



# Genotype Cluster Investigations

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# Learning Objectives

- Name at least three ways that genotyping results can be used in TB control
- Name the basic steps in a genotype cluster investigation
- Understand the importance of epidemiological links in genotype cluster investigation

# So what is genotyping?

- Laboratory method to examine tiny DNA variations in the genetic makeup of *mycobacterium tuberculosis*
- These variations distinguish different strains of the TB organism

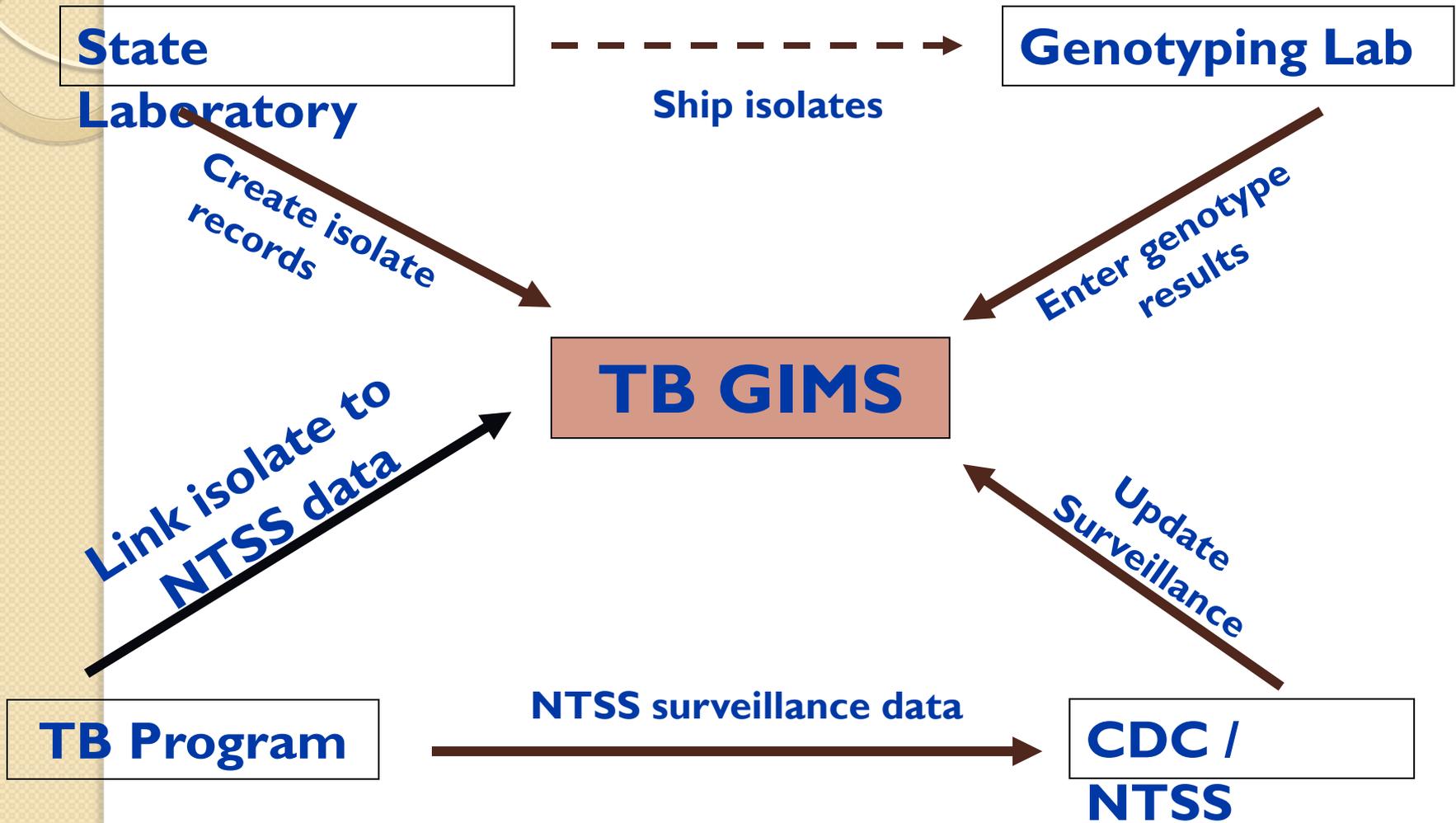
# National TB Genotyping Surveillance Network

