

A Fluoroquinolone-Resistant *Escherichia coli* Clinical Isolate without Quinolone Resistance-Determining Region Mutations Found in Japan[∇]

Fluoroquinolones are broad-spectrum and highly bactericidal antimicrobials agents that are used to treat various bacterial infections. *Escherichia coli* infections, especially in the urinary tract, are frequently treated with fluoroquinolones, and fluoroquinolone resistance has increased in the clinical field. Fluoroquinolone resistance is caused mainly by chromosomal mutations in the quinolone resistance-determining region (QRDR) of *gyrA* and *gyrB*, which encode DNA gyrase subunits, and *parC* and *parE*, which encode topoisomerase IV subunits. Moreover, plasmid-mediated quinolone resistance (PMQR) genes have been reported in Gram-negative bacteria, including *E. coli*. The acquisition of PMQR genes alone results in a low level of fluoroquinolone resistance and does not lead to MICs exceeding the breakpoints of these agents.

We isolated an *E. coli* strain, named HUE1, from the urinary catheter of a 77-year-old female patient in 2008 at Hokkaido University Hospital (Sapporo, Japan). The multilocus sequence type of this microorganism was ST171, and the phylogenetic group was A. The MICs of ciprofloxacin (CIP), levofloxacin (LVX), and nalidixic acid (NAL) exceeded the resistance breakpoints proposed by the Clinical and Laboratory Standards Institute (CLSI) (Table 1). The CLSI breakpoint for LVX is ≤ 2 $\mu\text{g/ml}$ susceptible and ≥ 8 $\mu\text{g/ml}$ resistant, that for CIP is ≤ 1 $\mu\text{g/ml}$ susceptible and ≥ 4 $\mu\text{g/ml}$ resistant, and that for NAL is ≤ 8 $\mu\text{g/ml}$ susceptible and ≥ 32 $\mu\text{g/ml}$ resistant (2). However, direct sequencing did not reveal any mutations in the QRDR of *gyrA*, *parC*, *parE*, or *gyrB*. We then screened for PMQR genes *qnrS*, *qnrA*, *qnrB*, *qnrC*, *qnrD*, *aac(6′)-Ib-cr*, *qepA*, and *oqxAB* by PCR. HUE1 was positive for *qnrS* and *oqxAB* (Table 1).

OqxAB is a new plasmid-encoded efflux pump belonging to the RND type and was first found in *E. coli* from swine manure

in 2003 (6). It confers resistance to several antimicrobial agents, such as olaquinox, trimethoprim, and chloramphenicol, and a slight decrease in susceptibility to fluoroquinolones (3). Isolation of *oqxAB*-harboring *Enterobacteriaceae* has been reported only in Sweden and Denmark, South Korea, and China (3, 5, 7), and isolates derived from human patients have been reported only in South Korea. This letter provides the first report of *oqxAB*-harboring *E. coli* in Japan. Zhao et al. reported the isolation of *E. coli* harboring both *qnrS* and *oqxAB* from pigs in China (7). These isolates showed no mutations in the QRDR of *gyrA* and *parC*, however, mutations in that of *parE* and *gyrB* have not been determined. These isolates showed CIP MICs of 1 to 2 $\mu\text{g/ml}$, and they are therefore susceptible or intermediate according to the CLSI breakpoints.

OqxAB and QnrS increase the MIC of CIP approximately 32-fold and 64-fold, respectively (1, 5). These reports suggest that fluoroquinolone resistance in HUE1 without mutations in QRDR is caused by the concomitant presence of *oqxAB* and *qnrS*. However, other mechanisms may be associated with fluoroquinolone resistance in HUE1; therefore, further investigations are needed.

In conclusion, we present the first report of fluoroquinolone resistance in an *E. coli* isolate that is independent of mutations in the QRDR. The isolate harbored two PMQR genes, *qnrS* and *oqxAB*.

We thank Hirotsugu Akizawa for providing *E. coli* clinical isolates.

This study was supported in part by a grant-in-aid from the Japanese Ministry of Health, Labor and Welfare (H21-Shokuhin-Ippan-013) and a grant from the Japan Ministry of Education, Culture, Sports, Science, and Technology for the program of developing supporting systems for upgrading education and research.

TABLE 1. Detection of fluoroquinolone susceptibility, QRDR mutations, and PMQRs in HUE1

Strain	QRDR mutations				PCR			MIC ($\mu\text{g/ml}$) ^b					
	<i>gyrA</i>	<i>parC</i>	<i>parE</i>	<i>gyrB</i>	<i>oqxA</i>	<i>oqxB</i>	<i>qnrS</i>	ENR	CIP	LVX	PUR	STX	NAL
HUE1	WT ^a	WT	WT	WT	+	+	+	8	4	8	4	2	128

^a WT, wild type.

^b ENR, enrofloxacin; PUR, prulifloxacin; STX, sitafloxacin.

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^v Published ahead of print on 13 June 2011.