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COMMENTARY

Recent advances in vaccine development against Ebola threat as bioweapon

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Abstract With the increasing rate of Ebola virus appearance, with multiple natural outbreaks of Ebola hemorrhagic fever, it is worthy of consideration as bioweapon by anti-national groups. Further, with the non-availability of the vaccines against Ebola virus, concerns about the public health emerge. In this regard, this review summarizes the structure, genetics and potential of Ebola virus to be used as a bioweapon. We highlight the recent advances in the treatment strategies and vaccine development against Ebola virus. The understanding of these aspects might lead to effective treatment practices which can be applied during the future outbreaks of Ebola.

Keywords Ebola virus · Ebola hemorrhagic fever · Bioweapon · Ebola vaccine · Ebola outbreak

Introduction

There is a growing risk that the science will be deliberately misused and that the consequences could be catastrophic. The global proliferation of biological weapon (BW) technologies remains a significant threat to public health and the environment. Unfortunately, many BW agents are unfamiliar to most clinicians and laboratory scientists, complicating appropriate responses [28]. Bioweapons are the biological entities or organisms which can be used as a weapon in the wars. Several countries are believed to have offensive biological weapons programs, and some independent anti-national groups have suggested their intention to use biological weapons. As the possibility of a terrorist attack using bioweapons is especially difficult to predict, detect, or prevent, it is among the most-feared terrorism scenarios.

Ebola virus hemorrhagic fever has been known to affect thousands of people worldwide with higher mortality rates. The first reported outbreak of Ebola virus disease (EVD) occurred in 1976 in Democratic republic of Congo (Northwestern Zaire). Since then many severe outbreaks occurred in other parts of the world, Sudan, central and west Africa. The recent outbreak of EVD was the first in densely populated area, infected the largest numbers, was of longest duration with high fatality rate and simultaneously hit three countries i.e. Guinea, Liberia, and Sierra [25]. The severity of the disease led WHO to seek greater efforts to fight against EVD and declare it as public health emergency of international concern (PHEIC).

EVD is a significant health concern worldwide because of the absence of specific effective treatments and vaccines against Ebola virus in addition to lack of early diagnostic methods, insufficient equipment for personal protection and deficient resources for infection control. The high rate of mortality associated with EVD, marked the potential of Ebola virus to be used as bioweapon by anti-national groups. The present review seeks to provide information on the potential of Ebola virus to be used as a bioweapon as well as the recent advances in vaccine development against Ebola virus to combat this risk.

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Epidemiology of Ebola virus

Ebola virus is a member of the virus family Filoviridae which contains five species such as Bundibugyo ebolavirus, Reston ebolavirus, Sudan ebola virus, Tai Forest ebola virus, and Zaire ebola virus [35], responsible for causing an infectious disease "Ebola hemorrhagic fever" with a high mortality rate. The name "Ebola" came from the river Zaire where it was first discovered in 1976. The virus actually occurs in the animal population but can be transmitted to the human populations by direct contact. The natural carriers of Ebola virus are thought to be fruit bats which carry the virus without being affected by it. Non-human primates like monkeys can also be the accidental host and can be infected with the virus as humans [26]. After its discovery in 1976, many of the Ebola outbreaks were reported in Sudan, Central and Western Africa; however, the most recent outbreak which simultaneously hit three countries Guinea, Liberia, and Sierra Leone infected the largest numbers, were of longest duration and possess high fatality rate. WHO also seeks greater efforts to fight against Ebola virus and declared this outbreak as a Public Health Emergency of International Concern (PHEIC) in 2014. Although most of the past Ebola outbreaks are mainly caused by Reston species but mortality rate may vary from highest with Zaire species (80%) and lowest with Bundibugyo species (40%).

The virus possesses a negative-sense, non-segmented RNA genome, 19 kb in length (800–1100 nm long and 80 nm diameter), that encodes seven structural proteins (3′ NP VP35 VP40 GP (including secreted soluble GP (sGP) and structural $GP_{1,2}$) VP30 VP24 L 5′) and at least one nonstructural protein [8, 31]. Components of the nucleocapsid are Nucleoprotein (NP), viral protein (VP) 35, VP30, and L, the RNA-dependent RNA polymerase are essential for viral replication and transcription [23]. VP40 is the matrix protein and is critical for viral budding [12]. VP24 is essential for the formation of nucleocapsids composed of NP, VP35, and viral RNA [15]. The viral surface glycoproteins secreted soluble GP (sGP) and structural $GP_{1,2}$, plays a role in viral attachment and entry [25].

