Experimental Persistent Infection of BALB/c Mice with Small-Colony Variants of *Burkholderia pseudomallei* Leads to Concurrent Upregulation of PD-1 on T Cells and Skewed Th1 and Th17 Responses

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Abstract

Background

*Burkholderia pseudomallei* (*B. pseudomallei*), the causative agent of melioidosis, is a deadly pathogen endemic across parts of tropical South East Asia and Northern Australia. *B. pseudomallei* can remain latent within the intracellular compartment of the host cell over prolonged periods of time, and cause persistent disease leading to treatment difficulties. Understanding the immunological mechanisms behind persistent infection can result in improved treatment strategies in clinical melioidosis.

Methods

Ten-day LD<sub>50</sub> was determined for the small-colony variant (SCV) and its parental wild-type (WT) via intranasal route in experimental BALB/c mice. Persistent *B. pseudomallei* infection was generated by administrating sub-lethal dose of the two strains based on previously determined LD<sub>50</sub>. After two months, peripheral blood mononuclear cells (PBMCs) and plasma were obtained to investigate host immune responses against persistent *B. pseudomallei* infection. Lungs, livers, and spleens were harvested and bacterial loads in these organs were determined.

Results

Based on the ten-day LD<sub>50</sub>, the SCV was ~20-fold less virulent than the WT. The SCV