

CLAIMS

1. A pharmaceutical composition comprising polyclonal immunoglobulin from an equine that has been hyper-immunized with a filovirus glycoprotein, wherein the equine is immunized with a mucin-like domain-deleted filovirus spike glycoprotein.
2. The composition of claim 1, wherein the immunoglobulin is purified from serum or plasma of the equine that has been hyper-immunized with the filovirus glycoprotein.
3. The composition of claim 2, wherein the purified immunoglobulin is IgG, or a fragment thereof.
4. The composition of claim 3, wherein at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 20%, or more of the purified IgG binds to the filovirus glycoprotein.
5. The composition of any one of claims 2 to 4, wherein the purified immunoglobulin can prevent or minimize symptoms in a subject infected with a filovirus.
6. The composition of any one of claims 1 to 5, wherein the filovirus is Ebola virus (EBOV), Sudan virus (SUDV), Bundibugyo virus (BDBV), Tai Forrest virus (TAFV), Reston virus (RESTV), or Marburg virus (MARV).
7. The composition of any one of claims 1 to 6, wherein the transmembrane domain of the spike glycoprotein is deleted.
8. The composition of claim 7, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 subunits thereof.

9. The composition of claim 7, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof and the GP2 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 and GP2 subunits thereof.
10. The composition of any one of claims 7 to 9, wherein the spike glycoprotein comprises an amino acid sequence that is at least 90%, at least 95%, or 100% identical to SEQ ID NOS: 2, 4, 6, 8, 10, or 12.
11. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NO: 2.
12. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NO: 4.
13. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NO: 6.
14. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NO: 8.
15. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NO: 10.
16. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NO: 12.
17. The composition of any one of claims 7 to 16, wherein the equine is immunized with the spike glycoprotein on days 0, 21, 42, and 63, respectively.
18. The composition of claim 17, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.

19. The composition of claim 17 or claim 18, wherein the spike glycoprotein comprises MARV GP-ΔTM, and wherein the recovered plasma has an EC50 titer for binding to MARV GP-ΔTM of at least 10^2 , at least 5×10^2 , at least 10^3 , at least 5×10^3 , at least 10^4 , at least 5×10^4 , at least 10^5 , or at least 5×10^5 , as determined by ELISA.
20. The composition of claim 18 or claim 19, wherein the spike glycoprotein comprises MARV GP-ΔTM, and wherein the purified IgG binds to MARV GP-ΔTM with an EC50 of less than 3 μg/ml, less than 2.5 μg/ml, less than 2 μg/ml, less than 1.5 μg/ml, or less than 1 μg/ml, or less than 0.5 μg/ml, as measured ELISA.
21. The composition of any one of claims 17 to 20, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.
22. The composition of any one of claims 7 to 10, wherein the equine is immunized with a prime-boost regimen.
23. The composition of claim 22, wherein the prime-boost regimen comprises priming with a filovirus virus-like particle (VLP) and boosting with the spike glycoprotein.
24. The composition of claim 23, wherein the VLP comprises a filovirus glycoprotein and a filovirus VP40.
25. The composition of claim 24, wherein the VLP further comprises the filovirus nucleoprotein (NP).
26. The composition of claim 23, wherein the prime dose is administered on day zero and day 21, respectively, and the boost dose is administered on day 42 and day 63, respectively.
27. The composition of claim 26, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.

28. The composition of any one of claims 22 to 27, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, or NP, the boost dose comprises EBOV GP-ΔMuc, and wherein the recovered plasma has an EC50 titer for binding to EBOV GP-ΔTM of at least 10^3 , at least 10^4 , at least 10^5 , or at least 5×10^5 , as determined by ELISA.

29. The composition of any one of claims 22 to 28, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, or NP, the boost dose comprises EBOV GP-ΔMuc, and wherein the purified IgG binds to EBOV GP-ΔTM or EBOV GP-ΔMuc with an EC50 of less than 1 μg/ml, less than 0.9 μg/ml, less than 0.8 μg/ml, less than 0.7 μg/ml, less than 0.6 μg/ml, less than 0.5 μg/ml, less than 0.4 μg/ml, less than 0.3 μg/ml, less than 0.2 μg/ml, less than 0.1 μg/ml, or less than 0.09 μg/ml, as measured ELISA.

30. The composition of any one of claims 22 to 29, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.

31. A method for preparing the composition of any one of claims 1 to 30, comprising administering an amount of a filovirus immunogen to an equine sufficient to hyperimmunize the equine against protective antigens of the filovirus, wherein the immunogen comprises a filovirus spike glycoprotein; and recovering immunoglobulin from the equine, wherein the filovirus glycoprotein is a mucin-like domain-deleted filovirus spike glycoprotein.

32. The method of claim 31, wherein the immunoglobulin is recovered as plasma.

33. The method of claim 31 or claim 32, further comprising purifying the immunoglobulin recovered from the equine.

34. The method of claim 33, wherein the purified immunoglobulin comprises IgG or a fragment thereof.

35. A polyclonal immunoglobulin from an equine that has been hyper-immunized with a filovirus glycoprotein for use in preventing, treating, or managing a filovirus-mediated disease in

a subject, wherein the filovirus glycoprotein is a mucin-like domain-deleted filovirus spike glycoprotein.

