TITLE: ANALYSIS OF THE INFLUENCE OF THE TRANSCRIPTIONAL REGULATOR COVR IN LOW SUSCEPTIBILITY OF *Streptococcus mutans* STRAINS ISOLATED FROM BLOOD TO OPSONIZATION BY THE COMPLEMENT SYSTEM.

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ABSTRACT:

Streptococcus mutans (SM) is a common bacterial species of the oral cavity of humans involved in the pathogenesis of dental caries, which can also promote infective endocariditis after accessing the bloodstream from oral niches. The SM transcriptional regulator CovR represses transcription of genes for evasion to complement system, an important host immune defense of the bloodstream. Recently we observed that SM strains involved in systemic infections show low expression of *covR*, associated with up-regulation of downstream genes involved in complement evasion.The aim of this study was to identify polymorphisms in *covR* locus among SM strains isolated from systemic infections, which could be associated with alteration in CovR expression or function. To this purpose, we amplified and sequenced the *covR* locus of seven SM strains isolated from blood of patients with systemic infections and from eleven strains isolated from the oral cavity. PCR reactions were performed with primers designed to amplify sequences of 1316 bp, which included *covR* promoter and CovR encoding regions. Amplicons were purified and subjected to DNA sequencing using ABI 3500 Genetic Analyzer. The sequences of the *covR* locus were then subjected to BLAST and clustalW multiple sequence alignment for polymorphism identification. A total of ten *covR* mutations were identified. These included nine silent mutations in *covR* ORF and one missense mutation. The promoter regions of *covR* accounted for the highest frequency of polymorphisms. A total of fourteen polymorphisms were detected in these regulatory regions, and 71,43% of these were detected in three strains isolated from blood (SA13, SA14 e SA18). These results show that whereas the encoding region of *covR* is highly conserved, the *covR* regulatory region is more variable, specially among strains associated with systemic infections. This study was supported by FAPESP; proc. 2015/22967-6 and 2015/12940-3.

Keywords: Streptococcus mutans, CovR, systemic virulence, gene regulation.

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