Ebola antibody treatment, produced in plants, protects monkeys from lethal disease

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A new Ebola virus study resulting from a widespread scientific collaboration has shown promising preliminary results, preventing disease in infected nonhuman primates using monoclonal antibodies.

In this week's online edition of the Proceedings of the National Academy of Sciences (*PNAS*), the research team describes a proof-of-concept for using a "cocktail" of monoclonal antibodies, or mAbs, to prevent lethal disease in rhesus macaques. When administered one hour after infection, all animals survived. Two-thirds of the animals were protected even when the treatment, known as MB-003, was administered 48 hours after infection.

Ebola virus, which causes hemorrhagic fever with human case fatality rates as high as 90 percent, has been responsible for numerous deaths in central Africa over the past several months. In addition to being a global health concern, the virus also is considered a potential biological threat agent. Currently there are no available vaccines or treatments approved for use in humans.

The work is the culmination of more than a decade of effort between government and industry partners. According to lead investigator Gene Olinger, Ph.D., a virologist at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), this consortium of investigators has taken very distinct technologies and combined them to develop a cutting-edge medical countermeasure against a lethal viral disease.

"It is rare that an antiviral compound prevents Ebola virus infection with limited to no morbidity in treated animals at any point of treatment following infection by this lethal virus," said Olinger. "Until recently, attempts to utilize antibodies to provide protection against Ebola virus have been met with failure. The level of protection against disease that we saw with MB-003 was impressive."

In addition, the production method used in this study offers the potential to make an economical and effective medical countermeasure, according to the authors. Initially developed as a monoclonal antibody cocktail in the mouse model, MB-003 was successfully humanized and then produced in the tobacco plant-based production system.

"We were pleased to see how well the humanized mAbs of MB-003 performed," said Larry Zeitlin, Ph.D., president of Mapp Biopharmaceutical and senior author on the study. "We also were pleasantly surprised by the superiority of the plant-derived mAbs compared to the same mAbs produced in traditional mammalian cell culture."

Further improvement in antibody efficacy was developed at Kentucky BioProcessing (KBP). Using a fully automated production system that operates in accordance with good manufacturing practices (GMP), antibody is produced in a tobacco plant system. This new development process significantly decreases the amount of time required for production, increases the quantity of antibody produced, and slashes the cost of manufacturing, according to Barry Bratcher, chief operating officer of KBP and co-author on the *PNAS* study.

"Our GMP facility can generate a new antibody lot in two weeks to rapidly address new threats and new outbreaks," said Bratcher.

Olinger said efforts are underway to advance MB-003 to clinical safety

testing as his team at USAMRIID continues to determine the true therapeutic capability of the cocktail.

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