Title: IDENTIFICATION OF A MarR FAMILY TRANSCRIPTION FACTOR CONTROLLING VIRULENCE IN *Chromobacterium violaceum*

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Abstract:

Transcription factors play key role in gene expression control in all living organisms. MarR family transcription factors, found in Bacteria and Archaea, are able to sense small compounds as intracellular signals to control many biological processes, such as virulence, response to oxidative stress, antibiotic resistance and catabolism of aromatic compounds. In this work, our goal is identify and characterize MarR family transcription factors controlling virulence in *Chromobacterium violaceum*, an opportunistic pathogen of humans. Using i*n silico* analyzes in protein databases, we identified fifteen MarR family regulators in the *C. violaceum* genome. Five of these fifteen proteins have conserved cysteine residues, suggesting that they can be redox sensing transcription factors. Null mutants were generated for eight of these MarR genes by allelic exchange mutagenesis. It was also generated a mutant strain of *cilA* gene which encodes a global virulence regulator of the Cpi-1/-1a pathogenicity island. In viability tests, all eight MarR mutants and the *cilA* mutant were as viable as the wild-type strain, after 24 hours cultivation in LB medium. In virulence tests, when introduced by intraperitoneal injection in BALB/c mice, a MarR mutant strain, here called MarR1, was less virulent when compared to the wild-type strain ($p=0.0046$), while the other seven MarR mutants showed no difference. As expected, the *cilA* mutant was highly attenuated for virulence. Further analyses of the MarR1 gene indicate its co-localization with other possible virulence genes in the *C. violaceum* genome. In addition, the MarR1 protein has a highly conserved Cys77 residue, indicating that its activity can be modulated by oxidation-reduction. Therefore, we demonstrate that the MarR family transcription factor MarR1 is an important virulence determinant in *C. violaceum*.

Keywords: gene regulation, transcription factors, MarR family, *Chromobacterium violaceum*, bacterial virulence, oxidative stress.

Financial Support: FAPESP and **FAEPA**.