

**Identification and characterisation of toxin-antitoxin systems  
(TA) in *Burkholderiapseudomallei***

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as a thesis for the degree of  
Doctor of Philosophy in Biological Sciences  
In February 2013

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## Abstract

The aim of this study was to identify and characterise type II toxin-antitoxin (TA) systems in *Burkholderiapseudomallei*, the causative agent of the human disease melioidosis.

8 putative TA systems were identified within the genome of *B. pseudomallei*K96243. 5 of these were located within genome islands. Of the candidate toxins, BPSL0175 (RelE1) or BPSS1060 (RelE2) caused growth to cease when expressed in *Escherichia coli*, whereas expression of BPSS0390 (HicA) or BPSS1584 (HipA) (in an *E. coli*  $\Delta$ hipBA background) caused a reduction in the number of culturable bacteria. HicA also caused growth arrest in *B. pseudomallei*K96243 $\Delta$ hicAB. These toxin induced phenotypes were enhanced by an <3kDa extracellular factor that accumulated in the spent medium during growth. Expression of the cognate antitoxins could restore growth and culturability of cells.

Expression of *hicA* in *E. coli* gave an increased number of persister cells in response to ciprofloxacin or ceftazidime. Site directed mutagenesis studies identified two key residues within the HicA toxin that were essential for both the reduced culturability and increased persistence phenotypes. Deletion of *hicAB* from *B. pseudomallei*K96243 did not affect persister cell or survival frequencies compared to the wild type following treatment with a variety of stress conditions.

Deletion of the  $\Delta$ hipBA locus from *B. pseudomallei* K96243 also had no effect on bacterial persistence or survival under the conditions tested.

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