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The *prrAB* Two-Component System Is Essential for *Mycobacterium tuberculosis* Viability and Is Induced under Nitrogen-Limiting Conditions

Shelley E. Haydel[a,b], Vandana Malhotra[a], Garrett L. Cornelison[a], Josephine E. Clark-Curtiss[a,b]

[a]The Biodesign Institute Center for Infectious Diseases and Vaccinology, Arizona State University, Tempe, Arizona, USA
[b]School of Life Sciences, Arizona State University, Tempe, Arizona, USA

ABSTRACT The *Mycobacterium tuberculosis prrA-prrB* (Rv0903c-Rv0902c) two-component regulatory system is expressed during intracellular growth in human macrophages and is required for early intracellular multiplication in murine macrophages, suggesting its importance in establishing infection. To better understand the function of the *prrA-prrB* two-component system, we defined the transcriptional characteristics of the *prrA* and *prrB* genes during exponential and stationary growth and upon exposure to different environmental stresses and attempted to generate a *prrA-prrB* deletion mutant. The *prrA* and *prrB* genes constitute an operon and are cotranscribed during logarithmic growth, with transcriptional levels decreasing in stationary phase and during hypoxia. Despite the transcriptional differences, PrrA protein levels remained relatively stable throughout growth and in hypoxia. Under conditions of nitrogen limitation, *prrAB* transcription was induced, while acidic pH stress and carbon starvation did not significantly alter transcript levels. Deletion of the *prrAB* operon on the chromosome of *M. tuberculosis* H37Rv occurred only in the presence of an episomal copy of the *prrAB* genes, indicating that this two-component system is essential for viability. Characterization of the *prrAB* locus in *M. tuberculosis* Mt21D3, a previously described *prrA* transposon mutant, revealed that this strain is not a true *prrA* knockout mutant. Rather, Tn*5367* transposon insertion into the *prrA* promoter only decreased *prrA* and *prrB* transcription and PrrA levels in Mt21D3 compared to those in the parental Mt103 clinical strain. These data provide the first report describing the essentiality of the *M. tuberculosis prrAB* two-component system and reveal insights into its potential role in mycobacterial growth and metabolism.

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Address correspondence to Shelley E. Haydel, shelley.haydel@asu.edu.