POSTER - DNA AND GENOMICS

GENOME-WIDE ASSOCIATION STUDY IN CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII

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Acinetobacter baumannii, a ubiquitous environmental bacterium, is prevalent on various biotic and abiotic surfaces, including soil, water, and living organisms. Its presence extends to hospital environments, where it poses a significant risk, causing a series of infections, such as urinary tract, bloodstream and pneumonia, often resulting in high mortality rates. Nosocomial outbreaks of A. baumannii highlight its potential for virulence and antimicrobial resistance. Carbapenem-resistant strains of A. baumannii, in particular, have gained notoriety and are listed by the World Health Organization as critical organisms threatening global health, highlighting the urgent need for research and development of new treatment strategies. With the aim of finding genetic variants related to resistance to the carbapenem antibiotics imipenem and meropenem, we performed a genome-wide association analysis (GWAS) of A. baumannii resistant or sensitive to these antibiotics. The A. baumannii genomes used in this study were retrieved from the BV-BRC database. Only genomes of A. baumannii strains resistant or sensitive to both antibiotics together were included, for which the minimum inhibitory concentration (MIC), determined

experimentally, was available. All genomes were reannotated using the prokka v.1.14.5 program. Core-genome identification was done using the Roary v.3.13.0 program. The GWAS analysis was performed using the pyseer v.1.3.10 program based on the variability of kmers using the linear mixed model (LLM). The counting of kmers from the genomic sequences was performed using the fsm-lite program. To correct the population structure, the phylogenetic tree produced from the core-genome was used. 182 genomes of A. baumannii resistant to imipenem and meropenem and 169 genomes of A. baumannii sensitive to imipenem and meropenem were selected. Strains whose MIC for meropenem and imipenem was equal to or greater than 8 mg/ml were considered resistant, and strains with an MIC equal to or less than 4 mg/ml were considered resistant to meropenem and imipenem. In total, 7,836,737 kmers containing genetic variants related to resistance to imipenem/meropenem were identified, but only 3,278 were considered significant ($p < 6.38\text{-}9$). Of these, 1,676 kmers were identified and annotated in 227 genes. The mapping of significant kmers in the reference genome of the type strain of A. baumannii (ATCC19606) identified genetic variations related to resistance to imipenem/meropenem in 9 genes, including the transcriptional regulators adeL and fadR, the phage protein tpm and a tnsAB recombinase. The GWAS analysis performed in this study brought new information about genetic variants related to resistance to the carbapenem antibiotics imipenem and meropenem in A. baumannii. These findings are crucial to understanding the genetic basis of antimicrobial resistance in this critical pathogen, pointing to potential therapeutic targets and highlighting the continued urgency of research and development strategies to combat A. baumannii infections.

Palavras-chave: acinetobacter baumannii; carbapenem; gwas.