Structural and Functional Analysis of *Klebsiella pneumoniae* Ferric Uptake Regulator

Stuchi, L.P.¹; Gomes, A.E.I.¹; Borges, L.¹; Ribeiro, M.L.²; Pedrazzoli Jr, J.²; Vicentini, R.³; Ferraz, L.F.C.¹

¹Laboratório de Biologia Molecular e Farmacologia, e ²Laboratório de Biologia Molecular/UNIFAG, Universidade São Francisco, Bragança Paulista, SP; ³CBMEG, Universidade Estadual de Campinas, SP, Brazil.

*Klebsiella pneumoniae* is a gram-negative opportunistic pathogen that may causes a variety of infections, such as pneumonia, meningitis, septicemia, among others. An essential step during colonization is the ability of the pathogen to obtain iron from the host. The microorganisms have evolved iron acquisition systems that are closely linked to virulence-related genes. Transcriptional regulation by iron is mediated by Fur, the ferric uptake regulator. Fur, encoded by *fur* gene, regulates gene expression by binding to specific DNA sequences, named Fur boxes, located at the promoter region of target genes. Fur regulates not only genes involved in iron homeostasis but also genes related to bacterial pathogenesis. Here, we describe the structural and functional characterization of *Klebsiella pneumoniae* ferric uptake regulator. Firstly, bioinformatic analysis of *fur* gene promoter region revealed a putative Fur-binding site, which was validated by the FURTA assay. Next, the relative expression of *fur* was analyzed by real time quantitative PCR with *K. pneumoniae* cells kept in contact with iron or an iron chelator. Finally, a homology model of *K. pneumoniae* Fur was generated by homologous molecular modeling based on the crystal structure of *Vibrio cholerae* Fur (PDB code 2w57; 2.6 Å resolution; 77% sequence identity; E-value 7e-64). The constructed homology model was considered accurate according to the DOPE score. In summary, the results seem to suggest that Fur autoregulates its own expression. Also, the homology model of the *K. pneumoniae* Fur presents as a suitable model for further analysis on the molecular mechanisms by which Fur binds DNA.

Word Keys: Ferric uptake regulator, Homologous molecular modeling, *Klebsiella pneumoniae*

Supported by: FAPESP and CAPES/PROSUP.