Histone like protein HupB of *Mycobacterium tuberculosis* promote survival during stress conditions

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Abstract

Therapeutics treatment of TB patients has led to selective emergence of MDR- and XDR-Mtb strains. One such known target is Mtb's histone like protein, HupB belonging to class of Nucleoid associated proteins (NAP). NAPs are small, basic bacterial proteins that bind DNA to drive chromatin structure and DNA-dependent processes. In other bacterial sp., HU (a histone like protein) through nucleoid reorganization possibly inhibits cellular metabolism and reduces bacterial growth during adaptation to stress conditions. Histone-like protein (Hlp) of *Mycobacterium smegmatis* (Msmeg), a nonpathogenic soil variant of *Mycobacterium tuberculosis* (Mtb) play role in adaptation to environmental stress. Mtb encodes a histone-like protein HupB (*in-vivo* essential) that has also been targeted with drugs. However, its *in-vivo* functions are largely unexplored. Here, we explore role of Mtb HupB during stress imposed by macrophages. For this, we have set up host stimulated stress assays as well as *in vitro* infection assays in cell line. Our data supports the role of *hupB* during stress. To further evaluate its functionality, we generated the Mtb Δ*HupB* which showed growth defect and change in colony morphology in comparison to that of Mtb. Our mutant also showed susceptibility to host induced stress. Thus, targeting HupB may be an essential strategy that can be deployed to tackle this pathogenic bacterium. As of now, it is not a target either with any first line or second line drugs. Our study to understand HupB's role during macrophage-induced stress might lead way to further confirm if HupB must be considered a potential target.