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MOBILIZATION OF blaNDM-1 GENETIC PLATFORMS FROM A LOCAL *Acinetobacter bereziniae* CLINICAL ISOLATE

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Acinetobacter is an aerobic Gram-negative genus ubiquitous in nature. Some species are opportunistic human pathogens being carbapenem-resistant (*carbR*) *A. baumannii* (Ab) frequently isolated from nosocomial infections. However, other species have been associated with clinical infections including *A. bereziniae*. Aminoglycosides (AG) and carbapenems are commonly employed therapeutic options for *Acinetobacter* infections. The *carbR* *A. bereziniae* clinical local isolate HPC229, harboring pNDM229 plasmid was characterized in our group. pNDM229 carries *blaNDM-1* responsible of the *carbR*, inserted in a Tn125 transposon, and an AG-resistance gene, *aphA6*, upstream of Tn125. In addition, an ISAbA14 insertion sequence is located upstream of *aphA6*, resulting in the ISAbA14-*aphA6*-Tn125 structure, widely distributed in *carbR* *Acinetobacter* strains. In pNDM229, an extra ISAbA14-like was also found immediately downstream of Tn125, suggesting the formation of a new composite transposon, Tn14. Here we characterize the dissemination of *blaNDM-1* from *A. bereziniae* HPC229 to other *Acinetobacter* species by horizontal gene transfer (HGT). Sensitive strains such as *A. nosocomialis* M2 (An M2), *A. baylyi* ADP1 (ADP1) and Ab ATCC17978 were transformed employing the total HPC229 plasmid content (pHPC229), and further selected for *carbR* using imipenem (IMPR). The genetic context of *blaNDM-1* was characterized by PCR/sequencing. Transformation experiments with pHPC229 resulted in IMPR clones harboring *blaNDM-1* when Ab 17978 was used. Thus, indicating not only the mobilization of this resistance gene, but also its functionality in this host. Interestingly, some of these clones exhibited additional amikacin resistance (AKNR) or reduced sensitivity (AKNS*). PCR amplification of different marker regions for Tn125, Tn14 or pNDM229 in the Ab 17978/pHPC229 IMPR/AKNR/S* clones, suggested the successful mobilization of pNDM229 from *A. bereziniae* to *A. baumannii*. On the other hand, transformation assays did not yield IMPR clones when An M2 or ADP1 were used, suggesting pNDM229 as a non-permissive plasmid in these hosts. Additional An M2 transformation with plasmid content from both Ab 17978/pHPC229 phenotypes, resulted in An M2 IMPR clones with varying AKN sensitivities. PCR analysis in An M2 transformants with intermediate AKN resistance (AKNI), and AKN sensitive (AKNS), identified two distinct *blaNDM-1* mobilization platforms: pNDM229 and Tn125, respectively. Thus, suggesting that the *blaNDM-1* gene is located on different genomic platforms within the Ab 17978/pHPC229 plasmid content, capable of further dissemination by HGT and

replicating in An M2. Altogether, our results show for the first time that HPC229 resistance genes are susceptible to dissemination by HGT to other *Acinetobacter* species. Further characterization of Ab17978/pHPC229 and An M2 re-transformant clones will allow us to understand the diversity of plasmid structures carrying *bla*NDM-1 gene in clinical *Acinetobacter* strains.

Palabras clave: *Acinetobacter bereziniae* - NDM_1 - carbapenem resistance - plasmids