BURKHOLDERIA MALLEI CLH001 ATTENUATED VACCINE STRAIN IS IMMUNOGENIC AND PROTECTS AGAINST ACUTE RESPIRATORY GLANDERS.

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Burkholderia mallei is the causative agent of glanders, an incapacitating disease with high mortality rates in respiratory cases among animals and humans. Its endemicity and ineffective treatment options emphasize its public health threat and highlight the need for a vaccine. In this study, we constructed a B. mallei ΔtonB Δhcp1 (CLH001), a strain deficient in iron uptake and type six secretion function and investigated its ability to protect against acute respiratory Burkholderia murine infections. Intranasal (i.n.) administration of CLH001 (1.5x10^4 CFU) to BALB/c and immunodeficient NSG mice resulted in 100% survival with no detectable colonization or abnormal histopathology in the lungs, liver or spleen at day 21. BALB/c mice vaccinated i.n. with 1.5x10^5 CFU of CLH001 in a prime/boost regimen showed full protection at 35 days post-challenge with 1.5x10^4 CFU of B. mallei lux reporter strain CSM001. All organs analyzed from surviving mice were clear of bacterial colonization and histopathological abnormalities. Immunized mice showed high B. mallei-specific IgG serum titers and a Th1-biased response (IgG2a:IgG1 ratio = 4.0), a good predictor of protection. Additionally, pre-challenge sera displayed significant bactericidal activity over naïve serum (p=0.0062). Vaccinated BALB/c mice were also significantly protected (87.5% survival; p< 0.0001) against higher dose (3.5x10^5 CFU) of B. mallei 23344 challenge. Our studies show that CLH001 is attenuated and safe, and effective at providing protection against lethal B. mallei challenge. CLH001 is not only a viable vaccine platform for advancement into pre-clinical studies, but also represents the first Tier 1 Select Agent-excluded B. mallei strain.