Deadly Effects

Multi-pronged fight against anthrax

Quick read
To counter the deadly effects of the anthrax pathogen, multiple approaches are being pursued by Los Alamos, including development of a life-saving antitoxin.

By the time you know you've been infected with anthrax, it's likely too late. The pathogen is a favorite for bioterrorists.
In 2001, seven envelopes containing anthrax spores were sent to news organizations and U.S. senators. Five people died. Thousands of people were given precautionary medical treatment, and dozens of buildings were closed. Terrorists caused a multi-million dollar debt and widespread panic.
Los Alamos National Laboratory has been a key participant in the fight against the causative agent for anthrax (i.e., Bacillus anthracis). To counter the pathogen's deadly effects, multiple approaches are being pursued, including development of an antibody decoy that prevents production of the bacterium's deadly toxin. Other teams are finding vulnerabilities in the bacterium's metabolism.
Additionally, the Laboratory's expertise in DNA sequencing has made it a significant player in DNA forensics. Laboratory researchers are developing new medical treatments, including more effective vaccinations that can act more quickly—vital during a terrorist attack.
The most-prescribed current antibiotics cause side effects and mutated bacteria may be resistant to antibiotics. To defeat something like B. anthracis, you have to look for vulnerabilities.
A Formidable Opponent
Outside a living host, B. anthracis forms spores that are resistant to heat, dehydration and radiation. The spores can either be ingested or enter the body through a break in the skin. Their minuscule size makes inhalation easy.
Anthrax inhalation has a mortality rate of nearly 75 percent if not treated quickly and it's difficult to diagnose because early symptoms mimic a cold or flu.
The spores lodge in the lungs' tiniest air sacs, the alveoli, where they encounter mature white blood cells called macrophages. Macrophages normally envelop and devour invading pathogens. However, the spores resist being eaten and instead germinate into fully active B. anthracis bacteria, which ride along, undamaged, to the lymph nodes; there they burst out to multiply at a staggering rate—and secrete a deadly toxin—in the favorable environment of the bloodstream.

Breaking and Entering: Anthrax Toxin Invades a Cell. The anthrax toxin comprises three proteins (PA, EF, and LF) that work together to break through the cell's outer wall and set off a string of reactions that can ultimately kill the host.

The toxin is a complex set of three proteins working cooperatively to kill cells. The first one, called protective antigen (PA), initiates the attack and binds to a cell receptor, dragging along the other two proteins—edema factor (EF) and lethal factor (LF). Inside the cell, they set off a string of death-dealing events, including the malfunction and swelling of cells and disruption of the intercellular signals that would activate the immune system.
Launching a Decoy

Momchilo Vuyisich, co-developer of the Los Alamos antitoxin.

PA is the focus of an antitoxin being developed by a Los Alamos team of Goutam Gupta (project leader), Momchilo Vuyisich, and "Gnana" Gnanakaran. Team members want to block the toxin by keeping PA from attaching to a cell's receptors and preventing mutations from working. The current anthrax vaccine functions similarly, but not as well, and far too slowly.

The decoy has passed several major tests sponsored by the National Institute of Allergy and Infectious Diseases and by the National Institutes of Health's Biodefense Program.

Joining Forces: Metabolism and Mystery Proteins

Other Los Alamos researchers are pursuing the anthrax bacterium down different paths.

A team headed by Christy Ruggiero and Andy Koppisch is trying to develop new antibiotics that specifically target B. anthracis through its metabolism. The idea is to block the bacterium's acquisition of iron (a dietary requirement to function), effectively starving the bacterium.

"As far as we know," says Ruggiero, "Bacillus anthracis is the only pathogen that uses petrobactin."

Currently, the team is studying the effect of turning off several of the bacterium's genes that control petrobactin uptake; then antibiotics that block proteins expressed by these genes will be created.

Koppisch is also leading a separate team that is looking into other metabolic functions and investigating how the bacterium develops resistance to antibiotics, in the hope of preventing resistance before it happens.

Paul Langan's team is attacking one particular enzyme, DHFR, which is essential for the bacterium's survival.

Cliff and Pat Unkefer are working in a new field of study known as "metabolomics" that offers a window into the biochemical workings of an organism, providing new drug targets.

Ryszard Michalczyk's anti-anthrax team is studying six extra genes unexpectedly found on a circular piece of B. anthracis DNA—leading to additional drug targets.

A combination of these Los Alamos strategies may work in tandem for stronger results, leading to a future that is safe from anthrax.

Pushing Frontiers

In the second half of 2008, Los Alamos National Laboratory made significant advances in its primary mission: safeguarding the U.S. nuclear deterrent and pushing the frontiers of science on multiple fronts.

The national stockpile stewardship program achieved a major milestone in September with the production of the first life-extended W76-1 ballistic missile warhead for Trident submarines. The achievement culminated more than a decade of work by scientists and engineers at Los Alamos and across the nuclear weapons complex-including two crucial experiments conducted by the Laboratory's Hydrodynamic Experiments Division.

