ANALYSIS OF THE 3D STRUCTURE OF ELRR, A TRANSCRIPTIONAL ACTIVATOR OF A VIRULENCE FACTOR IN *Enterococcus fecalis*: LESSONS ON ALLOSTERIC REGULATION AND DNA BINDING SPECIFICITY.

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We have determined the crystallographic structure of ElrR, a transcriptional regulator (TR) (see poster in this meeting). It has an N-terminal DNA-binding domain, a 5-helix central domain and a C-terminal domain built of traritopeptide (TPR)-like repeats. At least two families of TRs (RNPP and Rgg) present this fold. The interface between central and C-terminal domains presents a large and deep groove which builds the allosteric site. In five proteins with this fold, four have a peptide as allosteric ligand (three linear, one cyclic) and are quorum sensors. In spite of these similarities, the allosteric mechanisms regulating DNA binding are very different. These mechanisms include: a) In PrgX, Tetramerization allowed by ligand binding, b) In PtcR, reduction of HTH domain flexibility, achieved through breaking a long alpha helix connecting HTH and central domains, c) In ElrR, strong interaction between HTH and central domains, propagating changes in the allosteric site conformation, to the DNA-binding helices. Only two proteins of the RNPP family (PrgX and PrcL) share its folding with the only two structures determined in Rgg family (Rgg2sd and now ElrR). Different to the allosteric mechanisms, these proteins are homo-dimers (or homo-tetramers) and both HTH domains in a dimer bind to DNA. This binding form, imply very high restrictions in DNA binding sequence, symmetry and length. Furthermore, the N-terminal amino acid of the second helix (in the HTH domain) is always the key residue in the specific interaction with a particular base-pair in the DNA sequence. The aim of these studies is to understand the activation mechanism of virulence gens as the operon including ElrA and in a longer time-scale to design inhibitors of ElrR, which can help in controlling the *Enterococcus fecalis* growth.

Rgg and RNPP families, Transcriptional regulator, *Enterococcus fecalis*.

We acknowledge FAPESP, USP/COFECUB, LNLS, CAPES.