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Overcoming Anthrax Bacterium's Natural Defenses Could Hold Key to New Treatments

Army scientists have discovered a way to "trick" the bacterium that causes anthrax into shedding its protective covering, making it easier for the body's immune system to mount a defense. The study, which appears in this month's issue of the journal MICROBIOLOGY, could lead to new approaches for treating anthrax infection.

Bacillus anthracis, the causative agent of anthrax, is particularly lethal because of its protective coating, or capsule, which enables the pathogen to escape destruction by the host's immune system. A key bacterial enzyme called capsule depolymerase, or CapD, anchors the capsule to the cell surface. CapD also cuts and releases part of the capsule into small fragments that are thought to interfere with specific parts of the immune system, offering further protection to the bacterium. The rest of the capsule remains intact.

Finding a way to cause *B. anthracis* to unmask itself, using the bacterium's own machinery, would be a novel approach to defeating the pathogen. So scientists at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) induced *B. anthracis* to make higher-than-normal amounts of CapD, resulting in release of the capsule fragments. This left very little capsule attached to the bacterial cells. As a result, the unprotected bacteria were left vulnerable to immediate detection and destruction by the cells of the immune system.

"By engineering B. anthracis to over-produce CapD, we are effectively turning the bacterium's own weapon on itself," explained Dr. Arthur Friedlander, one of the study's principal investigators. He believes the USAMRIID group's findings could have significant clinical impact.

"Many pathogenic bacteria, including *B. anthracis*, produce a capsule surrounding them that prevents the infected host from killing them, improving their chances of causing disease," he explained. "Understanding the mechanisms of virulence used by the anthrax bacterium is vital to developing medical countermeasures against it."

Anthrax most commonly occurs in wild and domestic mammals, although it has the potential to be used as a biological threat agent. Symptoms vary depending on the route of exposure; however, mild fever, fatigue and muscle aches usually begin within 4-6 days of exposure. As the bacteria multiply in the lymph nodes, toxemia progresses and the potential for widespread tissue dissemination, destruction and organ failure increases. Severe breathing difficulty, meningitis and shock can follow. Up to 90 percent of untreated cases of inhalational anthrax result in death.

"This study provides significant insight into the pathogenesis of anthrax infection, tracing the connection between *B. anthracis* gene expression to its effect on host response," said Colonel John P. Skvorak, commander of USAMRIID.

USAMRIID, located at Fort Detrick, Maryland, is the lead medical research laboratory for the U.S. Department of Defense Biological Defense Research Program, and plays a key role in national defense and in infectious disease research. The Institute conducts basic and applied research on biological threats resulting in medical solutions (such as vaccines, drugs and diagnostics) to protect the warfighter. While USAMRIID's primary mission is focused on the military, its research often has applications that benefit society as a whole. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command. For more information, visit www.usamriid.army.mil

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Reference: **Capsule depolymerase overexpression reduces *Bacillus anthracis* virulence:** Angelo Scorpio, Donald J. Chabot, William A. Day, Timothy A. Hoover, and Arthur M. Friedlander. *Microbiology*, May 2010; 156: 1459 - 1467.