Another highlight: Roadrunner reached a new performance record of 1.105 petaflops, keeping it atop the list of the world's fastest supercomputers. Built by IBM for the Lab, Roadrunner was the first computer the crack the petaflop barrier: one thousand TRILLION operations per second. Initial applications will range widely: studying in great detail the evolution of HIV... exploring deeply the formation—as well as deformation—of metallic nanowires...and-toward producing biofuels more efficiently-unraveling the processes by which bacteria break down cellulose.

Safety and environmental stewardship were again a major theme for our work in the latter half of 2008. In November, the last group of unvented high-activity drums left Los Alamos for the Waste Isolation Pilot Plant near Carlsbad. That shipment fulfilled a commitment to the Defense Nuclear Facilities Safety Board to prioritize disposal of the highest-activity transuranic wastes stored at the Lab.

Los Alamos also strengthened security, ensuring that nearly six dozen classified and unclassified computing systems are managed and operated securely. The Lab has now complied with all 14 security actions mandated two years ago by the Department of Energy.

And, through our program to recruit cognizant systems engineers, we met the crucial need for sufficient numbers of engineers to keep vital mechanical and electrical safety systems functioning properly in our nuclear facilities.

The latter half of 2008 proved once again why Los Alamos is the nation's premier institution for scientific research. Capping the list of accomplishments was a new technology called MagViz that could eventually provide increased security at major airports. Based on medical MRI technology, MagViz can identify contents of bottles and other containers, distinguishing potentially hazardous liquids from the harmless shampoos and perfumes a traveler might carry onboard a jet. MagViz was demonstrated successfully in December at Albuquerque's airport.

We continued a long tradition of supporting U.S. space exploration. A NASA mission, launched in October to probe the far edge of the solar system from a high Earth orbit, carried a Los Alamos device called the High Energy Neutral Atom Imager. Its goal: to detect atoms emitted from a region where the outermost reaches of our solar system meet the vast interstellar space-giving us a panoramic view of this gateway to the galaxy.

Closer to home, Los Alamos continues to explore solutions to the energy needs of tomorrow. For example, scientists at the Lab hope to use tiny semiconductors called quantum dots to convert sunlight to electricity more efficiently than is possible with current solar panels-and to create new, efficient solid-state lighting.

Equally electrifying, Los Alamos materials scientists are helping unravel the mysteries of superconductivity. During the latter half of the year, LANL researchers identified entirely new mechanisms for superconductivity that could form the basis for new superconducting materials.

Underscoring the wealth of scientific talent at the Lab, Bob Albers, Paul Johnson, and Kurt Sickafus were named Laboratory Fellows in December. These three Fellows represent diverse disciplines, including theoretical physics, energy science, and geophysics.

Los Alamos may be one of the world's great technology incubators, yet we also strive to help others develop new ideas and products. In January, the Lab selected four young local companies as the newest recipients of awards from the LANS Venture Acceleration Fund. LANS, which manages and operates the Lab, supports the fund through donations from its earnings.

The Lab and LANS also teamed last September with a venture capital firm and a local venture capital fund to spin off technology developed by Lab scientists, with an emphasis on creating companies in Northern New Mexico. The Lab could contribute up to one million dollars to the initiative over the first three years.

We also are pushing to build top-flight research facilities for the future. In July 2008, workers hoisted the final steel beam atop the skeleton of what will be the Radiological Laboratory Utility Office Building, part of the Lab's Chemistry and Metallurgy Research Replacement Project. Once completed, the CMRR nuclear facility will house several of the Lab's mission-critical projects, including analytical chemistry, materials characterization, and actinide research and development capabilities. They'll be relocated from their current location in the historic—yet antiquated—Chemical and Metallurgy Research building at Technical Area 3.

In December, Los Alamos welcomed hundreds of employees who transferred from KSL, the subcontractor whose work the Lab brought in-house. The move was geared to improve efficiency and reduce costs associated with site-support services, including maintenance, waste removal, and custodial work.

Throughout the Lab's history, Los Alamos has helped play a vital role in the surrounding communities, and in 2008, that tradition continued. Lab employees pledged a million dollars, and LANS matched one hundred percent: a record Los Alamos contribution to United Way of TWO MILLION dollars. Contributions from the Lab and LANS also helped fund dozens of nonprofit organizations and scholarship programs, including a LANS donation of $500,000 to a LANL Foundation scholarship named for former long-time New Mexico Senator Pete Domenici.

These accomplishments and many more added up to a strong year. Our customer, the National Nuclear Security Administration, reached the same conclusion in its very favorable assessment of the Lab's performance for fiscal year 2008. It's unmistakable: the extraordinary talent, commitment, and creativity that Los Alamos employees dedicate every day to national security science and the betterment of their communities.