## CAMO (COMPARING ANIMAL MODELS TO ORGANOIDS) - TE STING MEDICAL COUNTERMEASURES WITH MICROPHYSIOLOGICAL SYSTEMS AND COMPARING TO TRADITIONAL ANIMAL MODELS AND CLINICAL TRAILS

# Characterization Of Virulence Of The Burkholderia Pseudomallei ATS2021 Strain Isolated From Aromatherapy Spray Unintentionally Imported To The United States From India

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An outbreak of Burkholderia pseudomallei, the etiologic agent of melioidosis, resulted in multiple deaths in the United States (US) during 2021-2022 caused by isolate ATS2021 identified in an aromatherapy spray purchased at a national retailer. The unintentional importation of the Tier one select agent within an aromatherapy spray manufactured in India demonstrates the importance of understanding this bacterium as an emerging disease in the U.S. We have assessed several aspects of virulence of isolate ATS2021 and established that it represents a virulent strain of B. pseudomallei capable of robust formation of biofilm in vitro at physiological temperatures which may contribute to virulence, particularly in the inhalational route of infection. By using the C57BL/6 mouse model of inhalational melioidosis, we have determined median lethal dose estimates and performed in depth bacteriological and histopathological characterization with an emphasis on potential neurological pathogenesis that is likely associated with the bimABm allele identified in this isolate of B. pseudomallei. After being inhaled as small-particle aerosols, we characterized the ability of this bacterium to disseminate to and replicate in the brain soon after exposure. Histopathological analyses indicated that the bacteria were quickly associated with the nasal cavity (e.g. nasal turbinates) and were then identified in the olfactory bulb of the brain within three days (depending upon the dose inhaled). These data presented here, previous case-reports, and the identification of endemic strains of B. pseudomallei in Mississippi, support the idea that B. pseudomallei is an emerging infectious disease in the U.S. Thus, it is imperative that we understand these new isolates in context of inhalational (and neurological) melioidosis to accurately predict the hazards associated with this emerging pathogen for both the biodefense and public health communities. Furthermore, clinical laboratories must continue to be on the alert for melioidosis within the U.S., and new B. pseudomallei isolates should be used to develop and test novel medical countermeasures and novel diagnostic strategies. Lastly, these data will be important when attempting to recapitulate aspects of melioidosis pathogenesis using oganoids or other microphysiological systems in future research.

Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the U.S. Army or the Department of Defense Health Agency. Research was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, National Research Council, 2011. The facility where this research was conducted is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

Funding: US Defense Threat Reduction Agency