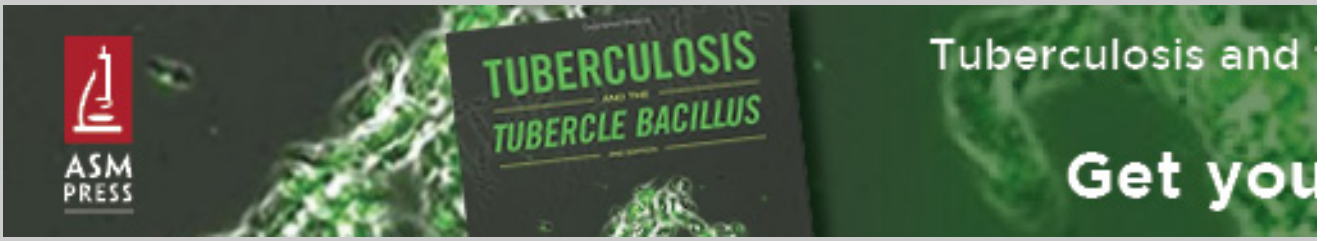

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

Characterization of a New Metallo- -Lactamase Gene, *bla*$_{NDM-1}$, and a Novel Erythromycin Esterase Gene Carried on a Unique Genetic Structure in *Klebsiella pneumoniae* Sequence Type 14 from India

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ABSTRACT

A Swedish patient of Indian origin traveled to New Delhi, India, and acquired a urinary tract infection caused by a carbapenem-resistant *Klebsiella pneumoniae* strain that typed to the sequence type 14 complex. The isolate, *Klebsiella pneumoniae* 05-506, was shown to possess a metallo- -lactamase (MBL) but was negative for previously known MBL genes. Gene libraries and amplification of class 1 integrons revealed three resistance-conferring regions; the first contained *bla*$_{CMY-4}$ flanked by IS*EcP1* and *blc*. The second region of 4.8 kb contained a complex class 1 integron with the gene cassettes *arr-2*, a new erythromycin esterase gene; *ereC*; *aadA1*; and *cmlA7*. An intact IS*CR1* element was shown to be downstream from the *qac*/*sul* genes. The third region consisted of a new MBL gene, designated *bla*$_{NDM-1}$, flanked on one side by *K. pneumoniae* DNA and a truncated IS*26* element on its other side. The last two regions

lie adjacent to one another, and all three regions are found on a 180-kb region that is easily transferable to recipient strains and that confers resistance to all antibiotics except fluoroquinolones and colistin. NDM-1 shares very little identity with other MBLs, with the most similar MBLs being VIM-1/VIM-2, with which it has only 32.4% identity. As well as possessing unique residues near the active site, NDM-1 also has an additional insert between positions 162 and 166 not present in other MBLs. NDM-1 has a molecular mass of 28 kDa, is monomeric, and can hydrolyze all -lactams except aztreonam. Compared to VIM-2, NDM-1 displays tighter binding to most cephalosporins, in particular, cefuroxime, cefotaxime, and cephalothin (cefalotin), and also to the penicillins. NDM-1 does not bind to the carbapenems as tightly as IMP-1 or VIM-2 and turns over the carbapenems at a rate similar to that of VIM-2. In addition to *K. pneumoniae* 05-506, $bla_{\text{NDM-1}}$ was found on a 140-kb plasmid in an *Escherichia coli* strain isolated from the patient's feces, inferring the possibility of in vivo conjugation. The broad resistance carried on these plasmids is a further worrying development for India, which already has high levels of antibiotic resistance.

FOOTNOTES

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