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MOBILIZATION OF XER MODULES IN *Acinetobacter baumannii*: IMPLICATIONS FOR PLASMID DYNAMICS AND EVOLUTION

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Acinetobacter baumannii (Ab) is a Gram-negative opportunistic pathogen that represents a major cause of nosocomial infections. The alarming increase in multidrug-resistant (MDR) Ab strains reported worldwide highlights the urgency of understanding the evolutionary dynamics of the pathogen in clinical settings. In this context, mobile genetic elements (MGE) such as plasmids, transposons, insertion sequences, etc. promote the dissemination of antimicrobial resistant genes (ARG), heavy metals-detoxification systems and other traits such as virulence factors, as they play a vital role in facilitating horizontal gene transfer (HGT) within a microbial population. In recent years, it has been discussed that XerC/D-site specific recombination (SSR) represents an alternative pathway mediating ARGs transfer within plasmids in Ab. Ab244, Ab242, and Ab825 are MDR A. baumannii strains belonging to the CC15 clonal complex (CC) isolated from patients hospitalized in Clemente Alvarez Emergency Hospital in Rosario, Argentina. Ab825 and Ab242 also display carbapenem resistance (*carbR*). They harbor plasmids endowed with blaOXA-58- and TnaphA6-containing resistance modules bounded with pXerC/D sites. We recently described how pXerC/D-mediated recombination generates structural variants of the carbR plasmid. We have developed a series of methodologies that allowed us to disclose the existence of bona fide pairs of recombinationally-active pXerC/D sites in these plasmids, some of which mediate reversible intramolecular inversions and others reversible plasmid fusions/resolutions. Here, we describe additional plasmid architectures from pXerC/D site-mediated fusion and resolution events involving circular Xer modules in these carbR strains. Using transformation assays and PCR amplification, we identified a novel mechanism for intragenomic plasmid rearrangements, resulting in gene mobilization between co-resident plasmids of Ab242 and Ab825, mediated by circular Xer modules. Furthermore, we were able to show that these dynamic events are not limited to our clinical isolates, but also occur in another Ab strain. Sequence analysis of the involved Xer module revealed a high degree of conservation across the Acinetobacter genus, despite variability in the surrounding genomic environments. This suggests that this Xer module plays relevant roles during evolution and that the mobilization mechanism is also conserved within the genus. Although more work is needed to uncover the role of pXerC/D sites in plasmid evolution, our findings indicate that this mechanism significantly contributes to genetic diversity within *Acinetobacter* species and likely promotes the spread of resistance determinants.

Palabras clave: *Acinetobacter baumannii* - plasmid dynamic - Xer recombination
- blaOXA-58