INTRODUCTION

Since the discovery of penicillin in 1928, antibiotics have been used worldwide to treat illness resulting from colonization of pathogenic bacteria. The most widely prescribed penicillin-based antibiotics are β-lactams (Figure 1A).1 β-lactams work by interfering with cell-wall synthesis by inhibiting penicillin-binding proteins (PBPs). Numerous resistance mechanisms oriented toward β-lactams have emerged over the years. The most common resistance mechanism is the expression of β-lactamases, enzymes that are able to hydrolyze the β-lactam ring, which renders the antibiotic useless.2 These resistance mechanisms pose a massive threat to the effectiveness of β-lactams. Even with the development of carbapenems, β-lactams designed to bypass β-lactamases, carbapenem-resistant Enterobacteriaceae (CRE) such as Klebsiella pneumoniae have arisen. The emergence of CRE highlights the need for a better understanding of the various mechanisms of resistance towards β-lactam antibiotics.

In addition to β-lactamases, many species of Enterobacteriaceae also express L,D-transpeptidases (Ldt) which are structurally and functionally different enough from D,D-transpeptidases (PBPs) to not be recognized by β-lactams.3 Ldts form a different crosslink in the peptidoglycan layer of the cell-wall of bacteria than PBPs (Figure 1B). While Ldts do not normally serve as the primary pathway of cell-wall biosynthesis, it is hypothesized that while under pressure from a β-lactam, Ldts can assume a primary role and allow the bacteria to survive. CRE are an ever-growing problem in the umbrella of antibiotic resistance, as they are a large source of hospital-acquired infections and are often life-threatening.4 Because of this, it is important to determine which, if any, β-lactam antibiotics are able to retain activity against the Ldts expressed by CRE organisms.

REFERENCES & FUNDING

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