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Smallpox as A Weapon of Bioterrorism

Penn Researchers Receive NIH Grant to Lessen the Threat

(Philadelphia, Pa.) - University of Pennsylvania School of Medicine researchers have received a grant from the National Institutes of Health (NIH) to investigate how the U.S. could combat a possible outbreak of smallpox. Stuart N. Isaacs, MD, Assistant Professor of Medicine in the Penn Division of Infectious Diseases and John D. Lambris, PhD, Professor in the Department of Pathology & Laboratory Medicine, will lead the research into creating new therapies to protect against the disease. The researchers were awarded $1.1 million for the four-year study.

"Smallpox may be largely forgotten, but it certainly isn't gone," said Isaacs. "There is a possibility, however slight, that terrorists could obtain the virus and release it within the U.S."

Despite the existence of a working vaccine, smallpox could still serve as powerful weapon for bioterrorists interested in attacking the U.S. The U.S. population is becoming highly susceptible since Americans are no longer vaccinated against the disease and older people who were previously vaccinated are losing their immunity to the virus.

There is very little vaccine stockpiled either in the U.S. or globally to respond to a terrorist attack, and there is no drug currently available to treat smallpox. Death rates from a smallpox infection among an unvaccinated population can be as high as 30%.

Currently, vaccination remains the only way to protect an at-risk civilian population, however, a

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portion of the population can have serious complications with the vaccine, particularly pregnant women, infants, and people with poor immune systems. There is a treatment for these complications, a preparation of human immune globulin - a protein taken from healthy vaccinated people - but it is in very short supply.

Instead, Isaacs and Lambris will develop new therapies that target related, yet functionally distinct, virus proteins. "We are looking at a combination punch to knock-out the effects of the smallpox virus," said Lambris. "We will create therapeutics which will attack two proteins that the virus produces." One therapy would prevent the virus from entering cells and the other will neutralize a protein that the virus produces to bypass the human immune system.

VCP, the vaccinia complement-control protein, inactivates the human complement system, a complex system of circulating proteins that attack invading organisms in the human body. The complement system serves as the first line of defense for the immune system and when the virus disables complement proteins, it makes it easier for it to invade and survive in human cells. By neutralizing VCP, the researchers hope to create a therapy that would allow a patient's complement system to control a smallpox virus infection.

The researchers are also looking at B5R, a specific protein on the surface of the virus. The virus uses B5R as a key to unlock the walls of human cells, and is essential for further spreading the virus within an infected host. The researchers plan to create therapeutics that will attach to B5R and prevent it from functioning, thereby disabling the virus.

"I find it morbidly ironic that smallpox, the first disease ever to be purposely immunized against - and successfully eradicated - might come back from the dead to pose a threat now, " said Isaacs. "Fortunately, we now have the tools and understanding to help take the risk out of smallpox vaccinations and potentially combat the threat of smallpox bioterrorism."