BRIEF SUMMARY ~~OF THE INVENTION~~

[0011] The present disclosure~~invention~~ is related to a new method for the production of live PRRS virus for use in the manufacture of such vaccines. The methods described herein may be used in the large scale production of any PRRS virus, including but not limited to including but not limited to PRRSV 94881 PRRSV strain 94881 deposited with the European Collection of Cell Cultures (ECACC) under the Accession Numbers ECACC 11012501 and ECACC 11012502 each deposited on January 25, 2011 in accordance with the provisions of the Budapest Treaty, or any descendant or progeny of one of the aforementioned strains.

[0012] More particularly, the present disclosure, in a first aspect,~~invention~~ relates to a method for the commercial scale production of porcine reproductive and respiratory syndrome virus (PRRSV) comprising:

[0013] a) concurrently seeding a large scale culture media with a mammalian cell line that is permissive to PRRSV infection into a bioreactor and infecting the mammalian cells with a PRRSV.

[0014] b) propagating virus for 5 to 7 days post infection;

[0015] c) performing a first harvesting step by removing the media from the bioreactor and isolating propogated virus therefrom;

[0016] d) replenishing the media in the bioreactor and propagating virus for 1 to 4 days;

[0017] e) performing a second harvesting step by removing the media from the bioreactor and isolating propogated virus therefrom;

[0018] f) replenishing the media in the bioreactor and propagating virus for 1 to 4 days and

[0019] g) performing a third harvesting step by removing the media from the bioreactor and isolating propogated virus therefrom.

[0020] In certain embodiments, the method may further comprise at least one re-feeding and harvest steps subsequent to the third harvesting step

Accession No. I-1140, CNCM Accession No I-1387, CNCM Accession No I-1388, ATCC VR 2332, VR 2385, VR 2386, VR 2429, VR 2474, and VR 2402; CNCM I-1102, CNCM I-1140, CNCM I-1387, CNCM I-1388, or ECACC V93070108; ATCC deposit VR-2332, ATCC deposit VR-2368; ATCC VR-2495; ATCC VR 2385, ATCC VR 2386, ATCC VR 2429, ATCC VR 2474, and ATCC VR 2402, , or any descendant or progeny of one of the aforementioned strains.

[0027] The present disclosure, in a second aspect, relates to~~Also contemplated is~~ a commercial-scale production method for the preparation of a PRRSV comprising:

a. a concurrent seeding of both mammalian cells permissive to infection by the PRRSV and the PRRSV into a bioreactor containing a media suitable for the growth of the cells; and

b. performing three consecutive harvesting steps wherein PRRSV is harvested wherein after each of the first and second harvests, the media is replenished, and wherein:

i. the first harvest is performed on the first day that the dextrose concentration of the media decreases to less than 0.1 g/L;

ii. the second harvest is performed 1 or 2 days after addition of the media following the first harvest; and

iii. the third harvest is performed between 1 and 4 days after addition of the media following the second harvest.An alternative method is also contemplated that uses a concurrent roller bottle prodcess that is equivalent to the bioreactor process described above. ~~More particularly, t~~The present disclosure, in a third aspect,~~invention~~ relates to a method for the commercial scale production of porcine reproductive and respiratory syndrome virus (PRRSV) comprising: a) concurrently seeding a large scale culture media with a mammalian cell line that is permissive to PRRSV infection into a roller bottles and infecting said mammalian cells with a PRRSV; b) propagating virus for 5 to 7 days post infection;c) performing a first harvesting step by removing the media from said roller bottle and isolating propogated virus therefrom; d) replenishing the

media in said roller bottle and propagating virus for about 2 days; e) performing a second harvesting step by removing the media from said roller bottle and isolating propogated virus therefrom; f) replenishing the media in said roller bottle and propagating virus for about 2 days and g) performing a third harvesting step by removing the media from said bioreactor and isolating propogated virus therefrom.

[0028] ~~Another aspect of t~~The disclosure also~~invention~~ relates to a PRRSV MLV comprising a PRRSV produced according to the methods described herein formulated with an acceptable adjuvant or carrier for delivery to a pig.

BRIEF DESCRIPTION OF SEVERAL VIEWS OF THE DRAWINGS

[0029] Figure 1: Concurrent process for large-scale production of PRRSV 94881.

[0030] Figure 2: Definition and Timelines of the concurrent process for the 300L Bioreactors

[0031] Figure 3 Viral titers and dextrose profiles for the three concurrent runs in the 300L Bioreactors.

[0032] Figure 4: Viral titers and glutamine profiles for the three concurrent runs in the 300L Bioreactors.

[0033] Figure 5: Viral titers and DO profiles for the three concurrent runs in the 300L Bioreactors.

[0034] Figure 6: Shows RT-PCT Time PCR results depicting % viremia in animals vaccinated with PRRSV 94881.

[0035] Figure 7: Concurrent process for roller bottle production of PRRSV 94881.

[0036] Figure 8:Definition and Timelines of the concurrent process for the roller bottle process.