（英文）

Abstract

In this study, using reference and clinical strains has standardized methods for drug resistance surveillance of *Mycobacterium tuberculosis*. A P3 level negative pressure laboratory has been constructed and verified. We have analyzed various mutations, in-frame deletions and insertions of the *rpoB* gene associated with rifampin resistance by DNA sequencing 162 multiple drug-resistant (MDR) and 40 anti-tuberculosis drug sensitive clinical strains of *Mycobacterium tuberculosis* isolated in Taiwan. The relative mutation frequencies of specific mutations found in this study were different from those previously reported in Asia countries. In our case, 90.1% (146/162) MDR isolates showed a total of 32 distinct changes, including 30 single-nucleotide substitutions, one insertion, and one deletion, in an 81-bp region of the *rpoB* gene. 93.8% (137/146) of the mutated isolates showed a single mutation site. The changes in codons Ser_{531}, His_{526} and Asp_{516} accounted for the majority of rifampin resistance, as previously documented for isolates analyzed in other geographic regions of the world. Our results indicate distinct frequencies of mutations compared to those of other studies, that we found 80 MDR strains (54.8%, $P < 0.05$) carrying a mutated codon at position 531, 33 MDR strains (22.6%, $P < 0.05$) having mutated codon at position 526, and 14 MDR strains (9.6%, P value 0.59) showing mutated codon at position 516. Altogether eleven novel alleles within the 81-bp region of *rpoB* were recognized in this investigation. All studied isolates were also characterized by methods using other genetic markers, such as IS*6110* RFLP and spoligotyping, to gain further genetic information on the generation and transmission of MDR strains. There was 60% of the studied isolates belongs to Beijing family genotypes. The results of RFLP also indicate that the MDR strains isolated in Taiwan are genetically diverse and implicate most of the MDR strains were isolated from previously treated patients rather than recent transmissions.

Key Words: drug resistance surveillance, *Mycobacterium tuberculosis*, multiple-drug resistance,