Correspondence

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Comment on: Quinolone resistance determinant qnrA3 in clinical isolates of Salmonella in 2000–2005 in Hong Kong

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Sir,

In their recent correspondence, Chu et al.,1 noted the first observation of qnrA3 in salmonellenae in Hong Kong,3 underlining the spread and diversity of plasmidic quinolone-resistance determinants worldwide. Such determinants now include qnrA1–5, qnrB and qnrS, some of which, at least, protect DNA gyrase,2 as well as the fluoroquinolone-acetylating variant of the aminoglycoside-modifying enzyme AAC(6′)Ib, named AAC(6′)Ib-cr.1 These proteins may influence the development of high-level resistance to at least some fluoroquinolones. In our recent article,5 we sought to explore the unexplained significant association between chromosomal fluoroquinolone resistance and plasmidic resistances to other antibiotic classes (such as ESBLs), which is seen in several bacterial genera.

We were pleased to note that Chu et al.1 cited our article,4 but would like to clarify a misinterpretation of our hypothesis. Multiresistance plasmids can encode toxin–antitoxin systems to prevent their own loss from the cell, and some toxins target DNA gyrase. We asked whether the development of quinolone resistance by plasmid-bearing strains might be associated with such DNA gyrase-targeting toxins. We speculated on whether a cell might escape addiction to toxin–antitoxin systems by developing resistance to the toxin. Mutational events in DNA gyrase could play a role in cells escaping addiction to plasmids with gyrase-targeting toxins, and we suggested that these mutations might fortuitously confer a degree of cross-resistance to quinolones. Notably, whilst at least three qnrA variants likely originated from the chromosome of Shewanella algae,3 and although Qnr-type proteins inhibit/protect DNA gyrase,6,7 their precise cellular role(s) remains unknown. We would like to emphasize that we did not state, or wish to imply, that Qnr proteins could be part of a toxin–antitoxin pair as was attributed to our article by Chu et al. Rather, we postulated that gyrase ‘inhibitors/protectors’ such as Qnr might give some cross-resistance to gyrase-targeting toxins in addition to the more obvious resistance to quinolones. By so doing these proteins might open a ‘window’ and influence the frequency at which cells could eject the toxin–antitoxin encoding replicons without suffering apoptosis, thereby providing the host organism with a toxin–antitoxin evasion mechanism. This might provide a competitive advantage in demanding psychrophilic aquatic environments, the natural environment of S. algae, by allowing enhanced ejection of ‘accessory’ replicons.

References

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Comment on: Human intravenous immunoglobulin for experimental streptococcal toxic shock: bacterial clearance and modulation of inflammation

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