36. Use of a polyclonal immunoglobulin from an equine that has been hyper-immunized with a filovirus glycoprotein in the manufacture of a medicament for the treatment, prevention or management of a filovirus-mediated disease, wherein the filovirus glycoprotein is a mucin-like domain-deleted filovirus spike glycoprotein.

37. The use of claim 36, wherein the immunoglobulin is purified from serum or plasma of the equine that has been hyper-immunized with the filovirus glycoprotein.

38. The use of claim 37, wherein the purified immunoglobulin is IgG, or a fragment thereof.

39. The use of claim 38, wherein at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 20%, or more of the purified IgG binds to the filovirus glycoprotein.

40. The use of any one of claims 37 to 39, wherein the purified immunoglobulin can prevent or minimize symptoms in a subject infected with a filovirus.

41. The use of any one of claims 36 to 40, wherein the filovirus is MARV, EBOV, SUDV, BDBV, TAFV, or RESTV.

42. The use of any one of claims 36 to 41, wherein the equine is immunized with a mucin-like domain-deleted filovirus spike glycoprotein.

43. The use of any one of claims 36 to 42, wherein the filovirus glycoprotein is a spike glycoprotein, and wherein a transmembrane domain of the spike glycoprotein is deleted.

44. The use of claim 42 or claim 43, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 subunits thereof.

45. The use of claim 42 or claim 43, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof and the GP2 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 and GP2 subunits thereof.
46. The use of any one of claims 42 to 45, wherein the spike glycoprotein comprises an amino acid sequence that is at least 90%, at least 95%, or 100% identical to SEQ ID NOS: 2, 4, 6, 8, 10, or 12.
47. The use of any one of claims 42 to 46, wherein the spike glycoprotein comprises an amino acid sequence of SEQ ID NOS: 2, 4, 6, 8, 10, or 12.
48. The use of any one of claims 42 to 47, wherein the equine is immunized with the spike glycoprotein on days 0, 21, 42, and 63, respectively.
49. The use of claim 47 or claim 48, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.
50. The use of claim 49, wherein the spike glycoprotein comprises MARV GP- Δ TM, and wherein the recovered plasma has an EC₅₀ titer for binding to MARV GP- Δ TM of at least 10^2 , at least 5×10^2 , at least 10^3 , at least 5×10^3 , at least 10^4 , at least 5×10^4 , at least 10^5 , or at least 5×10^5 , as determined by ELISA.
51. The use of claim 49 or claim 50, wherein the spike glycoprotein comprises MARV GP- Δ TM, and wherein the purified IgG binds to MARV GP- Δ TM with an EC₅₀ of less than 3 μ g/ml, less than 2.5 μ g/ml, less than 2 μ g/ml, less than 1.5 μ g/ml, or less than 1 μ g/ml, or less than 0.5 μ g/ml, as measured ELISA.
52. The use of any one of claims 49 to 51, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.

53. The use of any one of claims 42 to 47, wherein the equine is immunized in a prime-boost regimen.
54. The use of claim 53, wherein the prime-boost regimen comprises priming with a filovirus VLP and boosting with the spike glycoprotein.
55. The use of claim 54, wherein the VLP comprises a filovirus glycoprotein and a filovirus VP40.
56. The use of claim 55, wherein the VLP further comprises the filovirus nucleoprotein (NP).
57. The use of any one of claims 53 to 56, wherein a prime dose is administered on day zero and day 21, respectively, and a boost dose is administered on day 42 and day 63, respectively.
58. The use of any one of claims 53 to 57, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.
59. The use of claim 57 or claim 58, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, and NP, the boost dose comprises EBOV GP- Δ Muc, and wherein the recovered plasma has an EC₅₀ titer for binding to EBOV GP- Δ TM of at least 10^3 , at least 5×10^3 , at least 10^4 , at least 5×10^4 , at least 10^5 , or at least 5×10^5 , as determined by ELISA.
60. The use of claim 57 or claim 58, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, or NP, the boost dose comprises EBOV GP- Δ Muc, and wherein the purified IgG binds to EBOV GP- Δ TM or EBOV GP- Δ Muc with an EC₅₀ of less than 1 μ g/ml, less than 0.9 μ g/ml, less than 0.8 μ g/ml, less than 0.7 μ g/ml, less than 0.6 μ g/ml, less than 0.5 μ g/ml, less than 0.4 μ g/ml, less than 0.3 μ g/ml, less than 0.2 μ g/ml, less than 0.1 μ g/ml, or less than 0.09 μ g/ml, as measured ELISA.
61. The use of any one of claims 53 to 60, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.

62. The use of any one of claims 35 to 61, wherein the filovirus-mediated disease comprises one or more symptoms selected from the group consisting of: fever, internal hemorrhaging, edema, organ failure, headache, malaise, myalgia, nausea, vomiting, bleeding of needle puncture sites, hematemesis, melena, petechiae, ecchymosis, maculopapular rash, disseminated intravascular coagulation, shock, jaundice, conjunctivitis, diarrhea, pharyngitis, convulsions, delirium, coma, oliguria, and epistaxis.

63. The use of any one of claims 36 to 62, wherein the subject is a human.