

Structural and Functional Characterization of the Transcriptional Regulator Rv1176 of Mycobacterium tuberculosis H37Rv

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Abstract : Microorganisms have self-defense mechanisms to protect themselves from toxic environments. Phenolic acid decarboxylase(pad) is responsible for the defense against toxicity caused by phenolic acids, converting them into less toxic vinyl derivatives. The transcription of the pad gene is regulated by a negative transcription factor, phenolic acid decarboxylase regulators (PadR), in a substrate-inducible manner. The PadR family members share the conserved DNA-binding features and interact with the operator DNA using a winged helix-turn-helix (wHTH) motif, which contains a three-helix motif and a β -stranded wing. The members of this family function as transcriptional regulators that are involved in various cellular survival processes, such as toxin production, detoxification, multidrug resistance, antibiotic biosynthesis, and carbon catabolism. Rv1176 of Mycobacterium tuberculosis H37Rv has been assigned to the PadR family protein that remains to be structurally and functionally uncharacterized. To reveal the structural mechanism by which Rv1176 could regulate effector-responsive transcription, several experiments were performed, including Electrophoretic Mobility Shift Assay (EMSA) for DNA protein interaction, differential scanning calorimetry (DSC) and Differential Scanning Fluorimetry (DSF) for temperature and ligand-dependent protein stability, Circular Dichroism (CD) spectroscopy for secondary structure analysis. Further, to evaluate the functional role of Rv1176, the intracellular survival of recombinant *M. smegmatis* was examined in murine macrophage cell line J774A.1 and different stressed conditions like oxidative, pH, and nutritive stress. All these studies demonstrated that Rv1176 could behave as a transcription regulator and its expression in recombinant *M. smegmatis* increases intracellular survival.

Keywords : EMSA, Mycobacterium tuberculosis, PadR family protein, transcriptional regulator

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