Biology

New clue hints at how anthrax kills

Nicholas S. Duesbery never expected to find a clue to the deadliness of a microorganism feared by biological warfare experts. His studies focus on a signaling pathway inside cells that depends upon a protein called mitogen-activated protein kinase (MAPK). This pathway is employed by many kinds of cells, including cancer cells and immature mammalian eggs, or oocytes.

"I wanted to find something that inhibits the MAPK pathway so that I could see what happens to cancer cells and oocytes," says Duesbery, who works at the National Cancer Institute (NCI) in Frederick, Md.

Searching through an NCI database that stores information on how thousands of compounds affect 60 kinds of cancer cells, Duesbery and his colleagues found one whose actions closely resembled those of a previously identified inhibitor of the MAPK pathway. Much to their surprise, this compound turned out to be a key component of the deadly toxin made by the bacterium *Bacillus anthracis*.

Though microscopic, *B. anthracis* could prove a devastating weapon in the hands of armies or terrorists. Its toxin, commonly known as anthrax, acts swiftly. A small dose can kill a rat in less than hour, apparently by destroying immune cells called macrophages.

Yet investigators have not had many clues as to how the toxin kills cells. It consists of three proteins, the most deadly of which is named lethal factor (LF). It was LF that Duesbery came upon in his quest for a MAPK pathway inhibitor.

Duesbery and his colleagues next obtained a sample of LF and tested whether it disrupts the MAPK pathway in oocytes. "It blocked the oocytes' ability to develop into eggs," says Duesbery. In further experiments, described in the May 1 SCIENCE, the scientists discovered that LF inhibits the MAPK signaling pathway by cleaving other proteins that would normally activate MAPK.

The scientists are still working to confirm that LF's inhibition of the MAPK pathway explains the deadliness of anthrax. They're investigating how macrophages react to disruptions of this signaling system by other methods, for example. If MAPK inhibition is the explanation for anthrax's actions, says Duesbery, compounds that block LF's cleaving action—so-called protease inhibitors—might be a useful therapy for the disease. —*J.T.*

Patenting the Minotaur?

In a marriage of modern law and ancient mythology, a cell biologist and a long-time critic of biotechnology have filed for a broad patent on the making of human-animal chimeras. "We're challenging the patent system," says cell biologist Stuart A. Newman of New York Medical College in Valhalla, who is joined on the patent application by Jeremy Rifkin, president of the Foundation on Economic Trends in Washington, D.C.

Since a controversial 1980 Supreme Court decision that living creatures are patentable, scientists and companies have patented many genetically engineered life-forms. Even though Newman and Rifkin oppose all such patenting, they hope to use this legal maneuver to prevent, or at least delay, any use of chimeras created by fusing human and animal embryonic cells. Such creatures have not been made yet, but Newman says they will soon be feasible. Examples of such chimeras might include pigs growing human organs for transplants or chimpanzee-human chimeras to be used for pharmaceutical testing.

"This is not a legal issue. It's a public policy issue. If we're going to have a policy of patenting these types of creatures, it ought to be based on a more vigorous public debate than we've had to date," says Patrick J. Coyne, a Washington, D.C., lawyer representing Newman and Rifkin in their patent application. —*J. T.*

Biomedicine

From a meeting in San Francisco of the Federation of American Societies for Experimental Biology

Get Granny to speed up those leg lifts

Aging brings an inexorable loss of muscle, known as sarcopenia (SN: 8/10/96, p. 90). Joseph Signorile of the University of Miami in Coral Gables, Fla., is investigating means of slowing this loss of strength, which can cripple older people. For instance, while weight lifting helps even 90-year-olds (SN: 6/25/94, p. 405), his new work suggests that performing those lifting exercises more rapidly can improve a person's ability to perform the so-called explosive movements needed to rise from a chair or catch one's balance.

To build muscle mass, trainers usually instruct people to lift weights or push against controlled-resistance equipment over the course of 2 seconds and then bring the weights back down over 3 seconds. However, Signorile says, to perform powerful moves quickly, football players and other athletes must practice those moves much more quickly.

Figuring that what works for athletes might work for the elderly, his team recruited 104 sedentary men and women age 62 to 78 for a 12-week program of resistance training. Three times a week, each person did 10 exercises with weights equal to about 75 percent of the maximum that he or she could lift. While half raised the weights to the standard count of 2, the rest were told to hoist them as quickly as possible.

At the end of the training period, the volunteers' ability to push levers, move their limbs, and perform powerful work was compared to their previous strength. Those who trained at the slower speed improved their ability to perform slow tasks, such as moving an arm through a 60° arc in 1 second or lifting slowly. Only those who trained at high speed improved substantially in their ability to exhibit power and torque (such as pushing on a lever) at high speeds.

In daily living, speed counts, Signorile says, "because it does not matter how strong my arms are if I don't get them out in front in time to break a fall. That's what we're training for." —*J.R.*

Exercise does not spur AIDS course

People infected with HIV, the virus responsible for AIDS, tend to develop muscle wasting. Though their surviving muscle can be strengthened with exercise, many AIDS sufferers have been reluctant to pump iron for fear that the muscle injury accompanying this training might initiate an immune response that would cause HIV to replicate.

A new study indicates that such worries may be unfounded.

Ronenn Roubenoff of the Tufts University School of Medicine in Boston and his colleagues recruited 21 men and 4 women infected with HIV. They underwent a 15-minute step-climbing activity. Once every 5 seconds throughout the trial they stepped onto and off of a 30-centimeter-high platform. While it was rigorous work, all of the volunteers finished it (although they reported feeling sore for days afterward).

Comparing the results of laboratory tests performed during the week after the exercise trial to those before, "we did see activation of the immune system, muscle damage, and activation of muscle protein turnover—all things that we know are part of the response to exercise," Roubenoff says. "What we didn't see was a rise in [HIV]. "In fact, there was a statistically significant, but not biologically significant, decline."

Studies by others have shown that if one stimulates the immune system—for example, by vaccinating people who have HIV—"you can get a walloping increase" in the number of HIV-infected cells, he notes. Doctors were concerned that HIV-positive people who move from inactivity to exercise, as weekend athletes or gardeners do, might experience a similar increase. "But this level of exercise doesn't seem to be that strong a stimulus," Roubenoff says. "That's reassuring," he notes, because earlier research by his team has shown that any follow-up exercise will have a far smaller impact on immunity. —*J.R.*