

# Transferable Quinolone Resistance in Enterobacteria from Argentina: *aac(6')-Ib-cr* and a Novel *qnrB* Allele (*qnrB6*) Are Located in a Complex Class 1 Integron

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## INTRODUCTION

The worldwide emergence of transferable quinolone resistance, i.e. *qnr*, *qepA* and *aac(6')-Ib-cr*, is becoming one of the major threats in bacterial resistance. In Argentina, these mechanisms are not reported yet.

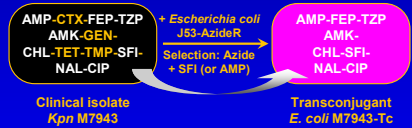
## METHODS

The multiresistant *Klebsiella pneumoniae* (Kpn) M7943 was isolated at the Fundación Favalaro (Buenos Aires, May 2006) from a blood culture of a patient with bacteremia, after 14-days course with piperacillin-tazobactam (TZP). MICs were determined by the agar dilution method (CLSI). Conjugations, PCR and DNA sequencing were performed by standard methods. Long PCR conditions were used for fragments > 4 kb. Phylogenetic tree was done with Clustal X.

## RESULTS

### 1 RELEVANT RESISTANCE PHENOTYPE AND CONJUGATION

Disk diffusion: resistance or reduced susceptibility are indicated. AMP, ampicillin; CTX, cefotaxime; FEP, cefepime; AMK, amikacin; GEN, gentamicin; CHL, chloramphenicol; TET, tetracycline; TMP, trimethoprim; SFI, sulfisoxazole; NAL, nalidixic acid; CIP, ciprofloxacin



### Relevant susceptibility profiles

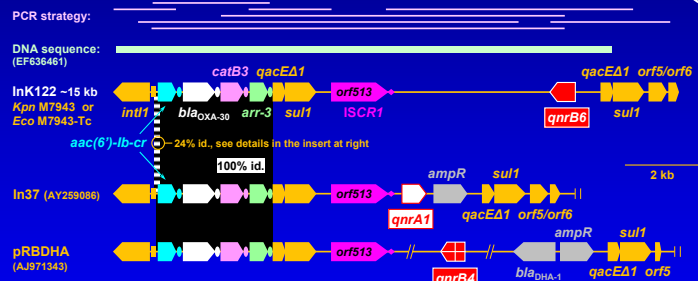
Antibiotics	MICs (µg/ml)				
	Kpn M7943	E. coli M7943-Tc	E. coli J53-AzR	E. coli DH10β (pCROB6)*	E. coli DH10β (pCR2.1)*
Nalidixic acid	128	16	4	8	2
Ciprofloxacin	32	2	0.015	0.125	0.004
Norfloxacin	32	2	0.03	0.125	0.008
Levofloxacin	4	0.5	0.03	0.06	0.004
Oxfloxacin	8	0.5	0.06	0.06	0.004
Gatifloxacin	4	0.5	0.03	0.06	0.004
Moxifloxacin	8	1	0.06	0.125	0.004
Amikacin	16	4	0.5	2	2
Kanamycin	128	64	2	≥256	≥256
Tobramycin	16	16	0.25	0.25	0.25

\* The complete *qnrB6* gene was cloned into the vector pCR2.1 in sense with respect to the *lac* promoter; MICs were analyzed under the induction by 1 mM isopropyl-1-thio-β-D-galactopyranoside (IPTG).

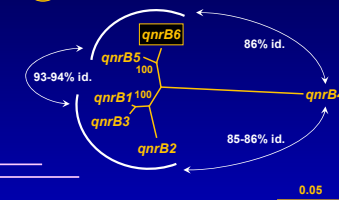
### 2 QUINOLONE RESISTANCE DETERMINANTS

	PCR			PCR + sequencing	
	<i>qnrA</i>	<i>qnrB</i>	<i>qnrS</i>	<i>aac(6')-Ib-cr</i>	<i>gyrA(QRDR)</i>
Kpn M7943	-	+	-	+	WT
E. coli M7943-Tc	-	+	-	+	ND

### 4 THE *qnrB6*-HARBORING COMPLEX CLASS 1 INTEGRON (InK122)



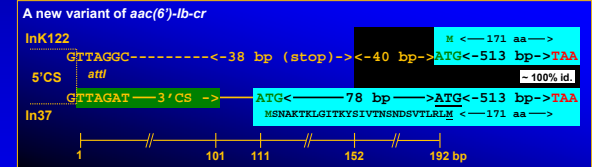
### 3 THE NEW *qnrB6* ALLELE



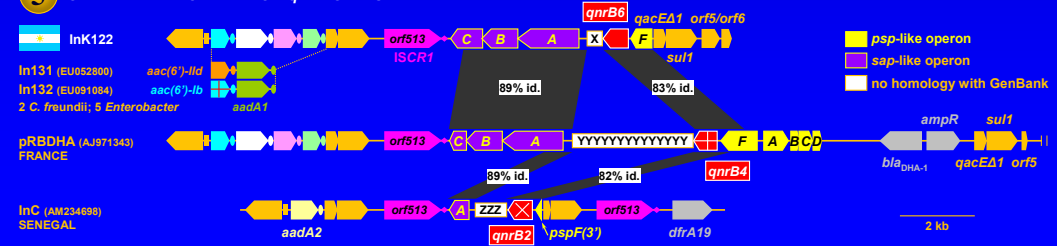
### Protein comparisons

	% of amino acid identity					
	QnrB1	QnrB2	QnrB3	QnrB4	QnrB5	QnrB6
QnrB1 (226 aa)	97.7	99.1	93.5	95.6	95.6	95.6
QnrB2 (214 aa)	5	97.7	93.0	96.7	96.7	96.7
QnrB3 (226 aa)	2	5	93.5	95.6	95.6	95.6
QnrB4 (216 aa)	14	15	14	95.3	95.3	95.3
QnrB5 (226 aa)	10	7	10	10	98.2	98.2
QnrB6 (226 aa)	10	7	10	10	4	98.2

No. of amino acid differences



### 5 GENETIC ENVIRONMENT OF *qnrB* GENES



## CONCLUSIONS

1. First report of *qnrB* and *aac(6')-Ib-cr* in Latin America.
2. New variants of *aac(6')-Ib-cr* and *qnrB* (*qnrB6* is now named *qnrB10*) were found in enterobacteria from Argentina.
3. A national surveillance is essential to estimate their prevalence.