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学位論文の題名

Moxifloxacin resistance and genotyping of Mycobacterium avium and Mycobacterium intracellulare isolates in Japan
（日本国内のMycobacterium avium及びMycobacterium intracellulareの遺伝子型とモキシフロキサシン耐性について）

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論文審査担当者

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Abstract

Although fluoroquinolones are considered as an alternative therapy of pulmonary
*Mycobacterium avium* complex (MAC) disease (1), association of fluoroquinolone
resistance and MAC genotypes in clinical isolates from individuals not previously
treated for MAC infection has not been fully shown. A total of 154 *M. avium* isolates
and 35 *Mycobacterium intracellulare* isolates were obtained from treatment-naïve
patients with pulmonary MAC disease at the diagnosis of MAC infection at 8 hospitals
in Japan. The susceptibility of moxifloxacin was determined by broth microdilution
methods. Moxifloxacin-resistant isolates were examined for mutations of *gyrA* and *gyrB.*
Variable numbers of tandem repeats (VNTR) assay was performed using 15 *M. avium*
VNTR loci and 16 *M. intracellulare* VNTR loci. Moxifloxacin susceptibility was
categorized as resistant and intermediate for 6.5% and 16.9% of *M. avium* isolates and
8.6% and 17.1% of *M. intracellulare* isolates, respectively. Although *M. avium* and *M.*
*intracellulare* isolates had amino acid substitutions of Thr 96 and Thr 522 at the sites
corresponding to Ser 95 and Gly 520 in the *M. tuberculosis* proteins GyrA and GyrB,
respectively, these substitutions were observed irrespective of susceptibilities and did
not confer resistance. VNTR assays showed three clusters among *M. avium* isolates and
two clusters among *M. intracellulare* isolates. No significant differences in
moxifloxacin resistance were observed among these clusters. In conclusion, although resistance to moxifloxacin was observed in approximately one-fourth of *M. avium* and *M. intracellulare* isolates, this resistance was not associated with mutations in *gyrA* and *gyrB* or with VNTR genotypes.