

Using Whole Genome Sequencing to Establish Epi Links among Individuals with Tuberculosis

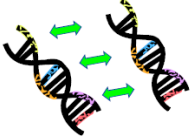
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 In commemoration of World TB Day

Theodore Bonau, MPH
 Epidemiologist III, Tuberculosis Program
 Chicago Department of Public Health

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What is TB Genotyping?

- Laboratory method that examines DNA variations to determine genetic relatedness of TB strains from different patients who have TB disease
- Can only be performed with culture-positive cases
 - N=106 2017 (83%)
- Genotyping helps identify transmission relationships between TB cases
- Genotypic matches are expected from known epi links (household contacts)




Genotype Cluster

- Two or more cases with matching TB genotypes may be considered part of a genotype cluster
 - Usually restricted by place and time
- Patients in a genotype cluster are more likely to be in the same chain of transmission
- Transmission among patients in a genotype cluster may be recent or remote
- Ruling out transmission vs. confirming
 - Easier to rule out

National TB Genotyping Service (NTGS)

- NTGS started in 2004
 - TB GIMS launched March 2010
 - As of January 2017, contains genotyping results for over 105,000 patients
- State labs submit TB isolates for genotyping
 - "Universal Genotyping"- genotype one isolate from every culture-positive TB case in the United States
- In 2016, 99% of Chicago culture positive cases were genotyped (97% US)



U.S. Tuberculosis Genotyping Nomenclature

2 0 0 4	Spoligotype:¹ 000000000003771	Initial 12-locus MIRU-VNTR¹ MIRU: 223325173533
2 0 0 9	PCRTyp^e: PCR00002	Additional 12-locus + MIRU-VNTR (MIRU2) MIRU2: 444534423428 ²
	GENType G00010	

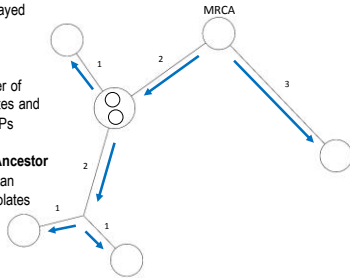
¹ Spacer oligonucleotide type (spoligotype) and mycobacterial interspersed repetitive unit-variable number tandem repeat.
² The complete set of 24 loci is referred to as 24-locus MIRU-VNTR and is used for GENType designation.

Whole Genome Sequencing (WGS)

- WGS started universally in 2018
 - CDC will WGS previous isolates upon request
- WGS analysis was performed for GENType clustered isolates to further assess the genetic relatedness.
- Expands coverage of the genome to ~90% (i.e., compared to ~1% coverage with conventional genotyping).
- WGS data identifies SNPs (single nucleotide polymorphisms), DNA change at a single position, that are useful for examining the genetic relationship among isolates.
- SNPs that are identified in WGS analysis are mapped on to a phylogenetic tree to diagram genetic relatedness

WGS Phylogenetic Tree

- Isolates are shown as circles (called nodes)
- Isolates with the same genome type (i.e., same sequence) are displayed together in one node
- Nodes are connected by lines proportional in length to the number of SNPs that differ between the isolates and are labeled with the number of SNPs



- MRCA= Most Recent Common Ancestor**
- Hypothetical genome type (not an actual isolate) from which all isolates on the tree are descended

G20467 in Illinois

- First case: in 2012 (not WGS), 24 year old, Male, Honduras -> US in 2007
- 2nd case: 64 year old, Male, Mexican-born



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- 2nd case: 64 year old, Male, Mexican-born
- 3rd case: 33 year old, male, Mexican-born
- 4th Case: 44 year old, male, Mexican-born, father-in-law to 1st case, main "focal point" of transmission
- Determined 2nd and 3rd case are social contacts to 4th case



G20467 in Illinois

- Case 4 ("super spreader") upon initial CI fails to identify some household contacts
- 5th case: 4 month old, Male, US-born
 - ED with cough, vomiting, w/ fever
 - Under DCFS and "safe home" was Case 4's




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- 6th case: 17 year old, Female, US-born
 - Girlfriend to one of Case 4's sons, lived in household




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 - ED with cough, vomiting, w/ fever
 - Under DCFS and "safe home" was Case 4's
- 6th case:** 17 year old, Female, US-born
 - Girlfriend to one of Case 4's sons, lived in household
- 7th case:** 15 year old, Male, US-born
 - Brother to 5th case, social contact to 4th
 - Clinical case, intrathoracic lymphnode TB




G20467 in Illinois

- 8th case:** 44 year old, Male, Mexican-born
 - Social contact to 4th case



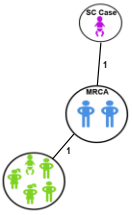
G20467 in Illinois

- 8th case:** 44 year old, Male, Mexican-born
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- 9th case:** 41 year old, Female, Mexican-born
 - Wife of 8th case




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- 10th case:** 6 year old, Female, US-born
 - From SC, visited family in Chicago
 - Unknown epi link




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- 9th case:** 41 year old, Female, Mexican-born
 - Wife of 8th case
- 10th case:** 6 year old, Female, US-born
 - From SC, visited family in Chicago
 - Unknown epi link
- 11th case:** 11 year old, Female, US-born
 - Lives in DuPage County
 - Spent time in family's restaurant




G20467 in Illinois

- CDPH TB Staff re-interview several cases and contacts
 - Identify restaurant social hang out spot
 - Identify new contacts
- 12th case:** 51 year old, Male, Mexican-born
 - Played cards at restaurant



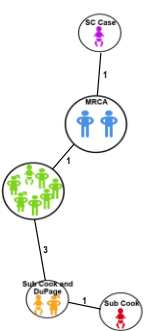
G20467 in Illinois

- CDPH TB Staff re-interview several cases and contacts
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- 12th case:** 51 year old, Male, Mexican-born
 - Played cards at restaurant
- 13th case:** 34 year old, Male, Mexican-born
 - Connected to card playing via nickname




G20467 in Illinois

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 - Identify restaurant social hang out spot
 - Identify new contacts
- 12th case:** 51 year old, Male, Mexican-born
 - Played cards at restaurant
- 13th case:** 34 year old, Male, Mexican-born
 - Connected to card playing via nickname
- 14th and 15th cases:** 28 year old, Female, US-Born and her infant
 - Live in Suburban Cook County



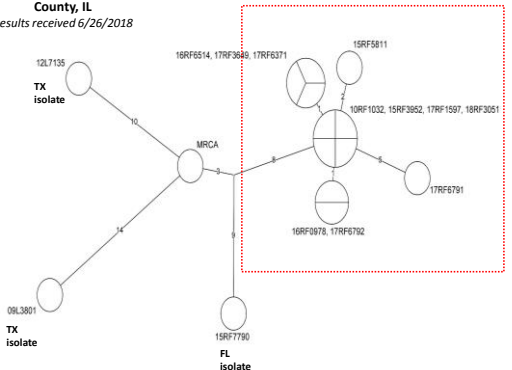
Next Steps

- Follow-up with newly identified contacts
 - Interview former restaurant owner
 - Testing and evaluations
- Held Conference Call with CDC, IDPH, DuPage, and CCDPH
 - Same last names identified for family members of Sub Cook Cases
 - Re-interview individuals at next clinic visit to establish any connections to Chicago



G10296 in Cook County, IL

Results received 6/26/2018




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