

## INFORMATION OF DOCTORAL DISSERTATION

**Thesis name:** *Molecular mechanisms associated with nosocomial carbapenem-resistant Acinetobacter baumannii in Thonghat General hospital of Dongnai province.*

**Major:** Medical Microbiology - Biotechnology

**Major Code:** 60420201

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### *The main results of the thesis:*

1. All 105 strains of multidrug-resistant *A. baumannii*, which cause infectious diseases in Dong Nai General Hospital, were not 100% sensitive to most antibiotics for the treatment of Gram-negative bacilli. *Acinetobacter baumannii* was 100% sensitive to only one antibiotic, named colistin and 99.1% to tigecycline. Meropenem/colistin and meropenem/rifampicin showed strong synergistic and additive effects on *A. baumannii*, accounted for 94.3% and 81.9%, respectively. However, the combination of tigecycline and colistin only showed synergistic and additive effects at just 36.2%. Effects of colistin at concentrations of 1 µg/ml or rifampicin at 2 µg/ml under MIC are likely to transfer the *A. baumannii* from meropenem insensitivity to meropenem in a high. Considering group of gens related to carbapenem resistance, the study showed that genes encoding the class-D carbapenemase, namely *bla*<sub>OXA-51</sub>, *bla*<sub>OXA-23</sub>, *bla*<sub>OXA-58</sub> were distributed in *A. baumannii* with 97.1%; 79% and 7.6% respectively. Meanwhile, the figure for *bla*<sub>NDM-1</sub>, genes encoding class B carbapenemase were about 13.3% and gene *bla*<sub>KPC</sub> encoding the A-type carbapenemase in *A. baumannii* has not been reported. In this study, 93.3% of multidrug-resistant *A. baumannii* strains had an

*Aba1* insertion sequence (*ISAbal*). Furthermore, carbapenem resistant in multidrug-resistant *A. baumannii* is due to the accumulation of resistant genes, with 80% of those containing three genes associated with carbapenem resistance simultaneously and 97.6% of which have *ISAbal* in three genes.

2. Assembly of whole-genome shotgun sequences of strain DMS06669 and DMS06670 yielded an estimated genome size of 4.2Mb and 3.8 Mb. In this manner, the identification of potential antibiotic resistance genes was conducted, and we predicted that the probability of *A. baumannii* DMS06669 (our strain in previous study) and DMS06670 as a human pathogen is 85.8% and 85.3%, with 632 and 622 pathogenic families, respectively. Additionally, the clusters of orthologous groups (COGs) analysis in protein sequence of *A. baumannii* strain DMS06669 and DMS06670 was compared with the other four genomes showed that the orthologous protein clusters responsible for multi-drug exist inside highly antimicrobial resistant strains. Phylogenetic analysis revealed that, based on the average nucleotide identity value, *A. baumannii* DMS06670 is a sister group to the LAC-4 and BJAB0715 strains of *A. baumannii* while *A. baumannii* strain DMS06669 is a sister group to strains ATCC\_17978, D1279779, ZW85-1, ab031, and SDF.

3. Comparative analysis of twenty-three available genomes of *A. baumannii* strains revealed a pan-genome consisting of 15,883 genes. Antibiotics resistance genes *in-vitro* (19 genes) were isolated by PCR and re-confirmed by improved Sanger method.

### ***The new scientific findings***

1. In this research, *A. baumannii* shows low susceptibility with Bactrim (26,4%), intermediate with rifampicin (59,5%) and high susceptibility with tigecycline (99,1%).

2. The efficacy of Tigecycline/Colistin on carbapenem-resistant *A. baumannii* is lower than that of meropenem/colistin and meropenem/rifampicin.
3. Knowing some genes associated with carbapenem resistance in *A. baumannii* contributes more information about carbapenem-resistant status in Dong Nai Province.
4. There are 9 antibiotic resistance genes that have not been previously published in *A. baumannii* strains, including 2 novel genes related to beta-lactam antibiotic resistance. Whole genome sequencing data also provided prophage regions in *A. baumannii*, species-specific proteins and virulence factors can be the basis for further research on molecular pathogenesis studies and research for *A. baumannii* vaccine.
5. The research supplies 19 nucleotide sequences of drug-resistant genes in *A. baumannii* and one of them is *bla*<sub>CARB-2</sub> which has never been isolated before. *Bla*<sub>CARB-2</sub> genes encoding for beta lactamase and is proved to be a factor responsible for beta-lactam resistance in *A. baumannii*.

**Advisors**

**PhD Student**

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