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O0399 *De novo* mutations in lipopolysaccharide biosynthesis pathways reveal the colistin resistance mechanism in *Acinetobacter baumannii* strains

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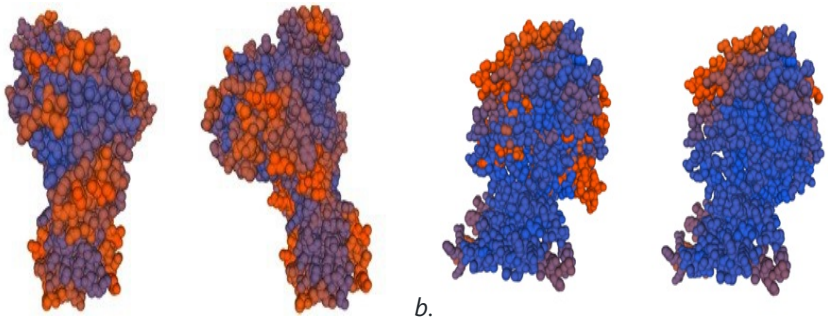
***de novo* mutations in lipopolysaccharide biosynthesis pathways reveal the colistin resistance mechanisms in *Acinetobacter baumannii* strains**

Background: Multidrug resistant gram negative bacteria especially *A. baumannii* cause infections with limited therapeutic alternatives and high mortality worldwide. In recent years "colistin" -as an old drug that fell out of favor due to its nephrotoxicity- has begun to be used again for the treatment of such infections. Nowadays with the increased use of colistin, resistant pathogenic strains have emerged. This situation extremely narrows down the treatment options and strategies to mitigate the colistin resistance in *A. baumannii* are in need. In this study, two colistin resistant and one colistin susceptible *A. baumannii* strains isolated from patients hospitalized an University Hospital Intensive Care Units between June 2014-June 2015 were considered to be whole-genome sequenced and subject to comparative genomics to discover the genetics origins of colistin resistance mechanisms.

Materials/methods: The species and antimicrobial susceptibility validation were conducted by conventional methods. The DNA isolation of the chromosomes and the plasmids via commercial kits were followed by whole genome sequencing using Illumina-MiSeq sequencer. The genomes were assembled and annotated using IDBA assembler, GeneMark, and RAST software. Annotated genetic elements were compared to 3027 previously sequenced *A. baumannii* using blast. Protein modeling was performed by SWISS-MODEL.

Results: Mobile genetic genes of colistin resistance were not detected in the strains. Comparing lipopolysaccharide biosynthesis pathway genes to the rest of the sequenced strains, novel mutations resulting in structural changes in the tertiary structure of the corresponding proteins were detected. Residual changes in *PmrB* and *vacJ* genes were prediced to alter the structure of these pathway proteins in one strain, while similar characteristics was observed for *eptA* gene in the second.

Conclusions: The detected mutations are in accordance with the variations in previously reported colistin resistant strains, although those mutations were not annotated. These results might provide insight for colistin resistance mechanisms in *A. baumannii*.



a. *b.*

Figure 1. a. 3D protein structure of pmrB gene (a) and eptA gene (b) in colistin resistant (rigth) and susceptible (left) *A. baumannii* strains