Worldwide emergence of colistin resistance in Klebsiella pneumoniae from healthy humans and patients in Lao PDR, Thailand, Israel, Nigeria and France owing to inactivation of the PhoP/PhoQ regulator mgrB: an epidemiological and molecular study

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Résumé en anglais	The emergence of colistin-resistant *Klebsiella pneumoniae* (CRKP) is a major public health concern worldwide. In this study, the prevalence and molecular basis of colistin resistance in CRKP isolated from healthy individuals and patients in Lao PDR, Thailand, Nigeria and France were investigated. Stool samples were screened by culture for the presence of colistin-resistant *Klebsiella spp.* Whole-genome sequence analysis was used to decipher the molecular mechanism of colistin resistance in a blaNDM-1-positive in vitro-selected CRKP mutant. PCR amplification and sequencing of the mgrB genetic environment was performed for all CRKP isolates as well as control colistin-susceptible *K. pneumoniae* (CSKP) isolates recovered from the same stools. A total of 869 stool samples were screened for colistin-resistant Klebsiella spp., yielding 32 CRKP and 2 colistin-resistant *Klebsiella oxytoca*. Comparative whole-genome sequence analysis revealed that an in vitro-selected CRKP mutant had an insertion sequence in its mgrB gene, as well as missense mutations in other selected clones. Of the 34 colistin-resistant *Klebsiella spp.* isolates, 14 (41.2%; 13 CRKP and 1 *K. oxytoca*) from the four countries also had various defects in their mgrB genes, but no such defects were found in the CSKP controls (P<10(-4)). Few mutations were observed in pmrAB compared with mgrB among the CRKP isolates. The worldwide emergence of CRKP is a major public health concern. Detection and surveillance of such strains are warranted to prevent an uncontrollable pandemic. Inactivation of the PhoP/PhoQ regulator gene mgrB is associated with ≥40% of colistin resistance among the CRKP isolates observed in this study.
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