

**TITLE:** THE TRANSCRIPTION FACTORS OF UrtR subfamily ARE INVOLVED WITH THE CONTROL OF VIRULENCE IN *Chromobacterium violaceum*

**AUTHORS:** PREVIATO-MELLO, M.; DA SILVA NETO, J.F.

**INSTITUTION:** DEPARTAMENTO DE BIOLOGIA CELULAR E MOLECULAR E BIOAGENTES PATOGÊNICOS, FACULDADE DE MEDICINA DE RIBEIRÃO PRETO, UNIVERSIDADE DE SÃO PAULO (AV. BANDEIRANTES, 3900 - MONTE ALEGRE - CEP: 14049-900 RIBEIRÃO PRETO, SÃO PAULO, BRAZIL)

**ABSTRACT:**

Transcription factors have an important role in gene expression control in all organisms. MarR family transcription factors, found in Bacteria and Archaea, act as intracellular sensors of multiple signals and control many processes in bacteria, such as virulence, response to oxidative stress, antibiotic resistance, and catabolism of aromatic compounds. *Chromobacterium violaceum*, an environmental bacterium found in water and soil in tropical and subtropical areas, is an opportunistic pathogen of humans that has fifteen MarR family transcription factors, but the function of many of them remains unknown. We have previously generated null mutant strains for most of these MarR genes and tested some of them in virulence assays. In this work, we studied two members of this family in *C. violaceum*, named here *urtR1* and *urtR2*. Using *in silico* analyzes in protein databases, we identified two MarR family regulators in the *C. violaceum* genome belonging to the UrtR subfamily, which covers the urate-responsive MarR family transcription factors. Multiple alignments of the amino acid sequence of these UrtR proteins of *C. violaceum* revealed conservation pattern in the primary amino acid sequence, with the characteristic N-terminal extension, absent in the classic MarR transcription factors, and the presence of the conserved amino acids tryptophan (W), aspartic acid (D) and two arginines (R), involved in the binding to urate. In virulence tests, when introduced by intraperitoneal injection in BALB/c mice, the  $\Delta urtR1$  mutant strain were less virulent, while the  $\Delta urtR2$  was more virulent, when compared to the wild-type strain. Unexpectedly, the  $\Delta urtR1/urtR2$  double mutant was highly attenuated for virulence. To define the regulon of UrtR2 transcription factor, the gene expression profiles were determined by DNA microarray analysis and Northern blot assays. The UrtR2 regulon contains dozens of genes, many of them related to amino acid catabolism, but there are few candidates for classical virulence factors (*pecM*, *escU*). Some genes related to catabolism/utilization of purine were regulated by both UrtR1 and UrtR2 and responded to the presence of urate. In conclusion, we have defined that *C. violaceum* uses the transcription factors of the UrtR subfamily, UrtR1 and UrtR2, to modulate its virulence.

**Keywords:** Bacterial virulence, transcription factors, MarR family, UrtR subfamily, *Chromobacterium violaceum*.

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