

# Acquisition of Colistin Resistance Links Cell Membrane Thickness Alteration with a Point Mutation in Lpxd Gene in Acinetobacter BaumanniLinn

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## Abstract

*Acinetobacter baumannii* is one of the most common causes of nosocomial infections in intensive

care units. Its ability to acquire diverse mechanisms of resistance limits its therapeutic choices. Multi-drug resistant *A. baumannii* became a critical challenge for common antibiotic treatments. Colistin is an old antibiotic that has been reused recently, as a last resort drug, for *A. baumannii*. In this study, we explored the impact of gaining colistin resistance on the susceptibility to other antibiotics and linking the resistance acquisition to its genetic basis. The susceptibility of 95 *A. baumannii* isolates revealed that 89 isolates were MDR with five isolates resistant to colistin. Subsequently, three isolates, -MS48, MS50, and MS64-, exhibited different resistance pattern, when exposed to colistin resistance induction. The susceptibility profiles reevaluation showed the gain of resistance to almost all tested antibiotics for MS50Col-R and MS64Col-R isolates, while the resistance pattern of MS48Col-R remained unchanged. Upon TEM examination, morphological alterations compared to parent sensitive strains, have been reported for all of the induced isolates, also to an isolated colistin-resistant clinical isolate (MS34Col-R). Finally, genetic alterations in PmrB and LpxACD were assessed, in which a point mutation in LpxD in MS64Col-R mutant and the colistin-resistant isolate MS34Col-R at Lys117Glu was identified in the lipid-binding domain. Our findings shed light on the implications of using colistin in the treatment of *A. baumannii*, especially in sub-MIC concentrations, where co-resistance to other classes of antibiotics may emerge beside the rapid acquisition of resistance against colistin itself due to distinct genetic events

## Article Information

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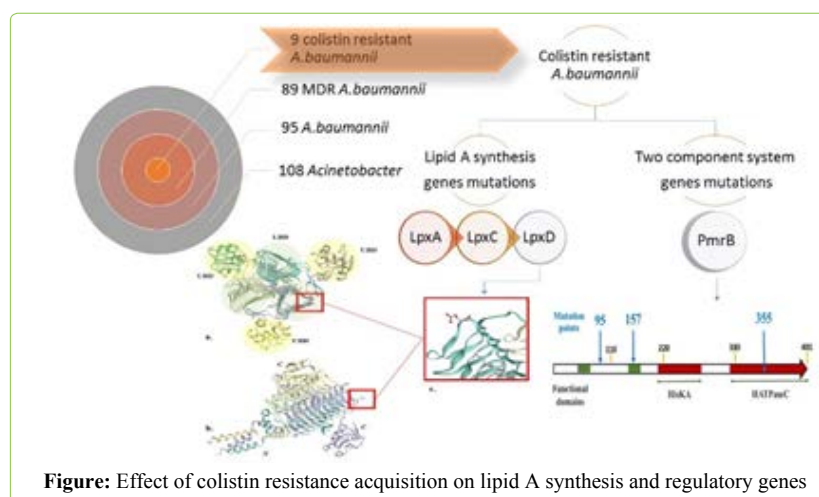
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**Figure:** Effect of colistin resistance acquisition on lipid A synthesis and regulatory genes