Symptoms of Ebola virus infection include high fever, chills, asthenia (), headache, muscle aches, anorexia, conjunctivitis, abdominal pain, nausea, vomiting and diarrhea, pharyngitis, sore throat and chest pain and an erythematous macules rash. After three days of fever, the hemorrhagic manifestation of the disease usually begins. The signs are characterized by hemorrhage (blood escape from ruptured blood vessel, ecchymoses (bruising), conjunctival hemorrhage, gingival bleeding, bleeding from an injection site, frank bleeding from the gastrointestinal tract with melaena (blood loss in faeces), vaginal bleeding, haematemesis (vomiting of blood), and bleeding from other sites such as internal organs). The incubation period of the virus ranges from 2 to 21 days. The symptoms of Ebola hemorrhagic fever are typical of any common tropical disease which makes it misdiagnosed and mistreated, and thus poses a public health threat [11].

Ebola threat as bioterrorist attack

Since the death rate of this highly contagious infectious disease, Ebola hemorrhagic fever is 25–90% for those who contract Ebola virus, and because of its easy transmittance from person to person, this virus possess the potential to be used as bioweapon [19]. The virus is classified as category A bioterrorism threats by Centers for Disease Control and Prevention (CDC) for several reasons [1]. First, the filoviruses are highly lethal, causing severe hemorrhagic fever disease in humans and apes with high mortality rates (up to 90%). Second, in addition to being extremely pathogenic, filoviruses are highly infectious as aerosol droplets [33]. However, till now there is no report of bioterrorism event using Ebola virus as the virus possess certain constraints to be used effectively. It is difficult to prepare and becomes ineffective quickly when exposed to open air. Only an expert can handle the virus having the skills like obtaining the correct strain, growing the strain with the desired characteristics, storing and effectively dispersing the virus [20].

Although the threat of terrorism by preparing Ebola virus is low but still policies are required to prevent the potential threat. To be used for bioterrorism, Ebola virus is either obtained naturally or synthetically produced and weaponized to kill. There were eight instances reported till 2001 where terrorists have tried to acquire this virus. One obtained from legitimate supplier, one stolen, and one was self-manufactured, two were obtained from natural sources and three had unknown sources [4].

Development of vaccines against Ebola virus

Ebola -infected person is a source of spreading the disease till his body secretions contain the virus. Although intensive research has been done, till now there is no vaccine available for the Ebola hemorrhagic fever (WHO report, Ebola haemorrhagic fever fact sheet 103; 2012). Therefore, an effective vaccine is needed to be developed in order to immunize the population against this deadly virus. An important therapeutic strategy is to target virus proteins which interact with host and critically regulate virus life-cycle. Ebola virus matrix protein, VP40, which is

abundantly expressed in infection and regulates virion assembly and budding in infected cells, is critical in this regard [22]. In 2007, Warfield and colleagues developed a vaccine which provides immunity against the Ebola virus. They produced the virus like particles from the co-expression of the viral glycoprotein and matrix protein VP40 in mammalian cells which resembles the wild type virus and are immunogenic in nature. These viruses-like particles were found to be effective against many viral infections like papilloma virus, HIV and rotavirus [36].

The Ebola virus is very lethal as the virus can be handled under the BSL-4 cabinets only. The lack of sufficient BSL-4 space and trained personnel and the rigors of working in BSL-4 laboratories have severely hampered basic research with Ebola virus as well as the development of vaccines and large-scale screening for effective antiviral compounds. Halfmann and coworkers developed a biologically-contained Ebola virus which has a reporter gene instead of VP30 gene useful in transcription. The viruses which lack the VP30 gene do not show any morphological difference from the wild type virus. Due to these changes in the virus, the engineered strain is safe for handling outside the BSL-4 cabinet [10].

