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The Rebel with a Mysterious Cause

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DEFENSE THREAT REDUCTION AGENCY

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Front cover: Warfighters conduct a training scenario during the Patriot Warrior 2019 exercise at Fort McCoy, Wisconsin, on August 16, 2019. Photo courtesy of the U.S. Air Force. Photo by Tech. Sgt. Gregory Brook.

Inside cover: A U.S. Army medical laboratory technician prepares to draw a blood sample from a patient at Joint Base Langley-Eustis, Virginia, on June 26, 2017. Photo courtesy of the U.S. Air Force. Photo by Staff Sgt. Teresa J. Cleveland.

Back cover: U.S. Air Force medical laboratory technician tests a blood sample at Joint Base Langley-Eustis, Virginia, on June 26, 2017. Photo courtesy of the U.S. Air Force. Photo by Staff Sgt. Teresa J. Cleveland.

The Rebel with a Mysterious Cause:

DTRA CB is learning why one stubborn bacterium just loves humans so much.

In a large family, there is at least one rebel. In the bacterial family of *Burkholderia*, which includes over 100 siblings, *Burkholderia pseudomallei* is this outlier because of its ability to virulently infect humans. The U.S. Centers for Disease Control and Prevention labels *B. pseudomallei* as a Category B bioterror agent; however, the bacterium is problematic to U.S. warfighters even if it is not released for nefarious reasons. The bacterium is endemic to the tropics, though it has spread to other areas of the world, such as the Caribbean; the organism causes the disease melioidosis for which a prolonged adherence to antimicrobial treatment is critical. In 2012, a warfighter deployed around Australia was diagnosed with the disease and needed antimicrobial therapy for 12 months.[1] To ensure that future protective measures against melioidosis are as effective as possible, the Defense Threat Reduction Agency's Chemical and Biological Technologies Department (DTRA CB) is supporting research to better understand the environmental and ecological signatures (signs) of *B. pseudomallei*.

1. Larson DT, Schully KL, Spall A, et al. 2020. Indirect detection of *Burkholderia pseudomallei* infection in a US Marine after training in Australia. *Open Forum Infectious Diseases.* 7(5):ofaa103. doi: 10.1093/ofid/ofaa103.

The DTRA CB-funded research began at the University of California, Los Angeles, and is now taking place at Northern Arizona University. Investigators are identifying the flora and fauna that can be associated with the presence of *B. pseudomallei* and the effects of these flora and fauna on the bacterium's virulence. They seek to identify the ecological and environmental signatures of the bacterium, understand how it evolves to survive in its environmental niche, and learn why it is especially virulent in humans.

B. pseudomallei lives in the rhizosphere, the soil area surrounding and influenced by plant roots. The rhizosphere, while rich in nutrients, can be a very competitive environment for the bacterium because its predators are also potentially present. The bacterium must evolve and adapt to survive, and the evolution and adaptations it undergoes may explain why it is infectious and virulent in humans when many of its family members are not. The investigators recently published a peer-reviewed article that discusses potential ecological and environmental explanations for the bacterium's virulence as found in the rhizosphere.[2] The authors posit that the virulence is likely a result of the bacterium's adaptations to evade destruction by natural predators, such as unicellular protozoa, thereby enabling the bacterium to select for evolutionary traits that 'incidentally' promote infections in humans. However, the virulence features of *B. pseudomallei* that distinguish it from its nonpathogenic close relatives are still not clear.

Investigators at Northern Arizona University are identifying rhizosphere-based species that cohabit with *B. pseudomallei* and influence genetic selection for traits that promote human disease. The investigators isolated the living fraction of soil — insects, larvae, nematodes, protozoa, and bacteria — from the soil's inorganic components. They are investigating field sites in Southeast Asia and other locations where melioidosis is endemic — including sites in the Caribbean — and aim to identify environmental factors and relevant predator-host systems to understand the mechanisms that promote *B. pseudomallei*'s virulence.

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Data on how *B. pseudomallei* adapts and evolves in the environment will enable scientists to develop effective protective measures against melioidosis, which is necessary given the bacterium's presence near U.S. shores and its potential to spread to the mainland United States. As illustrated by the case of the Marine deployed around Australia, warfighters are at risk of acquiring melioidosis depending on where they are stationed. The more scientists can learn about how this bacterium thrives in its natural environment, the better the chances of developing protective measures, including therapeutics, to safeguard warfighters and the nation from this dangerous bacterium. ●

2. French CT, Bulterys PL, Woodward CL, et al. 2020. Virulence from the rhizosphere: ecology and evolution of *Burkholderia pseudomallei*-complex species. *Current Opinion in Microbiology*. 54:18–32. doi: 10.1016/j.mib.2019.12.004.

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Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department. This publication highlights the department's advancements in protecting warfighters and citizens from chemical and biological threats through the innovative application of science and technology. DTRA.mil