- Started in January 2004
- Genotype at least 1 isolate for each new culture positive TB case
- ▶ About 115,000 isolates have been genotyped in the United States, 86% are linked to TB patients

# National TB Genotyping Surveillance Network

- **March 2010 TBGIMS implemented**
  - Compare aggregate data for a PCRtype or Gentype
  - Generate reports on specific genotypes
    - Includes distribution of the genotype nationally or within state
    - Snapshots that combine genotype and demographic information

# TB GIMS Data Flow



# So what is a genotype cluster?

- Two or more patients with a matching genotype within a geographic area and time frame, usually 2-3 years

# What if the genotype does not match?

- When the a new TB isolate does not match, it is called “unique”
- In Virginia, 42% of the isolates in our library are unique

# What does a genotype cluster tell us about transmission?

- By itself, very little
- It could represent different chains of transmission
- Transmission might not be recent or direct

# Distinguish Reactivation from New Infection

- If a person has TB at different times and they have culture results, the genotype may help distinguish break down of old disease or recent reinfection
- A recent study of people with recurrent TB found that about 15% of cases were new infections and in a subset of the study population, 60% were reinfection\*

*\*Interrante, J, et. al. Exogenous Reinfection as an Etiology of late Recurrent Tuberculosis in the United States.*

# Detect false positive cultures

- Estimated 2-3% of positive cultures for MTB are actually cross contamination
- Suspicious for contamination
  - Negative sputum smear and only one positive specimen
  - Clinically the patient does not exhibit expected TB signs and symptoms
  - Possibility of exposure has been explored and ruled out

# So we have a genotype cluster, now what?

- Prioritize clusters that have the highest likelihood that you can intervene.
- For example, two cases in cluster that are separated by 10 years would be a lower priority than a cluster with three cases within two years

## Step One: Review cluster data and national reports on that genotype

- Review the state and national data to see if any other TB cases have the same genotype
- If this is a new isolate in an existing cluster, consider whether it is an outbreak

## Step Two

- Discuss the match with the nurses, outreach workers and physicians who manage the cases
- Determine next steps based on what is known

# Step Three

- Medical chart abstraction with a standardized locations questionnaire
- Establish precise period of infectiousness for each case
- Review contact investigations

# Step Four

- Summarize the data and brainstorm
- Note possible locations of transmission
- Are there any clues of an epi-link between the cases in the clusters?
  - Consider re-interviewing the clients
  - Develop some additional questions based on the investigation to combine with the locations questionnaire

# Shoe leather epi

- Person
  - Demographic characteristics, behaviors, social networks
- Place
  - Are cases in same geographic area, do they share workplace, gathering place
- Time
  - Recent transmission is generally defined as within 2-3 years

# Things to consider....

- Did any of the cases name the other in the contact investigation?
- Did any of the cases spend time in the same location during the infectious period
- Are there other characteristics that may link them: e.g. substance abuse, chronic medical issues, public transit, same neighborhood....

# Is there an opportunity for intervention?

- Do you need to expand the contact investigation based on the genotype cluster investigation?
- Are there additional evaluation criteria for the contact investigations?

# Virginia Genotype Clusters of Note

- PZA monoresistant genotype cluster over a 5 year period with 30 cases, including 7 clinical cases
- Fairfax Cluster associated with index case with long infectious period
- Tidewater cluster that involves a social and family network
- Central Virginia cluster that includes several family members

# Conclusions

- TB genotype cluster investigation depends on shoe leather epidemiology to find chains or locations of transmission and to develop interventions
- By itself the genotype does not prove recent transmission nor does it prove direction and timing of transmission