In 2007, Jones and coworkers assessed the vaccine based on vesicular stomatitis virus (VSV) by using mouse model of Ebola virus hemorrhagic fever. Mice were injected with various doses of vaccine. Doses decreasing from 2×10^4 to 2 plaque-forming units (PFU), with both systemic and mucosal vaccination routes were used. Mice were challenged with 10^3 to 10^6 lethal doses of mouse-adapted live attenuated vesicular stomatitis virus expressing the Zaire Ebola virus (ZEBOV) glycoprotein. Severely immune-compromised mice were injected with 2×10^5 pfu, which was 10 times greater than the immunization dose normally used to test vaccine safety. Two plaque-forming units of the vaccine protected against lethal challenge, and mucosal immunization was found to be as protective as systemic injection. The replicating vaccine was never detected in the immunized animals, nor were there clinical signs after immunization. Vaccination of severely immune-compromised mice with 200,000 pfu resulted in no clinical symptoms [17]. In 2008, Geisbert and coworkers also developed a vaccine against Ebola virus based on vesicular stomatitis virus (VSV) and tested against Zaire Ebola virus in macaques infected with simian HIV. It was found to be effective against immune-compromised non-human primates [7]. A recent study has also evaluated the efficacy of recombinant rVSV-ZEBOV in preventing Ebola disease with substantial protection [13].

Swenson and coworkers produced a pan filovirus vaccine which was based on a complex adenovirus technology and expressed multiple antigens from five different filoviruses de novo. Vaccination of nonhuman primates demonstrated 100% protection against infection by two species of Ebola virus and three Marburg virus subtypes, each administered at 1000 times the lethal dose. This study indicates the feasibility of vaccination against all current filovirus threats in the event of natural hemorrhagic fever outbreak or biological attack [33]. A study has also demonstrated the use of monoclonal antibodies against cross-protective epitopes with cross-reactivity to several filoviruses, exhibiting protection against Ebola virus and other filoviruses [14].

Sun and coworkers produced Ebola virus like particles (VLP) using recombinant baculovirus expression system in insect cells. The efficacy was checked in mice with a vaccination regime which includes two immunizations of high dose level (50 μg) inducing high levels of antibodies against viral glycoprotein while two immunizations of low dose level (10 μg) inducing five fold less level of antibodies against viral glycoprotein. High production yield of VLP in insect cells with effective protection was observed. If three immunization of low dose is administered, it gives the results similar to those of high dose [32]. A thermostable nano-VLP vaccine is also produced against Ebola virus which can be effectively used in tropical countries [3].

Mucosal vaccination can offer several advantages over conventional intramuscular immunization to protect against Ebola virus (EBOV) infection, such as immune protection at sites of viral entry into susceptible individuals, and can be administered using needle-free devices [27]. A study had evaluated the oral and nasal vaccination of mice with human adenovirus serotype 5 (Ad) expressing the Zaire Ebola virus glycoprotein (Ad-ZGP), in terms of their protection against and underlying immune responses to Ebola virus. Similar to intramuscular administration, oral or nasal vaccination of mice with Ad-ZGP fully protected the mice against a lethal challenge with mouse-adapted EBOV. Both T and B cell responses developed in mice receiving oral or nasal vaccination in different body compartments, indicating qualitative improvement of the immune responses which includes stimulation of CD8+ T cells or effector memory T cells from the gastrointestinal tract or the lungs and was superior to that noted after intramuscular administration of the vaccine [27]. Recently an intranasal Ebola vaccine was evaluated that contained attenuated recombinant human parainfluenza virus type 1 (rHPIV1) and expressed the membrane-anchored form of EBOV glycoprotein GP. It was found to be safe and immunogenic in African green monkeys (AGMs) and set to be further be evaluated in clinical trials [21]. The attempts were also made to form edible Ebola vaccine [2].

In 2010, Pratt and coworkers developed a multivalent vaccine which expresses the glycoprotein of Zaire and Sudan Ebola virus based on adeno virus vector. This

vaccine provides protection against both viruses by either of the route [29]. Passive antibody had also been used effectively for the treatment of Ebola hemorrhagic fevers, with encouraging results [24]. Furthermore, considerable evidences from animal studies indicate that passive antibody administration prevents or ameliorates disease caused by viral agents of hemorrhagic fever. Studies in mice suggest that the protective efficacy of passive antibody against Ebola virus (EBOV) is a result of suppression of viral growth which allows development of immunity [9]. Hyper immune goat serum was generated by immunization with live EBOV-protected guinea pigs against lethal challenge [18]. Passive antibody therapy for EBOV infection may be effective in humans, as suggested by lower death rates in recipients of blood transfusions from convalescent patients [5].

