

Scientists show how anthrax bacteria impair immune response

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Researchers from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, have determined a key mechanism by which *Bacillus anthracis* bacteria initiate anthrax infection despite being greatly outnumbered by immune system scavenger cells. The finding, made by studying genetically modified mice, adds new detail to the picture of early-stage anthrax infection and supports efforts to develop vaccines and drugs that would block this part of the cycle.

To start an infection, anthrax bacteria release a toxin that binds to <u>immune cells</u> through two receptors, TEM8 and CMG2, found on the cell surface. The binding allows two additional bacterial toxins to enter the cells, setting off a chain of events that impairs their ability to ingest and kill the bacteria.

In the new research, NIAID investigators Stephen Leppla, Ph.D., Shihui Liu, M.D., Ph.D., and colleagues bred <u>mice</u> that lacked CMG2 receptors on two kinds of immune cells, neutrophils and macrophages. These usually are the first cells to arrive at the site of an anthrax infection, where they engulf the invading bacteria and try to prevent the spread of infection.

Mice without CMG2 receptors on these immune cells were completely resistant to infection by B. anthracis bacteria, experiencing only a temporary swelling at the site of infection, and fully clearing the infection within two weeks. In contrast, in normal mice, the level of



anthrax bacteria increased rapidly in the 48 hours following infection, and all the mice died within six days.

The researchers concluded that B. anthracis uses CMG2 <u>receptors</u> to impair the scavenging action of neutrophils and macrophages during early infection, giving the bacteria time to multiply to levels sufficient to overwhelm the body's defenses. Developing drugs and vaccines that block B. anthracis from establishing early infection via binding to the CMG2 receptor, say the study authors, may be crucial to success in treating and preventing anthrax disease.

More information: S Liu et al. Anthrax toxin targeting of myeloid cells through the CMG2 receptor is essential for establishment of Bacillus anthracis infections in mice. Cell Host and Microbe. DOI:10.1016/j.chom.2010.10.004 (2010).

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