

## Genotyping Information

CDPHE

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Tuberculosis remains a concerning infectious disease in our country affecting a variety of people. In 2004 there were over 14,000 cases of tuberculosis reported in the United States with approximately 700 deaths due to the disease<sup>1</sup>. However, the incidence rate worldwide is much higher. It is suspected that one third of the world population, approximately two billion people, carry TB, with eight million people developing active infection each year<sup>2,3</sup>. Although our country generally has a relatively low rate of TB, the disease remains prevalent among certain groups, such as people in prisons or institutions, and foreign-born persons.

Finding and treating TB can be a challenging task as most individuals who are infected have a latent form of the disease in which there are no obvious clinical symptoms. But once an individual with active disease is located, an epidemiologic investigation may try to identify the source of infection as well as possible contacts. This data helps determine the spectrum of contacts, and may be highly suggestive of transmission from one individual to another. Tuberculosis can also be tracked through the laboratory techniques of genotyping. Once a positive culture (from sputum or other site) has been obtained, it can be analyzed for its DNA content through a variety of methodologies. This laboratory data can then be compared to other cases of tuberculosis to determine similarity between DNA. The greater the homology between bacterial strains of tuberculosis, the more likely the bacterial strain was passed from one person to another. Genotyping, in conjunction with epidemiological tracking, is a powerful way to identify cases of tuberculosis and follow its transmission. It is changing the way we are currently investigating tuberculosis.

### What is genotyping?

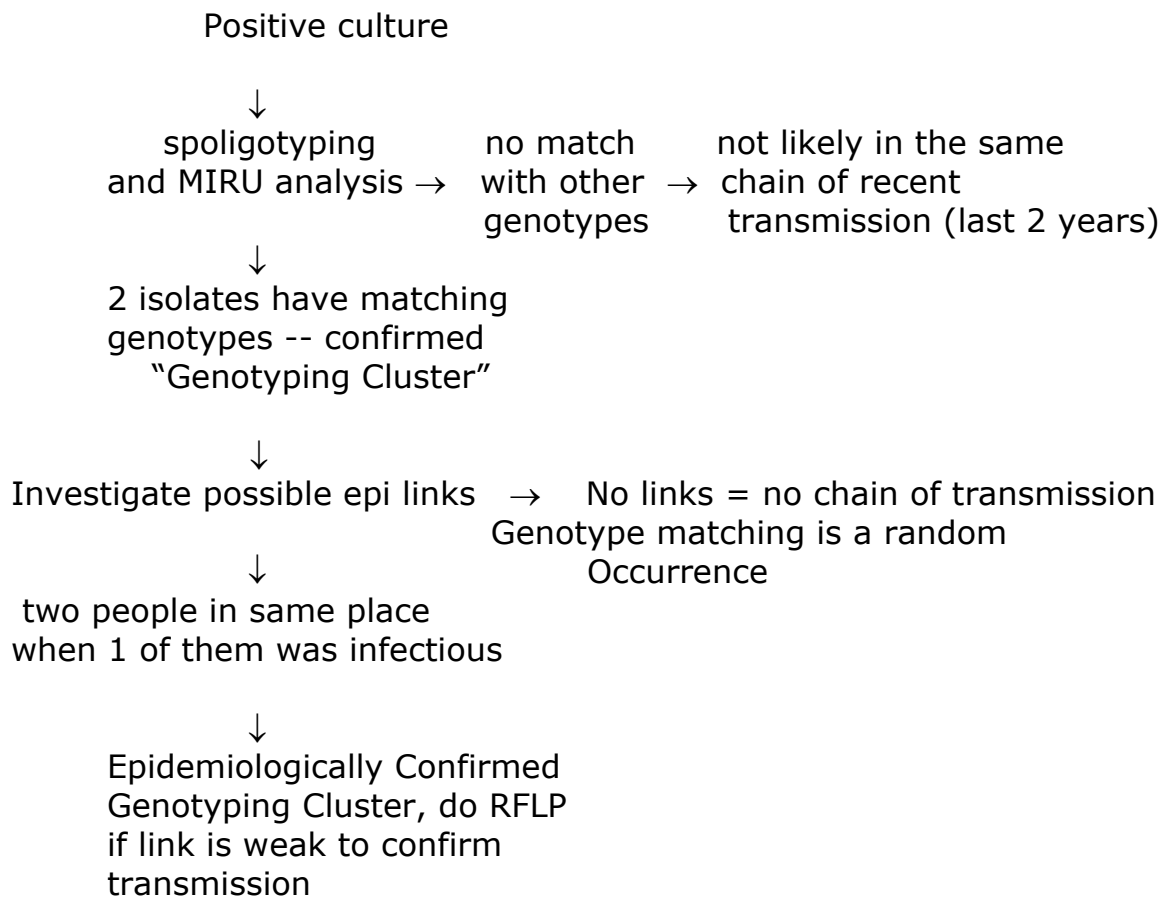
Genotyping is the process of analyzing genetic material of an organism. In the case of tuberculosis, a positive culture warrants sending a sample for further genomic testing. Three different laboratory tests may be done: spoligotyping, MIRU (mycobacterial interspersed repetitive units) testing, and RFLP (restriction fragment length polymorphism) analysis. All these tests look at variations within the DNA that occurs between strains of mycobacterium. MIRU testing and spoligotyping are PCR-based methods that look at repeated segments of DNA, or spacer DNA in between the repeat sequences, respectively. RFLP analysis compares specific sequences of DNA found in the bacteria. In most situations RFLP can differentiate strains of bacteria to a finer degree than the other two tests.

