

TITLE: ANALYSIS OF REGULATORS HOMOLOGOUS TO MarR IN

Bacteroides fragilis

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ABSTRACT:

Bacteroides fragilis is a Gram-negative rod found in humans microbiota. Despite this fact, it is the anaerobe most commonly isolated from endogenous infections in extraintestinal tissues. The expression of virulence factors contributes to the prevalence of this microorganism in clinical settings. Among anaerobes, *B. fragilis* is one of the most aerotolerant microorganisms, and can survive in aerobic environments for up to 72 hours. One of the consequences of exposure to oxygen is the formation of free radicals that are harmful to the microorganism. *B. fragilis* has a response that controls the expression of several genes involved in detoxification. The expression of these genes is controlled by transcriptional regulators, including those of the MarR family. Three homologues, BmoR, MarRI and MarRII, linked with the oxidative stress response and antimicrobial resistance in *B. fragilis* strain 638R were identified. However, much still needs to be studied regarding the mechanism involved in these regulatory processes. The aim of this work is to characterize the function of the regulators belonging to the MarR family in *B. fragilis*. *In silico* analyzes were carried out. Multiple alignment between these proteins showed little similarity between their amino acid residues, except for those located in the wHTH binding site. Secondary structure prediction showed that all of them have a fairly conserved secondary structure. Phylogeny prediction of these regulators also showed that, in evolutionary terms, the regulator BmoR followed a different evolutionary course when compared to MarRI and MarRII. Also, based on analyzes performed in the KEGG database, it is believed that the *marRI* and *marRII* genes are involved in antimicrobial resistance, and *bmoR* appears to be associated with regulation of oxidative stress response. Heterologous expression of MarRI, MarRII and BmoR were performed, and the purified proteins were used in EMSA assays to determine DNA binding sites. *bmoR* mutants were exposed to peritoneal and medullar macrophages, there were no difference in the survival of the mutant when compared to the wild-type strain independent of the cell that they were exposed, but when we evaluated the ability to form abscesses in C57BL/6 mice it was observed that the absence of *bmoR* led to decreased virulence. We hope that with these results we can contribute to the understanding of a vital mechanism for the survival of this microorganism that is the response to oxidative stress.

Keywords: *Bacteroides fragilis*, transcriptional regulation, oxidative stress, anaerobic bacteria, antimicrobial resistance

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