New vaccine against filoviruses

Filoviruses (Ebola and Marburg viruses) are highly infectious pathogens that cause hemorrhagic fever in humans and nonhuman primates. Their mortality rates approach 90% in humans. There are currently no approved vaccines against filoviruses.

New research presented at the 2008 American Society for Microbiology's Biodefense and Emerging Diseases Research Meeting in Baltimore, MD, shows that a vaccine that combines Ebola and Marburg virus-like particles (VLPs) protects macaques against the filoviruses. The work builds on previous studies using guinea pigs.

Kelly L. Warfield (United States Army Medical Research Institute of Infectious Diseases, Ft. Detrick, MD) and her colleagues previously showed that VLP-based vaccines could protect against filoviruses in guinea pigs. Given separately, the Ebola or Marburg VLPs protected guinea pigs against the corresponding filovirus, but not the other virus. Given together in a single dose, however, the Ebola and Marburg VLPs elicited strong immune responses and protected guinea pigs against both filoviruses.

Warfield's new research tested the combined Ebola and Marburg VLPs in more than 50 cynomolgus macaques. Vaccinated macaques developed strong Ebola- and Marburg-specific antibody titers and survived exposure to the filoviruses without developing clinical or laboratory signs of infection, whereas control animals succumbed to filovirus infection.

More studies are planned to determine how many doses of the vaccine are necessary and whether boosters are needed for long-term protection. In addition, investigators hope to develop a vaccine that will offer protection against all known pathogenic filovirus strains.

Traditional antiviral vaccines used whole viruses: either a virus genetically similar to the pathogen that would cause an immune response but not the disease, or the pathogen itself that had been weakened or killed in order to minimize risk of disease. These traditional vaccines carry a small risk of viral infection. Because the VLP-based vaccines do not use whole viruses, they carry no risk of infection, making them potentially safer than other antiviral vaccines. Some VLP-based vaccines are already available in the US, such as the vaccine against human papillomavirus.

Filoviruses present a potential bioterrorism threat because they are highly infectious, have high mortality rates and lack approved vaccines. The new VLP-based vaccine was safe and effective in protecting macaques against filovirus infection, making it "a leading candidate for use as a filovirus vaccine in humans," according to Warfield. Researchers hope to begin testing the vaccine in humans in coming years.

Monica Harrington

TOXICITY TESTING: THE NEXT GENERATION

Three federal agencies are joining forces in an effort to advance toxicity testing to the next level, with the hope of eventually shifting from animal experimentation to high-throughput *in vitro* assays.

The National Toxicology Program of the National Institutes of Health (NIH) and the US Environmental Protection Agency have been working together for several years to develop and implement a strategy that will enable more compounds to be tested, while relying increasingly on human rather than animal data. The two groups will now be joined by the NIH Chemical Genomics Center, which possesses the sophisticated technology that can help realize this vision: a high-throughput screening system, in which robots rapidly move well plates down an assembly line and subject them to automated assays (*Science* **319**, 906–907; 2008). The screening system, which has until now been used primarily to identify beneficial compounds for drug discovery, will be adapted to test the effects of potentially toxic chemicals. An informatics platform will compare results between assays and evaluate them against historical data, enabling scientists to fine-tune the system's output.

Toxicity tests traditionally involve "injecting chemicals into laboratory animals, watching to see if the animals get sick and then looking at their tissues under the microscope," said Francis Collins of the NIH National Human Genome Research Institute in a February teleconference announcing the collaboration. That approach uses many animals, and its relevance to toxicity in humans "is not as precise as we would like." The new screening technology enables *in vitro* testing of human and animal cells in massive quantities. According to Chemical Genomics Center Director Christopher Austin, the system would require only 2 days to test 100,000 compounds in 15 different concentrations. It would be "physically impossible," Austin said, to carry out the same number of tests in animals. In fact, over the past 30 years the NIH has been able to study only 2,500 chemicals in depth.

The system may also help scientists better understand data obtained from animal tests by elucidating the genetic pathways that are responsible for different human and animal responses to toxicants.

The collaboration is still in its preliminary stages, and it will take time to determine whether the new methods will be able to replace traditional animal testing. But if the joint effort is successful, said Collins, it "has the potential to revolutionize the way that toxic chemicals are identified."

Karen Marron