学位の種類	博士（医学）
報告番号	甲第１６８９号
学位記番号	第１２０６号
氏名	山羽　悠介
授与年月日	平成 31 年 3 月 25 日
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） Nagoya Medical Journal （accepted for publication）
論文審査担当者	主査：　長谷川 忠男 副査：　中西 良一，新実 彰男

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.

1. Koh WJ, Hong G, Kim SY, Jeong BH, Park HY, Jeon K, et al. Treatment of refractory *Mycobacterium avium* complex lung disease with a moxifloxacin-containing regimen. Antimicrob Agents Chemother 2013; 57: 2281-2285.