[0008] Despite the prevalence of HFMD in China, there is currently no vaccine against HFMD available, nor is there an effective antiviral therapy for infection. Treatment of HFMD has been focused only on alleviation of symptoms. Severe oral ulcerations can create painful stomatitis, which interferes with oral intake of both food and fluids, resulting in dehydration which may require hospitalization. Meningoencephalitis and cardiopulmonary arrest requires emergent and full supportive therapy and management.

BRIEF SUMMARY

[0009] Thus, there is a need to develop vaccines and immunogenic compositions for treating and/or preventing hand, food, and mouth disease, particularly in children. In order to meet this need, the present disclosure provides vaccines and immunogenic compositions for treating and/or preventing hand, foot, and mouth disease that include antigens from at least one virus that causes hand, foot, and mouth disease in humans, such as EV71, CA6, and CA16. Advantageously, the antigens may include at least one adaptation mutation that allows for production in cultured non-human cell lines such as Vero cells. Moreover, as disclosed herein, the vaccines and immunogenic compositions of the present disclosure have been demonstrated to induce a protective immune response against viruses that cause hand, foot, and mouth disease in humans.

[0009a] In one aspect of the present disclosure, there is provided a hand, foot, and mouth immunogenic composition or vaccine comprising one or more antigens from at least one virus that causes hand, foot and mouth disease in humans, wherein the one or more antigens comprise at least one non-human cell adaptation mutation.

[0009b] In another aspect of the present disclosure, there is provided a hand, foot, and mouth immunogenic composition or vaccine comprising one or more antigens from at least one inactivated virus that causes hand, foot and mouth disease in humans, wherein the at least one virus is EV71, and wherein the at least one virus was inactivated with beta-propiolactone (BPL).

[0009c] In yet another aspect of the present disclosure, there is provided a hand, foot, and mouth immunogenic composition or vaccine comprising one or more antigens from at least one virus that causes hand, foot and mouth disease in humans and an aluminum salt adjuvant, wherein at least 75%, at least 80%, at least 85%, at least 90%, at 95%, at least 97%, at least 99%, or 100% of the antigen is adsorbed to the aluminum salt adjuvant.

[0009d] In a further aspect of the present disclosure, there is provided use of an effective amount of the immunogenic composition or vaccine as described herein for the manufacture of a medicament for inducing an immune response in a subject in need thereof, or for treating or preventing hand, foot, and mouth disease in a subject in need thereof.

[0009e] In another aspect of the present disclosure, there is provided a method for preparing an adjuvanted hand, foot, and mouth immunogenic composition or vaccine, comprising:
(a) mixing the vaccine with an aluminum salt adjuvant, wherein the vaccine comprises one or more antigens from at least one virus that causes hand, foot and mouth disease in humans; and
(b) incubating the mixture under suitable conditions for a period of time that ranges from about 16 hours to about 24 hours,
wherein at least 75%, at least 80%, at least 85%, at least 90%, at 95%, at least 97%, at least 99%, or 100% of the antigen is adsorbed to the aluminum salt adjuvant, and
wherein the at least one virus that causes hand, foot and mouth disease is EV71.

[0009f] In yet another aspect of the present disclosure, there is provided a method for inactivating a hand, foot, and mouth virus preparation, comprising:
(a) isolating the hand, foot, and mouth virus preparation from one or more non-human cells, wherein the cells are used to produce the virus preparation;
(b) treating the virus preparation with an effective amount of beta-propiolactone (BPL); and
(c) treating the virus preparation with an effective amount of formalin, wherein the step of treating with formalin occurs concurrently with step (b) or after step (b), and
wherein the virus is EV71.

[0009g] In a further aspect of the present disclosure, there is provided a method for inactivating a hand, foot, and mouth virus preparation, comprising:
(a) isolating the hand, foot, and mouth virus preparation from one or more non-human cells, wherein the cells are used to produce the virus preparation;
(b) treating the virus preparation with an effective amount of formalin; and
(c) purifying the virus preparation from the formalin wherein the virus is EV71.

[0010] Accordingly, the present disclosure provides a hand, foot, and mouth vaccine containing one or more antigens from at least one virus that causes hand, foot

and mouth disease in humans, where the one or more antigens include at least one non-human cell adaptation mutation. Accordingly, the present disclosure also provides a hand, foot, and mouth immunogenic composition containing one or more antigens from at least one virus that causes hand, foot and mouth disease in humans, where the one or more antigens comprise at least one non-human cell adaptation mutation. The present disclosure further provides a method for treating or preventing hand, foot, and mouth disease in a subject in need thereof, by administering to the subject a therapeutically effective amount of any of the vaccines or immunogenic compositions disclosed herein. The present disclosure also provides a method for inducing an immune response in a subject in need thereof, by administering to the subject an immunogenic amount of any of the vaccines or immunogenic compositions disclosed herein.

[0011] The present disclosure provides a hand, foot, and mouth vaccine containing one or more antigens from at least one inactivated virus that causes hand, foot and mouth disease in humans, where the at least one virus is EV71, CA16, or both, and where the at least one virus was inactivated with beta-propiolactone (BPL). The present disclosure also provides a hand, foot, and mouth immunogenic composition containing one or more antigens from at least one inactivated virus that causes hand, foot and mouth disease in humans, where the at least one virus is EV71, CA16, or both, and where the at least one virus was inactivated with beta-propiolactone (BPL). The present disclosure further provides a method for treating or preventing hand, foot, and mouth disease in a subject in need thereof, by administering to the subject a therapeutically effective amount of any of the vaccines or immunogenic compositions disclosed herein. The present disclosure also provides a method for inducing an immune response in a subject in need thereof, by administering to the subject an immunogenic amount of any of the vaccines or immunogenic compositions disclosed herein. The present disclosure further provides a method for inactivating a hand, foot, and mouth virus preparation, by: (a) isolating the hand, foot, and mouth virus preparation from one or more non-human cells, where the cells are used to produce the virus preparation; (b) treating the virus preparation with an effective amount of beta-propiolactone (BPL); and (c) treating the virus preparation with an effective amount of formalin, where the step of treating with formalin occurs currently with step (b) or after step (b), and where the virus is selected from one or more of EV71, CA6, and CA16.

