

An Insight into the Interaction Study of a WhiB Protein and its Binding Partner

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Abstract : Tuberculosis is the deadliest disease worldwide. Millions of people lose their lives every year due to this disease. It has turned lethal due to the erratic nature of its causative organism, *Mycobacterium tuberculosis* (Mtb). Mtb tends to enter into an inactive, dormant state and emerge to replicating state upon encountering favorable conditions. The mechanism by which Mtb switches from the dormant state to the replicative form is still poorly characterized. Proteome studies have given us an insight into the role of certain proteins in giving stupendous virulence to Mtb, but numerous dots remain unconnected and unaccounted. The WhiB family of proteins is one such protein that is associated with developmental processes in actinomycetes. Mtb has seven such proteins (WhiB1 to WhiB7). WhiB proteins are transcriptional regulators; they regulate various essential genes of Mtb by binding to their promoter DNA. Biophysical parameters of the effect of DNA binding on WhiB proteins has not yet been appropriately characterized. Interaction with DNA induces conformational changes in the WhiB proteins, confirmed by steady-state fluorescence and circular dichroism spectroscopy. ITC has deduced thermodynamic parameters and the binding affinity of the interaction. Since these transcription factors are highly unstable in vitro, their stability and solubility were enhanced by the co-expression of molecular chaperones. The present study findings help determine the conditions under which the WhiB proteins interact with their interacting partner and the factors that influence their binding affinity. This is crucial in understanding their role in regulating gene expression in Mtb and in targeting WhiB proteins as a drug target to cure TB.

Keywords : mycobacterium tuberculosis, TB, whiB proteins, ITC

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