Interplay between the Xer system and the dissemination of antibioresistance in Acinetobacter baumannii

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Abstract

Antibiotic-resistant (AR) infections pose a pressing challenge in clinical settings. Plasmids are widely recognized for hastening the emergence of AR by facilitating horizontal gene transfer of antibiotic resistance genes (ARG) among bacteria (1,2). To comprehend the dynamics of ARG, it's crucial to grasp the evolution of plasmid strategies geared toward maximizing their persistence and dissemination within bacteria. These strategies may hinge not only on interactions with their bacterial hosts but also on interactions among plasmids themselves.
We explore this inquiry in *Acinetobacter baumannii* (*Ab*), given preliminary evidence suggesting positive interactions between plasmids during the emergence of AR in this bacterium. *Ab* is a globally emerging nosocomial pathogen responsible for a wide array of infections. Genomic scrutiny of the diversity of *Ab* plasmids has revealed that Rep_3 plasmids harbor adaptive genes within variable regions, whose acquisition or loss is believed to involve the Xer recombination pathway. An illustrative instance is the pABV01 plasmid, carrying the *blaOXA24* gene (conferring resistance to carbapenems) flanked by inverted Xer recombination sites (*xrs*). While the backbone of this plasmid closely resembles previously described ones, the region flanked by two *xrs* sites exhibits variability (1). Consequently, it has been postulated that these "*xrs*-cassettes" could constitute a novel mobile genetic element family, mobilized by the conserved Xer recombination system (2,3).

Employing genetic and molecular methodologies, we have tested this hypothesis. Our findings demonstrate that the Xer system of *Ab* is conventional, but "*xrs*-cassettes" do not constitute excisable genetic elements. Intriguingly, we reveal that Xer facilitates recombination between different types of *Ab* plasmids, generating and resolving cointegrate forms. This mechanism elucidates how "*xrs*-cassettes" are exchanged between *Ab*plasmids through interactions among distinct plasmids, offering a fresh perspective for comprehending the dynamics of ARG within bacteria.

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