



# NEWS RELEASE

U.S. Army Medical Research Institute of  
Infectious Diseases  
Fort Detrick, Maryland

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## **Gene-Specific Ebola Therapies Protect Nonhuman Primates from Lethal Disease**

Scientists have developed a successful strategy for interfering with Ebola virus infection that protected 75 percent of nonhuman primates exposed to the lethal disease. This is the first successful antiviral intervention against filoviruses like Ebola in nonhuman primates. The findings could serve as the basis for a new approach to quickly develop virus-specific therapies for known, emerging, and genetically engineered pathogens.

In today's online issue of the journal *Public Library of Science Pathogens*, a research team led by Sina Bavari and colleagues at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) reports using novel "antisense" drugs to interrupt normal Ebola virus replication. The work was performed in collaboration with AVI BioPharma, a U.S. biotechnology firm.

According to the study's authors, antisense drugs are useful against viral diseases because they are designed to enter cells and eliminate viruses by preventing their replication. The drugs, which act by blocking critical viral genetic sequences, may be more potent than anti-virals such as protease inhibitors, which seek to inhibit a protein needed for viral replication.

Ebola virus causes hemorrhagic fever with case fatality rates as high as 80 percent in humans. The virus, which is infectious by aerosol (although more commonly spread through blood and bodily fluids of infected patients), is of concern both as a global health threat and a potential agent of biological warfare or terrorism. Currently there are no available vaccines or therapies.

"One advantage of this strategy is that it directly targets the virus," said the paper's first author, Kelly L. Warfield. "With Ebola infection, the virus grows so fast that it overtakes the host immune system. What we did, essentially, was to hold off the viral replication long enough for the host to mount an immune response and clear the virus."

Working with a class of compounds known as antisense phosphorodiamidate morpholino oligomers, or PMOs, the team first performed a series of studies to identify PMOs that demonstrated activity against Ebola virus. Next, three of the PMOs were tested in mice, both individually and in combination. The combination of all three was found to be the most effective therapeutic approach in mice, whether the PMOs were administered before or after Ebola infection. Combination therapy was also tested in guinea pigs, where it appeared to be most effective when administered after infection.

To further evaluate the efficacy of the three-PMO combination, four rhesus monkeys were treated with the drug two days prior to Ebola virus exposure. Three of the four were protected from Ebola infection.

“These results, while preliminary, are very encouraging,” said Colonel George W. Korch, USAMRIID commander, “especially when you consider that Ebola virus has, to date, been fairly intractable to effective treatment. We look forward to additional findings of success using these PMOs.”

Collaborating on the study with Bavari and Warfield were Dana L. Swenson, Gene G. Olinger, Donald K. Nichols, William D. Pratt, and M. Javad Aman of USAMRIID, and Robert Blouch, David A. Stein, and Patrick L. Iversen of AVI BioPharma.

USAMRIID, located at Fort Detrick, Maryland, is the lead medical research laboratory for the U.S. Biological Defense Research Program, and plays a key role in national defense and in infectious disease research. The Institute’s mission is to conduct basic and applied research on biological threats resulting in medical solutions (such as vaccines, drugs and diagnostics) to protect the warfighter. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command.

AVI BioPharma, based in Corvallis, Oregon, develops therapeutic products for the treatment of life-threatening diseases using third-generation NeuGene® antisense drugs. AVI’s lead NeuGene® antisense compound is designed to target cell proliferation disorders, including cardiovascular restenosis, cancer and polycystic kidney disease. In addition to targeting specific genes in the body, AVI’s antiviral program uses NeuGene® antisense compounds to combat disease by targeting single-stranded RNA viruses, including West Nile virus, hepatitis C virus, dengue virus and Ebola virus.

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Reference: Warfield KL, Swenson DL, Olinger GG, Nichols DK, Pratt WD, et al. (2006) Gene-specific countermeasures against Ebola virus based on antisense phosphorodiamidate morpholino oligomers. PLoS Pathog 2(1): e1.

For more information on USAMRIID: [www.usamriid.army.mil](http://www.usamriid.army.mil)

For more information on AVI BioPharma: [www.avibio.com](http://www.avibio.com)