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Plasmid-mediated resistance to quinolones

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Quinolones are broad-spectrum antibacterial agents, commonly used both in human and veterinary medicine. Their extensive use has been associated with raising level of quinolone resistance. The two main mechanisms of quinolone resistance are chromosomally encoded, being either modification of the quinolone targets with changes of DNA gyrase (*gyrA*) and/or topoisomerase IV (*parC*) genes, or decreased intracellular concentration due to impermeability of the membrane or overexpression of efflux pump systems. Although considered by many as unlikely, plasmid-mediated quinolone resistance does exist, firstly identified in a *Klebsiella pneumoniae* clinical isolate from the USA. The first described Qnr protein (lately termed QnrA) is a 218-amino acid protein belonging to the pentapeptide-repeat family of proteins that protects DNA from quinolone binding to topoisomerases. QnrA confers resistance to quinolones such as nalidixic acid and increases MICs of fluoroquinolones up to 32-fold in *Escherichia coli*. In addition, it favours selection of associated chromosome-encoded quinolone resistance determinants that confer additional resistance to fluoroquinolones. The QnrA-like determinants have been reported worldwide from many enterobacterial species and six variants have been identified so far (QnrA1 to QnrA6). Other plasmid-mediated quinolone resistance determinants, QnrB (QnrB1 to QnrB6) and QnrS (QnrS1 and QnrS2) have been also identified in enterobacterial species, sharing 41% and 60% amino acid identity with QnrA, respectively. The plasmid-encoded *qnr*-like genes have so far been identified only in Enterobacteriaceae. Recent findings showed that those genes originate from environmental Gram-negative bacterial species, such as *Shewanella algae* being the progenitor of the *qnrA*-like genes and *Vibrio splendidus* being the progenitor of *qnrS*-like genes. It has also been shown that many Vibrionaceae species may harbour chromosome-encoded *qnr*-type genes. Besides these Qnr-like resistance determinants, other mechanisms at the origin of reduced susceptibility to fluoroquinolones have been recently identified, like the production of the acylyltransferase AAC(6')-Ib-cr that acetylates ciprofloxacin and the production of the QepA protein that acts as an efflux pump. Both these latter mechanisms do not affect the action of nalidixic acid.

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Selected References for Further Reading

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