Abstract

The use of whole genome single nucleotide polymorphisms (wgSNP) analysis in cluster investigation of tuberculosis outbreak cases

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Mycobacterium tuberculosis (M.tb) is a species of pathogenic bacteria in the family Mycobacteriaceae and the causative agent of tuberculosis. Understanding the dynamics of M.tb disease transmission through complex genotyping is critical to creating policies and monitoring the disease with the end goal of TB elimination. Current genotyping methods combine the results of two assays, spoligotyping and *Mycobacterium tuberculosis*-specific multiple locus (Variable Number of Tandem Repeats (MIRU-VNTR,) to give an M. tuberculosis TBG type. However, whole genome single nucleotide polymorphism (wgSNP) analysis was used to determine the genetic relatedness between strains is a preferred method due to its improved discrimination.

Between 2015 and 2018, a total of 11 strains were collected through TB contact investigation by four universities in a region in Korea. Analysis of spoligotyping and 24-loci MIRU-VNTR showed that all strains were of the same genotype, namely TBG0014. Patients at each university had an epidemiologic link, confirming that the event was an outbreak, but epidemiological relationships between universities could not be identified. In each outbreak case, the number of SNPs between tuberculosis strains was 0-1, but the number of SNPs between universities was 196-264.

A wgSNP analysis was performed to explore the genetic relationship between TB isolates that could not be confirmed through conventional methods. As a result, there were 0-1 SNPs between TB isolates in the outbreak. The number of SNPs between TB cases at the three universities was 196-264, and it was identified that there were no transmission cases among universities. A wgSNP analysis recommend performed to assess the potential of recent transmission and this information will be provided to the national TB management program.

Keywords: Mycobacterium tubercuosis, molecular typing, wgSNP



Figure 1. Phylogenetic tree of TBG0014 derived from Spoligotyping and 24-loci MIRU-VNTR

*Colored square reflect according to TB epidemiological investigation case. Red: A university, Purple: B university, Yellow: C university, Green: D university



Figure 2. Minimum spanning tree of TBG0014 derived from wgSNP

*The number indicates the SNPs and colored rings display according to TB contact tracing case. Red: A university, Purple: B university, Yellow: C university, Green: D university