or RFLP)	0	0

\*Year to date.

# Questions?

Laura.Lane@dshs.state.tx.us  
512-533-3162