

Comparative NanoUPLC-MS^E analysis between magainin I- susceptible and - resistant *Escherichia coli* strains

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INTRODUCTION. Nosocomial infections and the emergence of multidrug-resistant bacteria represent a serious public health problem. One of the strategies adopted to overcome the bacterial resistance phenomenon is the usage of antimicrobial peptides (AMPs) such as cecropins, batenecins and magainins. Interestingly, however, studies have shown that AMPs can also select resistant bacteria.

OBJECTIVE: Thus, in order to clarify these controversial ideas, we applied proteomics and transcriptomics tools to evaluate genes and proteins differentially expressed in *E. coli* (ATCC 8739) magainin I-resistant and -susceptible strains.

MATERIAL AND METHODS: Biochemical characterization was performed by broth microdilution, VITEK®, MicroScan® and MALDI-ToF. Transcripts and protein production were analyzed by RNA-seq, nanoUPLC-MS^E.

DISCUSSION AND RESULTS: Results demonstrated that resistant strains could be discriminated by MALDI-ToF. Also, VITEK® and MicroScan® analyses revealed that both susceptible and magainin-resistant strains were eliminated by all the 27 conventional antibiotics tested, indicating a specific resistance of these strains to magainin. Ten proteins were up regulated including OmpW, OmpF, OmpC and OmpC-1b fragment. Otherwise, fifteen proteins, including GlpB, GlpA, GdpD, transcriptional factor regulator kdgR, DPS and DnaK, were down regulated in the resistant strains. The up regulated proteins seem to be associated to membrane transport and signal transduction, while the down regulated proteins might participate in phospholipid metabolism and genetic information processing. It was also observed 60 unique proteins in the resistant strains involved in bacterial metabolism, genetic and environmental information processing. RNA-Seq analyses have also revealed 80 genes with differential expression in the resistant strain, mainly related to metabolism. Comparison between resistant vs susceptible groups showed five differential expressed genes, being three of them overexpressed (*pspA*, *secM*, *xdhB*) and the others subexpressed (*cdp*, *hldD*). **CONCLUSIONS:** These data suggest that the bacterium was able to develop an adaptation mechanism in response to magainin, probably regulating a complex net formed by multiple genes.

Keywords: HAIs, bacterial resistance, magainin I, *E. coli*, transcriptomics and proteomics tools

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