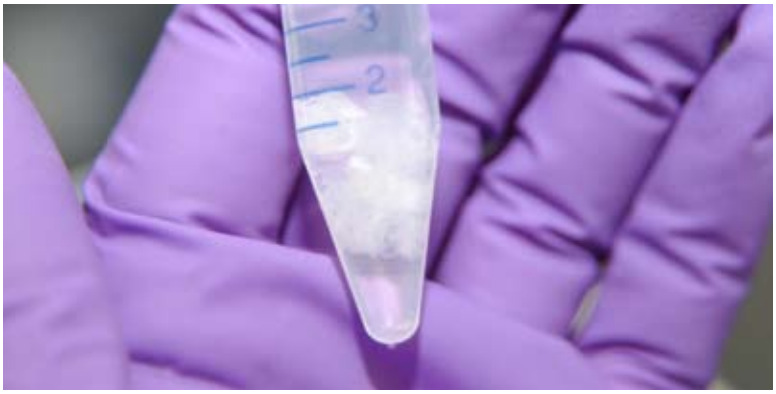
Understanding Anthrax

Infectious disease researchers show how anthrax paralyzes the body's "first responders"



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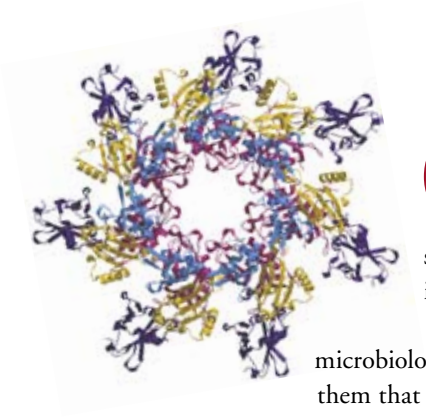

One of the first things people ask when they find out Russell During works with anthrax is "Isn't that dangerous?"

During, a doctoral student in microbiology and immunology, assures them that the purified form of anthrax toxin that he studies poses very little risk.

Working with Dr. Frederick Southwick, chief of infectious diseases at the UF College of Medicine, During helped uncover how the inhaled form of anthrax disarms bacteria-fighting white blood cells before they can fend off the disease, which kills most victims within days.

The lethal toxin in anthrax paralyzes neutrophils, the white blood cells that act as the body's first defense against infection, by impairing how they build tiny filaments that allow them to crawl throughout the body and eat invading bacteria.

Just two hours of exposure to the lethal toxin blocks the neutrophils' ability to produce these filaments by nearly 60 percent, paralyzing them and allowing the anthrax to move freely in the body, according to a paper by Southwick and During published last fall in the Journal of Infectious Diseases.

"If your neutrophils work normally, you might be able to shut down this infection," says Southwick, who worked on the study with a team of UF researchers and investigators from the Centers for Disease Control and Prevention and Emory University. "The overall goal is to understand how anthrax toxins paralyze the immune system."

The need to find new ways to treat victims of bioterrorism has increased since five people died in the fall of 2001 after they were exposed to anthrax powder through the mail. The UF findings could lead to treatments that block anthrax from paralyzing the much-needed neutrophils, says Southwick.

"Neutrophils are the first responders, like the ambulance going to the crash scene," says During. "For anthrax to get established, it has to be able to thwart those first responders, so we looked at what the toxin was doing to interfere with that process."

When researchers at the CDC looked at lung fluid from victims of the 2001 attacks, they noted that the victims did not have the elevated white blood cell counts typical for most infections, and a large number of the inhaled anthrax bacteria had spread from the lungs into the bloodstream.

This led Southwick and During to hypothesize that anthrax may be impairing the cells' ability to move and fight off the offending bacteria, an idea that had only been studied once before years earlier.

Using blood samples from volunteers, the researchers studied how neutrophils reacted when exposed to a purified

Mickey Cuthbertson

Dr. Frederick Southwick

form of anthrax lethal toxin. Unlike an intact inhalation anthrax spore, the pure toxin is not dangerous for researchers to use and allows them to isolate specifically how the toxin is affecting cells, Southwick says.

Low doses of the lethal toxin stopped the protein actin from building filaments to steer the neutrophils, blunting the body's immune response.

"Neutrophils crawl around in the body and roll around in the blood vessels and whenever they sense bacteria, they gobble them up like Pac-Man," says During. "If neutrophils are the first responders and they never get there, you're fighting a losing battle."

And inhalation anthrax works fast, which is one of the reasons why it is usually fatal, according to the CDC. The disease can be treated with antibiotics, but people often don't seek treatment until it is too late.

During, who has also studied West Nile Virus, says the team's findings could lead to faster diagnostic tools for anthrax.

"There's no quick test for anthrax, so a few of the early anthrax patients in 2001 were actually sent home with what doctors thought was the flu," During says. "Unfortunately, by the time the doctors realized what it was, it was too late."

The next step for UF researchers is to pinpoint the exact protein the lethal toxin is targeting in the neutrophil. There are more than 100 proteins that regulate actin-filament

Sarah Kiewel

Russel During

formation, and researchers have already isolated one that may be responsible, Southwick says.

The UF findings also could affect research on other diseases. Because actin is found in every cell, the study could lead researchers to know more about how tumors and other cells move in the body, Southwick says.

"It relates to wound healing, it may relate to many diseases and many problems."

Joseph Kays and April Frawley Birdwell