RV0792c; a potential drug target for Mycobacterium tuberculosis

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Tuberculosis (TB), remains a pervasive global health problem by being the seventh most frequent causes of death worldwide. The GntR family of transcription factors, one of the most abundant of helix-turn-helix regulatory proteins, involves in regulating various biological processes in diverse bacteria. Out of seven putative GntR genes in M. tuberculosis genome, this study focused on the gene Rv0792c, which lie between several hypothetical proteins, a monooxygenase and an oxidoreductase. This study was designed to analyze the regulatory mechanism of Rv0792c. Gene encoding RV0792c was cloned into pET28a and subsequently the protein was purified to near homogeneity by Nickel affinity chromatography. The intergenic region (BS) between Rv0792c and monooxygenase (Rv0793) was amplified and resulting PCR product was purified by electro elution. Increasing concentration of pure protein was titrated against BS-DNA under stoichiometric conditions in an EMSA. This resulted in binding of three RV0792c molecules within the BS region suggesting tight control of monooxygenase as well as its own gene. Further in silico analysis of the intergenic region reveals four probable sites with GntR recognition signature with which Rv0792c may interact. Since the binding sites interrupt both -10 and -35 regions of the putative shared promoter, it is proposed that this binding may play a significant role in regulating the adjacent genes organized in an operon. The natural ligand for this regulator is still under investigation. Since monoxygenases play a key role in metabolism, this gene may have a global regulatory role. This makes this transcriptional regulator a potential candidate for drug designing. Such new drug targets are of utmost importance in an era where TB is rapidly developing multi drug resistance.