All the genotyping tests evaluate the length and number of times certain DNA sequences occur, which provides a definitive means to compare

bacterial samples. These tests are like comparing fingerprints -- although DNA sequences may be similar, they are sufficiently unique to differentiate between all but the most homologous samples.

### When is it used?

If a person with active tuberculosis disease is culture-positive, an isolate is sent to a reference lab for genotyping. Generally, spoligotyping and MIRU analysis are done. If there are weak epidemiologic links between cases, RFLP may be performed as well.



### Why do it?

There are many advantages to genotyping in identifying, tracking, and controlling tuberculosis.

- It may help detect outbreaks earlier and more definitively by confirming linkages between cases when people share a genotype cluster. This will allow for earlier treatment and containing the spread of the disease.

- Unexpected or unusual transmissions will be easier to detect when people who would not normally be connected are both part of a genotypic cluster.
- It will be easier to identify false positives due to cross-contamination in labs between patient specimens and control strains.
- Cases of relapse versus re-infection can be decided based on the genotypic similarity of isolates.
- Prevalence of mycobacterial strains can be monitored. This may be particularly useful when a highly infectious strain is present.
- It may also be possible to correlate genotypes with multi-drug resistance and thereby track the prevalence and types of antibiotic resistance.
- May be useful for public health planning, evaluation, education.

### **Who does it?**

Currently there are two designated genotyping labs in the country, one in California, the other in Michigan, which are contracted by the CDC to perform genetic analysis on tuberculosis isolates. Beginning in 2004 all cases were tested in either California or Michigan, with all Colorado isolates being analyzed in California.

### **Outcomes**

Genotyping is improving our ability to identify links between cases. False positive cases can be identified preventing individuals from needlessly taking antibiotics for months. And on a broader scale, tuberculosis can be better tracked through our society and epidemiologic trends followed. This provides us greater ability to control tuberculosis in our society today, as well as plan for, and hopefully prevent, cases in the future.

### **References**

1. <http://www.cdc.gov/nchstp/tb/surv/surv2004/PDF/Table1.pdf>, accessed 11-04-05
2. <http://www.globalhealthreporting.org/tb.asp>, accessed 11-04-05
3. <http://www.lapublichealth.org/tb/faq/99Facts/99fact.htm>, accessed 11-04-05