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Ebola Virus Vaccines

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Abstract

Ebola hemorrhagic fever, an extremely fatal viral disease is caused by Ebola virus. The African subcontinent is experiencing the most fatal epidemic caused by this virus. Recently, a few cases have been detected outside Africa. Thus, this is of concern and has alerted World Health Organization (WHO). Currently there is no cure for Ebola, nor is there a vaccine approved yet for human use. A few vaccines are under clinical trials. Thus, there needs to be an integrated approach in prevention of this fatal disease by an effective vaccine formation.

Introduction

Ebola hemorrhagic fever, an extremely fatal viral disease is caused by Ebolavirus which is a highly infectious biological class 4 pathogen.¹ Though its discovery dates back to the year

1976, it is this year that the world experienced the most fatal epidemic caused by this virus. As present, this is confined to the African subcontinent with a great potential to spread globally. First case of Ebola hemorrhagic fever has been confirmed in Texas, US indicating its virulent potential. As per the latest WHO data, case fatality rate is as high as 90%, with a total number of cases being 3069, and deaths approximating 1552. The natural host for Ebola virus is being postulated as being fruit bats but there still seems to be no confirmation.²This has made it difficult for health care workers to implement programs to control or eliminate viral reservoirs of transmission to human populations. Currently there is no cure for Ebola, nor is there a vaccine approved yet for human use. Thus, there needs to be a more integrated approach in prevention of this fatal disease by an effective vaccine formation.

Challenges in vaccine development

A good vaccine for combating Ebola virus is a task which needs a lot of understanding of the pathogenesis of this disease, as well as the circulating Ebola virus strains. Recently, a report submitted on an outbreak in Guinea, West Africa revealed that the circulating strain was positioned in a different clade based on the phylogenetic analysis.³ Thus, this indicated that the strains of Zaire Ebola virus prevalent in Democratic Republic of Congo were different from the one in Guinea. This makes it extremely challenging to make an ideal vaccine to fight all the circulating strains. Another difficulty is preventing the virus from infecting monocytes, macrophages and dendritic cells which are the first cells to trigger the innate immune system to fight off infection.⁴ In addition, testing an Ebola vaccine is impractical and extremely hard, because the disease is so deadly and rare. Unlike other viruses of public health importance like hepatitis and measles virus, there is already a widespread population infected, so scientists can test the vaccine in those individuals. In contrast in case of Ebola virus, exposing a vast majority of population to the vaccine candidates under trial seems unethical.

Vaccine candidates

The target vaccine audience are district-level health-care workers (doctors, nurses, and paramedics), as well as intermediate- and central-level health-care workers responsible for

epidemic control, and International Health Regulations (IHR) and National Focal Points (NFPs).

Animal models

Several animal models have been developed to study the pathogenesis of Ebola virus infection and to assess the efficacy of various vaccine approaches. Guinea pigs and nonhuman primates represent the primary animal models for vaccine development because the progression and pathogenesis most closely resemble those of the human disease. A murine model was later developed by serial passage of virus in mice.⁴ Though the model allows the use of knockout and inbred strains to evaluate genetic determinants of disease, it is considered less predictive of human disease because it relies on a serially passaged, attenuated virus. While symptoms and time course of disease in guinea pigs parallel those in humans, nonhuman primate infection is considered the most predictive and useful for vaccine development.

Approach to vaccine development

Initial attempts to vaccine development was the use of an Ebola virus, which was rendered inactive. But not much success was achieved in the first attempts. In a few cases, the non-primate animals seemed to be protected, while the rest were killed. Since then a new approach used is the benign vaccine delivery system. In this approach, without using the actual infectious agent, the Ebola virus, proteins are delivered on the virus vector surface. This stimulates the IgG response and hence protection from Ebola virus disease.⁵

Current vaccine status

Some promising vaccine candidates include replication-deficient adenovirus vectors, replication-competent VSV (Vesicular Stomatitis Virus), HPIV-3 vectors (Human Parainfluenza virus) and virus-like particle preparations.¹ It is the adenovirus-based vaccine that will be tested on humans first. This looks promising, but there are some important caveats. For instance, the study shows something that correlates with protection from Ebola. That doesn't mean IgG is what is protecting the animals from the disease. It is still not clear

exactly how the immune system stops the virus from growing and spreading.⁶Also, the most talked about vaccine these days is the vaccine prepared by the scientists of National Microbiology Laboratory. Canada has donated this experimental Ebola virus vaccine to WHO and clinical trials will begin soon. Meanwhile, clinical trials of another vaccine cAd3, designed by scientists at the U.S. National Institute for Allergy and Infectious Diseases have already started. But the efficacy and safety results are still to be seen.

Conclusion

The rapid progression of Ebola virus infection has complicated the control of this disease, affording little opportunity to develop acquired immunity. There is currently no antiviral therapy or vaccine that is effective against Ebola virus infection in humans. Significant progress has been made in understanding the pathogenesis of Ebola virus infection and several promising vaccine candidates were shown to be successful in protecting non human primates against lethal infection. Recent advances in the generation of effective post-exposure immunization strategies highlight the possibility of developing a single dose vaccine that will confer full protection in humans following Ebola virus exposure.⁷ Post-exposure protection is particularly important in outbreak and biodefense settings, as well as clinical and laboratory settings in the case of accidental exposure.

References

1. Marzi A, Feldmann H. Ebola virus vaccines: an overview of current approaches. *Expert Rev Vaccines*. 2014 Apr;13(4):521-31.
2. Casillas AM, Nyamathi AM, Sosa A, Wilder CL, Sands H.A current review of Ebola virus: pathogenesis, clinical presentation, and diagnostic assessment.*Biol Res Nurs*. 2003 Apr;4(4):268-75.
3. Baize S, Pannetier D, Oestereich L, Rieger T, Koivogui L, Magassouba N et al. Emergence of Zaire Ebola virus disease in Guinea. *N Engl J Med*. 2014 Oct 9;371(15):1418-25.

4. Sullivan N, Yang ZY, Nabel GJ. Ebola virus pathogenesis: implications for vaccines and therapies. *J Virol.* 2003 Sep;77(18):9733-7.
5. Wilson JA, Hevey M, Bakken R, Guest S, Bray M, Schmaljohn AL et al. Epitopes involved in antibody-mediated protection from Ebola virus. *Science.* 2000 Mar 3;287(5458):1664-6.
6. Sullivan NJ, Sanchez A, Rollin PE, Yang ZY, Nabel GJ. Development of a preventive vaccine for Ebola virus infection in primates. *Nature.* 2000 Nov 30;408(6812):605-9.
7. Xu L¹, Sanchez A, Yang Z, Zaki SR, Nabel EG, Nichol ST. Immunization for Ebola virus infection. *Nat Med.* 1998 Jan;4(1):37-42.

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