In 2011, Zeitlina and coworkers have designed monoclonal antibodies (mAbs) which could be used in humans as immune-protectants for EBOV, starting with a murine mAb (13F6) which recognizes the heavily glycosylated mucin-like domain of the virion-attached glycoprotein(GP). The mAb was developed by introducing point mutation in the murine mAb variable region which removes the human T cell epitope. The efficacy of three variants of h-13F6 carrying different glycosylation patterns was evaluated in a lethal mouse EBOV challenge model. The pattern of glycosylation of the various mAbs was found to correlate to the level of protection [37].

An in vitro screening of the drugs and selected molecular probes had been done to identify the drugs which show antiviral activity against Zaire Ebola virus infection. Through this screening, selective estrogen receptor modulators were identified like clomiphene and toremifene, which were having antiviral activity against Ebola virus infections [16]. Food and drug administration (FDA) approves these selective estrogen receptor modulators (SERMs) which possess selective anti-Ebola activities for treatment of Ebola virus infections. It was observed that SERMs reduces cellular sphingosine concentration and accumulation of endo-lysosomal calcium, thus blocking Ebola entry [6].

Concluding remarks

With the increasing concern of using Ebola virus in bioterrorism, nations have become more concerned about developing an effective vaccine against this deadly virus. Although there is difficulty in obtaining and weaponizing the Ebola virus, the risk of using it as a bioweapon still exists. In spite of large research efforts with evaluation of several vaccine candidates and FDA approval to estrogen receptor modulators, none of the vaccine has been licensed yet. Some like DNA vaccines and adenovirus-based vaccines have entered Phase I clinical trials. A report has even shown the use of rVSV vaccine to protect one researcher with lab exposure of EBOV [34]. Furthermore, a recent report had shown that EBOV strains undergo adaptive mutations to escape itself from detection by T and B cells of host immune system [30]. These challenges remain to increase the effectiveness of vaccines and to reduce their adverse effects. Due to highly contagious nature of Ebola virus, as it can be transmitted easily through direct contact, effective preventive measures are required to prevent its spreading. These include educating people with classical approaches of disease prevention, isolation of patients or dead bodies, avoidance of funeral and burial rituals to prevent contact with the infected body. More funding and research efforts are also required for the identification of reservoir and potential hosts for Ebola viruses.

References

1. Ansari AA. Clinical features and pathobiology of Ebolavirus infection. J Autoimmun. 2014;55:1–9.
2. Arntzen C. Plant-made pharmaceuticals: from 'Edible Vaccines' to Ebola therapeutics. Plant Biotechnol J. 2015;13(8):1013–6.
3. Carra JH, Martins KA, Schokman RD, Robinson CG, Steffens JT, Bavari S. A thermostable, chromatographically purified Ebola nano-VLP vaccine. J Transl Med. 2015;13:228.
4. Carus WS. Bioterrorism and biocrimes: the illicit use of biological agents since 1900. Washington: National Defense University; 2001.
5. Casadevall A, Pirofski LA. The Ebola epidemic crystallizes the potential of passive antibody therapy for infectious diseases. PLoS Pathog. 2015;11(4):e1004717.
6. Fan H, Du X, Zhang J, Zheng H, Lu X, Wu Q, Li H, Wang H, Shi Y, Gao G, Zhou Z, Tan DX, Li X. Selective inhibition of Ebola entry with selective estrogen receptor modulators by disrupting the endolysosomal calcium. Sci Rep. 2017;7:41226.
7. Geisbert TW, Daddario-Dicaprio KM, Lewis MG, Geisbert JB, Grolla A, Leung A, Paragas J, Matthias L, Smith MA, Jones SM, Hensley LE, Feldmann H, Jahrling PB. Vesicular stomatitis virus-based ebola vaccine is well-tolerated and protects immunocompromised nonhuman primates. PLoS Pathog. 2008;4(11):e1000225.
8. Griffiths A, Andrew H, Robert D, Olena S, Ricardo C Jr, Jean LP. Chapter 24: Ebola virus infection. In: Singh SK, Ruzek D, editors. Viral hemorrhagic fevers. Boca Raton, CRC Press Taylor and Fracis Group; 2014. p. 435–56.
9. Gupta M, Mahanty S, Ahmed R, Rollin PE. Monocyte-derived human macrophages and peripheral blood mononuclear cells infected with ebola virus secrete MIP-1alpha and TNF-alpha and inhibit poly-IC-induced IFN-alpha in vitro. Virology. 2001;284(1):20–5.
10. Halfmann P, Ebihara H, Marzi A, Hatta Y, Watanabe S, Suresh M, Neumann G, Feldmann H, Kawaoka Y. Replication-deficient ebolavirus as a vaccine candidate. J Virol. 2009;83(8):3810–5.
11. Hartley MA, Young A, Tran AM, Okoni-Williams HH, Suma M, Mancuso B, Al-Dikhari A, Faouzi M. Predicting Ebola severity: a clinical prioritization score for Ebola virus disease. PLoS Negl Trop Dis. 2017;11(2):e0005265.

