

Characterization of Philippine Drug-susceptible and Multi-drug Resistant *Mycobacterium tuberculosis* Isolates through Combined 15-loci MIRU-VNTR Genotyping and Mutation Analysis of Drug Resistance Genes

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Molecular genotyping, an important strategy to characterize bacterial strain infecting a patient, allows identification of *M. tuberculosis* complex members with varied responses to anti-mycobacterial therapy. *M. tuberculosis* Interspersed Repeating Units – Variable Number of Tandem Repeats (MIRUVNTR) is a fast, reproducible and cost-effective PCR-based method capable of differentiating MTb strains. This study focused in evaluating the utility of MIRU-VNTRs to discriminate fifty-four MTB isolates from the Lung Center of the Philippines through amplification of twelve MIRU-VNTRs and three Exact Tandem Repeats (ETRs). Digital codes were determined per isolate through calculation of VNTR repeats and analyzed using online MIRU-VNTRplus program. Hunter Gaston Discriminatory Indices suggest that five out of fifteen (33.33%) MIRU-VNTRs are highly discriminatory (>0.75). All MIRU-VNTRs and ETRs except ETRC had HGDI indices ≥ 0.5 suggesting good resolving power. MIRU-VNTR profile of LCP isolates supplemented with mutation data of *rpoB*, *katG* and *gyrA* genes obtained through gene sequencing lead to identification of four clusters closely related to East African-Indian strain which confirmed previous reports regarding the existence of a distinct Manila family of MTb strains. These four clusters namely EAI-M1 to EAI-M4 are characterized by increasing propensity to develop drug resistance. *rpoB*, *katG* and *gyrA* mutations observed in the Philippine isolates were highly similar to reported literature. Our results show that combined 15-loci MIRU-VNTR genotyping strategy and mutation profiling of drug resistance-related genes could serve as a molecular epidemiology tool to characterize and monitor the drug susceptible and multi-drug resistant MTb strains in the country.