[0012] The present disclosure provides a hand, foot, and mouth vaccine containing one or more antigens from at least one inactivated virus that causes hand, foot and mouth disease in humans, where the at least one virus is CA6, CA16, or both, and where the at least one virus was inactivated with formalin. The present disclosure also provides a hand, foot, and mouth immunogenic composition containing one or more antigens from at least one inactivated virus that causes hand, foot and mouth disease in humans, where the at least one virus is CA6, CA16, or both, and where the at least one virus was inactivated with formalin. The present disclosure further provides a method for treating or preventing hand, foot, and mouth disease in a subject in need thereof, by administering to the subject a therapeutically effective amount of any of the vaccines or immunogenic compositions disclosed herein. The present disclosure also provides a method for inducing an immune response in a subject in need thereof, by administering to the subject an immunogenic amount of any of the vaccines or immunogenic compositions disclosed herein.

The present disclosure further provides a method for inactivating a hand, foot, and mouth virus preparation, by: (a) isolating the hand, foot, and mouth virus preparation from one or more non-human cells, where the cells are used to produce the virus preparation; (b) treating the virus preparation with an effective amount of formalin; and (c) purifying the virus preparation from the formalin where the virus is selected from one or more of EV71, CA6, and CA16.

[0013] The present disclosure provides a hand, foot, and mouth vaccine containing one or more antigens from at least one virus that causes hand, foot and mouth disease in humans and an aluminum salt adjuvant, where at least 75%, at least 80%, at least 85%, at least 90%, at 95%, at least 97%, at least 99%, or 100% of the antigen is adsorbed to the aluminum salt adjuvant. The present disclosure also provides a hand, foot, and mouth immunogenic composition containing one or more antigens from at least one virus that causes hand, foot and mouth disease in humans and an aluminum salt adjuvant, where at least 75%, at least 80%, at least 85%, at least 90%, at 95%, at least 97%, at least 99%, or 100% of the antigen is adsorbed to the aluminum salt adjuvant. The present disclosure further provides a method for treating or preventing hand, foot, and mouth disease in a subject in need thereof, by administering to the subject a therapeutically effective amount of any of the vaccines or immunogenic compositions disclosed herein. The present disclosure also provides a method for inducing an immune response in a subject in need thereof, by administering to the subject an immunogenic amount of any of the vaccines or immunogenic compositions disclosed herein. The present disclosure further provides a method for preparing an adjuvanted hand, foot, and mouth vaccine, by: (a) mixing the vaccine with an aluminum salt adjuvant, where the vaccine includes one or more antigens from at least one virus that causes hand, foot and mouth disease in humans; and (b) incubating the mixture under suitable conditions for a period of time that ranges from about 16 hours to about 24 hours, where at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the antigen is adsorbed to the aluminum salt adjuvant, and where the at least one virus that causes hand, foot and mouth disease is selected from one or more of EV71, CA6, and CA16. The present disclosure also provides a method for preparing an adjuvanted hand, foot, and mouth immunogenic composition, by: (a) mixing the immunogenic composition with an aluminum salt adjuvant, where the immunogenic composition includes one or more antigens from at least one virus that causes hand, foot and mouth disease in humans; and (b) incubating the mixture under suitable conditions for a period of time that ranges from about

or vaccine, a subunit immunogenic composition or vaccine, an inactivated whole virus immunogenic composition or vaccine, or an attenuated virus immunogenic composition or vaccine.

18. Use of an effective amount of the immunogenic composition or vaccine of any one of claims 1-17 for the manufacture of a medicament for inducing an immune response in a subject in need thereof, or for treating or preventing hand, foot, and mouth disease in a subject in need thereof.

19. The use of claim 18, wherein administration of the immunogenic composition or vaccine induces a protective immune response in the subject, optionally wherein:
    a. the immune response comprises an immune response against EV71; and/or
    b. the immune response comprises an immune response against one or more EV71 viral genotypes selected from B2, B4, B5, C2, and C4.

20. A method for preparing an adjuvanted hand, foot, and mouth immunogenic composition or vaccine, comprising:
(a) mixing the vaccine with an aluminum salt adjuvant, wherein the vaccine comprises one or more antigens from at least one virus that causes hand, foot and mouth disease in humans; and
(b) incubating the mixture under suitable conditions for a period of time that ranges from about 16 hours to about 24 hours,
wherein at least 75%, at least 80%, at least 85%, at least 90%, at 95%, at least 97%, at least 99%, or 100% of the antigen is adsorbed to the aluminum salt adjuvant, and wherein the at least one virus that causes hand, foot and mouth disease is EV71.

21. The method of claim 20, wherein the mixture is incubated at a temperature that ranges from about 2°C to about 8°C.

22. A method for inactivating a hand, foot, and mouth virus preparation, comprising:
(a) isolating the hand, foot, and mouth virus preparation from one or more non-human cells, wherein the cells are used to produce the virus preparation;
(b) treating the virus preparation with an effective amount of beta-propiolactone (BPL); and
(c) treating the virus preparation with an effective amount of formalin, wherein the step of treating with formalin occurs concurrently with step (b) or after step (b), and wherein the virus is EV71.