12. Harty RN, Brown ME, Wang G, Huibregtse J, Hayes FP. A PPxY motif within the VP40 protein of Ebola virus interacts physically and functionally with a ubiquitin ligase: implications for filovirus budding. Proc Natl Acad Sci US A. 2000;97(25):13871–6.
13. Henao-Restrepo AM, Camacho A, Longini IM, Watson CH, Edmunds WJ, Egger M, Carroll MW, Dean NE, Diatta I, Doumbia M, Draguez B, Duraffour S, Enwere G, Grais R, Gunther S, Gsell PS, Hossmann S, Watle SV, Kondé MK, Kéïta S, Kone S, Kuisma E, Levine MM, Mandal S, Mauget T, Norheim G, Riveros X, Soumah A, Trelle S, Vicari AS, Røttingen JA, Kieny MP. Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). Lancet. 2017;389(10068):505–18.
14. Holtsberg FW, Shulenin S, Vu H, Howell KA, Patel SJ, Gunn B, Karim M, Lai JR, Frei JC, Nyakatura EK, Zeitlin L, Douglas R, Fusco ML, Froude JW, Saphire EO, Herbert AS, Wirchnianski AS, Lear-Rooney CM, Alter G, Dye JM, Glass PJ, Warfield KL, Aman MJ. Pan-ebolavirus and pan-filovirus mouse monoclonal antibodies: protection against Ebola and Sudan viruses. J Virol. 2015;90(1):266–78.
15. Huang Y, Xu L, Sun Y, Nabel GJ. The assembly of Ebola virus nucleocapsid requires virion-associated proteins 35 and 24 and posttranslational modification of nucleoprotein. Mol Cell. 2002;10(2):307–16.
16. Johansen LM, Brannan JM, Delos SE, Shoemaker CJ, Stossel A, Lear C, Hoffstrom BG, Dewald LE, Schornberg KL, Scully C, Lehár J, Hensley LE, White JM. Olinger GG.FDA-approved selective estrogen receptor modulators inhibit Ebola virus infection. Sci Transl Med. 2013;5(190):190ra79.
17. Jones SM, Stroher U, Fernando L, Qiu X, Alimonti J, Melito P, Bray M, Klenk HD, Feldmann H. Assessment of a vesicular stomatitis virus-based vaccine by use of the mouse model of Ebola virus hemorrhagic fever. J Infect Dis. 2007;196(Suppl 2):S404–12.
18. Kudoyarova-Zubavichene NM, Sergeyev NN, Chepurnov AA, Netesov SV. Preparation and use of hyperimmune serum for prophylaxis and therapy of Ebola virus infections. J Infect Dis. 1999;179(Suppl 1):S218–23.
19. Lederberg J. Biological weapons. Cambridge: The MIT Press; 1999.
20. Leitenberg M. Biological weapons in the twentieth century: a review and analysis. Crit Rev Microbiol. 2001;27(4):267–320.
21. Lingemann M, Liu X, Surman S, Liang B, Herbert R, Hackenberg AD, Buchholz UJ, Collins PL, Munir S. Attenuated human Parainfluenza virus type 1 expressing Ebola Virus Glycoprotein GP administered intranasally is immunogenic in African Green Monkeys. J Virol. 2017;91:JVI.02469-16.
22. Madara JJ, Han Z, Ruthel G, Freedman BD, Harty RN. The multifunctional Ebola virus VP40 matrix protein is a promising therapeutic target. Future Virol. 2015;10(5):537–46.
23. Mühlberger E, Lötfering B, Klenk HD, Becker S. Three of the four nucleocapsid proteins of Marburg virus, NP, VP35, and L, are sufficient to mediate replication and transcription of Marburg virus-specific monocistronic minigenomes. J Virol. 1998;72(11):8756–64.
