P3-01 Manipulating *Brucella abortus* two-component regulatory system BvrR/BvrS promoter activity through environmental stimuli

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Abstract

The two-component regulatory system BvrR/BvrS is required for *Brucella abortus* transition from an extracellular to an intracellular lifestyle. BvrS is a sensor histidine kinase transducing unknown external stimuli to the BvrR transcriptional regulator through phosphorylation. Active BvrR then binds to gene regulatory regions, affecting their transcription. The system is a master regulator controlling the expression of genes related to cell envelope homeostasis, carbon and nitrogen metabolism, the virulence factor VirB and its regulator VjbR. *B. abortus* bvrR/bvrS mutants are avirulent in mice models. Low concentration of nutrients and pH were recently described as environmental cues affecting the BvrR transcriptional regulator activation through phosphorylation. Here, we describe the environmental cues that affect BvrR/BvrS promoter activity. Using a pbvrR::luxA/luxB transcriptional fusion, the promoter activity was determined during in vitro growth and ex vivo in a cellular infection model. Conditions and chemical compounds simulating the environment found during intracellular trafficking were evaluated: nutrient restrictions, different pH, presence of metals, carbon, and nitrogen sources, at different concentrations and time. The results obtained for each condition tested, individually or in combination will be presented in this report. Some of the assessed conditions affected bvrRp activity and demonstrated a similar effect on BvrR phosphorylation. A combination of conditions tested was found to repress bvrRp activity. Altogether, these results show that conditions that modulate bvrRp activity are not necessarily the same as those sensed by the BvrR/BvrS two-component system but might influence BvrR activation. This work provides a first attempt toin vitro manipulate the bvrRp activity and hence contribute to the understanding of the type of environmental signals need it for regulating bvrR/bvrS transcription.

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