

Project Title: Development and evaluation of next generation of molecular subtyping method (MLVA) for bacterial pathogens (*Shigella sonnei*)

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Principal Investigator(P.I.): Chiou, Chien-Shun

P.I. Position Title: Research Fellow

P.I. Institute: Research and Diagnostic Center, Centers for Disease Control

Abstract:

A multilocus variable-number tandem-repeat (VNTR) analysis (MLVA) method was developed and evaluated for the subtyping of *Shigella sonnei* isolates. A total of 26 VNTR loci were identified by exploring the repeat sequence loci in the genomic sequences of *S. sonnei* strains Ss046 and 53G and by testing 536 isolates that had previously been characterized by pulsed-field gel electrophoresis (PFGE). The discriminatory power of MLVA (Simpson's index of diversity [D], 0.9524; 95% confidence interval [CI], 0.9373 to 0.9564) for the 536 isolates was significantly higher than that of PFGE (D , 0.8882; CI, 0.8667 to 0.9097). MLVA typing with the four and eight most variable loci had D values of 0.9468 and 0.9481, respectively, results approaching that of 26 loci. The usefulness of MLVA for outbreak investigation was evaluated using 151 isolates from 10 shigellosis outbreaks and 22 PFGE-indistinguishable isolates collected from nine epidemiologically unrelated events in five different countries. The evaluations indicated that MLVA was a powerful typing tool to distinguish isolates for outbreak investigation and that it exhibited a good discrimination of the 22 PFGE-indistinguishable isolates. Single-locus variants did occur during the outbreak; therefore, *S. sonnei* isolates with MLVA profiles differing at no more than a single locus should be considered part of the same outbreak. The present study suggests that MLVA has the potential to replace PFGE as a standard method of typing *S. sonnei* isolates for disease surveillance and outbreak investigation.

Keyword: MLVA, VNTR, molecular typing, *Shigella sonnei*