24. Mupapa K, Massamba M, Kibadi K, Kuvula K, Bwaka A, Kipasa M, Colebunders R, Muyembe-Tamfum JJ. Treatment of Ebola hemorrhagic fever with blood transfusions from convalescent patients. International Scientific and Technical Committee. J Infect Dis. 1999;179(Suppl 1):S18–23.
25. Nanbo A, Imai M, Watanabe S, Noda T, Takahashi K, Neumann G, Halfmann P, Kawaoka Y. Ebolavirus is internalized into host cells via macropinocytosis in a viral glycoprotein-dependent manner. PLoS Pathog. 2010;6(9):e1001121.
26. Nidom CA, Nakayama E, Nidom RV, Alamudi MY, Daulay S, Dharmayanti IN, Dachlan YP, Amin M, Igarashi M, Miyamoto H, Yoshida R, Takada A. Serological evidence of Ebola virus infection in Indonesian orangutans. PLoS ONE. 2012;7(7):e40740.
27. Patel A, Zhang Y, Croyle M, Tran K, Gray M, Strong J, Feldmann H, Wilson JM, Kobinger GP. Mucosal delivery of adenovirus-based vaccine protects against Ebola virus infection in mice. J Infect Dis. 2007;196(Suppl 2):S413–20.
28. Peruski LF Jr, Peruski AH. Rapid diagnostic assays in the genomic biology era: detection and identification of infectious disease and biological weapon agents. Biotechniques. 2003;35(4):840–6.
29. Pratt WD, Wang D, Nichols DK, Luo M, Woraratanadharm J, Dye JM, Holman DH, Dong JY. Protection of nonhuman primates against two species of Ebola virus infection with a single complex adenovirus vector. Clin Vaccine Immun. 2010;17:572–81.
30. Ramaiah A, Arumugaswami V. Ebolavirus evolves in human to minimize the detection by immune cells by accumulating adaptive mutations. Virusdisease. 2016;27(2):136–44.
31. Sanchez A. Analysis of filovirus entry into vero e6 cells, using inhibitors of endocytosis, endosomal acidification, structural integrity, and cathepsin (B and L) activity. J Infect Dis. 2007;15(196 Suppl 2):S251–8.
32. Sun Y, Carrion R Jr, Ye L, Wen Z, Ro YT, Brasky K, Ticer AE, Schwegler EE, Patterson JL, Compans RW, Yang C. Protection against lethal challenge by Ebola virus-like particles produced in insect cells. Virology. 2009;383(1):12–21.
33. Swenson DL, Warfield KL, Negley DL, Schmaljohn A, Aman MJ, Bavari S. Virus-like particles exhibit potential as a pan-filovirus vaccine for both Ebola and Marburg viral infections. Vaccine. 2005;23(23):3033–42.
34. Takada A, Robison C, Goto H, Sanchez A, Murti KG, Whitt MA, Kawaoka Y. A system for functional analysis of Ebola virus glycoprotein. Proc Natl Acad Sci USA. 1997;94:14764–9.
35. Twenhafel NA, Mattix ME, Johnson JC, Robinson CG, Pratt WD, Cashman KA, Wahl-Jensen V, Terry C, Olinger GG, Hensley LE, Honko AN. Pathology of experimental aerosol Zaire ebolavirus infection in rhesus macaques. Vet Pathol. 2013;50(3):514–29.
36. Warfield KL, Swenson DL, Olinger GG, Kalina WV, Aman MJ, Bavari S. Ebola virus-like particle-based vaccine protects nonhuman primates against lethal Ebola virus challenge. J Infect Dis. 2007;196(Suppl 2):S430–7.
37. Zeitlin L, Pettitt J, Scully C, Bohorova N, Kim D, Pauly M, Hiatt A, Ngo L, Steinkellner H, Whaley KJ, Olinger GG. Enhanced potency of a fucose-free monoclonal antibody being developed as an Ebola virus immunoprotectant. Proc Natl Acad Sci U S A. 2011;108(51):20690–4.