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Zinc regulates the activity of kinase-phosphatase pair (BasPrkC/BasPrpC) in *Bacillus anthracis*

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Abstract *Bacillus anthracis* Ser/Thr protein kinase PrkC (BasPrkC) is important for virulence of the bacterium within the host. Homologs of PrkC and its cognate phosphatase PrpC (BasPrpC) are the most conserved mediators of signaling events in diverse bacteria. BasPrkC homolog in *Bacillus subtilis* regulates critical processes like spore germination and BasPrpC modulates the activity of BasPrkC by dephosphorylation. So far, biochemical and genetic studies have provided important insights into the roles of BasPrkC and BasPrpC; however, regulation of their activities is not known. We studied the regulation of BasPrkC/BasPrpC pair and observed that Zn^{2+} metal ions can alter their activities. Zn^{2+} promotes BasPrkC kinase activity while inhibits the BasPrpC phosphatase activity. Concentration of Zn^{2+} in growing *B. anthracis* cells was found to vary with growth phase. Zn^{2+} was found to be lowest in log phase cells while it was highest in spores. This variation in Zn^{2+} concentration is significant for understanding the antagonistic activities of BasPrkC/BasPrpC pair. Our results also show that BasPrkC activity is modulated by temperature changes and kinase inhibitors. Additionally, we identified Elongation Factor Tu (BasEf-Tu) as a substrate of BasPrkC/BasPrpC pair and assessed the impact of their regulation on BasEf-Tu phosphorylation. Based on these results, we propose Zn^{2+} as an important regulator of BasPrkC/BasPrpC mediated phosphorylation cascades. Thus, this study reveals additional means by which BasPrkC can be activated leading to autophosphorylation and substrate phosphorylation.

Keywords *Bacillus anthracis* · PrkC · PrpC · Zinc · Phosphorylation · Ef-Tu · Kinase inhibitors · Thermostability · ICP-OES

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Introduction

Ser/Thr and Tyr mediated phosphorylation is one of the most important post-translational events in signaling of bacteria. We had earlier reported that in *Bacillus anthracis*, the etiological agent of anthrax, loss of key Tyrosine kinase(s) may lead to gain of novel dual specificity protein kinases (phosphorylates Ser/Thr and Tyr) (Arora et al. 2012; Mattoo et al. 2008). In wake of

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