WHAT IS CLAIMED IS:

1. A method of generating attenuated, recombinant alphavirus, comprising the step of:

cloning internal ribosomal entry site of encephalomyelocarditis virus (EMCV IRES) between the end of nonstructural protein 4 (nsP4) coding sequence and initiating AUG of a subgenomic RNA coding sequence of an alphavirus, instead of natural 5' UTR of the subgenomic RNA.

2. The method of claim 1, further comprising:

inactivating the subgenomic promoter of the alphavirus by clustered point mutations and deletion of the natural 5'UTR in the subgenomic RNA.

3. The method of claim 2, wherein the inactivation of the subgenomic promoter does not modify the carboxy terminus of non-structural protein 4.

4. The method of claim 2, further comprising:

introducing adaptive mutations in non-structural protein 2 (nsP2) effective to increase virus replication, release and virus titers.

5. The method of claim 4, wherein the adaptive mutations are $Y_{370}\rightarrow C$, $K_{371}\rightarrow Q$, $P_{349}\rightarrow T$, $D_{41}8\rightarrow A$, $K_{423}\rightarrow T$ or combinations thereof.

6. The method of claim 1, wherein the alphavirus is Chikungunya virus.

7. The method of claim 1, wherein the alphavirus is Eastern Equine Encephalitis Virus.

8. The method of claim 1, wherein the alphavirus is Venezuelan Equine Encephalitis virus.

9. The method of claim 1, wherein the alphavirus is Western Equine Encephalitis virus.

10. An attenuated recombinant alphavirus generated by method of claim 1.

11. The attenuated recombinant alphavirus of claim 10, wherein said alphavirus is incapable of replicating in mosquitoes, incapable of transmission by

mosquito vectors, capable of inducing high levels of IFN alpha/beta, slow growth in IFN alpha/beta cells, slow growth in IFN signaling-deficient BHK-21 cells or a combination thereof.

12. A vector comprising a nucleotide sequence encoding the attenuated recombinant alphavirus of claim 10.

13. A host cell comprising and expressing the vector of claim 12.

14. A pharmaceutical composition, comprising:

the attenuated recombinant alphavirus of claim 10 and a pharmaceutically acceptable carrier.

15. An immunogenic composition, comprising:

the attenuated recombinant alphavirus of claim 10.

16. A method of protecting a subject from infections resulting from exposure to an alphavirus, comprising the step of:

administering immunologically effective amount of the immunogenic composition of claim 15, thereby protecting the subject from infections resulting from exposure to the alphavirus.

17. The method of claim 16, wherein the subject is a human or a livestock.

18. A method of generating attenuated, recombinant alphavirus incapable of infecting mosquitoes, comprising the step of:

cloning internal ribosomal entry site of encephalomyelocarditis virus and capsid genes downstream of the envelope glycoprotein genes with said capsid gene at the 3' end of the subgenomic region just upstream of the 3' UTR, wherein the capsid is expressed in a cap-independent manner and the envelope protein genes is translated in a cap-dependent manner but the capsid protein translated in an IRES-dependent manner.

WHAT IS CLAIMED IS:

1. An attenuated, recombinant alphavirus, comprising: an alphavirus nucleic acid having (i) an inactivated subgenomic promoter, and (ii) an insertion of an internal ribosomal entry site (IRES) between the end of nonstructural protein 4 (nsP4) coding sequence and initiating AUG of a subgenomic RNA coding sequence of the recombinant alphavirus, wherein the IRES is capable of expression in mammalian cells but not insect cells; and wherein the alphavirus is attenuated.

2. The attenuated alphavirus of claim 1, wherein the alphavirus' natural 5' UTR in the subgenomic RNA between the end of nonstructural protein 4 (nsP4) coding sequence and initiating AUG of the subgenomic RNA coding sequence is deleted.

3. The attenuated alphavirus of claim 1,-wherein the subgenomic promoter is inactivated by clustered point mutations introduced to the nucleic acid sequence of the subgenomic promoter.

4. The attenuated alphavirus of claim 2, wherein the clustered point mutations include two or more mutations at positions 5, 8, 11, 12, 14, 17, 20, 22, 24, 25, 26, 27, 28 of SEQ ID NO:1, 5' ccccuauaacucucuacggcuaaccugaauggacuacg 3'.

5. The attenuated alphavirus of any of the preceding claims, wherein the mutation of the subgenomic promoter does not modify the amino acid sequence of the carboxy terminus of non-structural protein 4.

6. The attenuated alphavirus of claim 2, further comprising: adaptive mutations in the nucleic acid sequence encoding the non-structural protein 2 (nsP2) effective to increase virus replication, release and virus titers.

7. The attenuated alphavirus of claim 6, wherein the adaptive mutations are nucleic acid mutations that result in one or more amino acid changes corresponding to $Y_{370}\rightarrow C$, $K_{371}\rightarrow Q$, $P_{349}\rightarrow T$, $D_{418}\rightarrow A$, $K_{423}\rightarrow T$ in the TC-83 virus nsP2 protein or combinations thereof.

8. The attenuated alphavirus of any of the preceding claims, wherein the IRES is an encephalomyelocarditis virus (EMCV) IRES.

9. An attenuated recombinant alphavirus comprising;

a) a capsid gene positioned at the 3' end of the subgenomic region, downstream from envelope glycoprotein genes and upstream from the 3' UTR of the subgenomic RNA of the alphavirus; and

b) an internal ribosomal entry site (IRES) introduced between the end of the envelope glycoprotein genes and the positioned capsid gene, wherein the IRES is capable of expression in mammalian cells but not insect cells; and

wherein the capsid is expressed in an IRES-dependent manner and the envelope protein genes are expressed in a cap-dependent manner; and wherein the alphavirus is attenuated.

10. The attenuated recombinant alphavirus of claim 9, wherein the subgenomic promoter of the alphavirus is inactivated.

11. The attenuated alphavirus of claim 1 or 9, wherein the alphavirus is Chikungunya virus.

12. The attenuated alphavirus of claim 1 or 9, wherein the alphavirus is Eastern Equine Encephalitis Virus.

13. The attenuated alphavirus of claim 1 or 9, wherein the alphavirus is Venezuelan Equine Encephalitis virus.

14. The attenuated alphavirus of claim 1 or 9, wherein the alphavirus is Western Equine Encephalitis virus.

15. The attenuated alphavirus of claim 1 or 9, wherein the alphavirus is incapable of replicating in mosquitoes and mosquito cells.

16. A vector comprising a nucleotide sequence encoding the attenuated, recombinant alphavirus of claims 1 or 9.

17. A host cell comprising and expressing the vector of claim 16.

18. A pharmaceutical composition comprising: the attenuated, recombinant alphavirus of claims 1 or 9 and a pharmaceutically acceptable carrier.

19. An immunogenic composition, comprising: the attenuated, recombinant alphavirus of claims 1 or 9.

20. The pharmaceutical composition of claim 18 of use in protecting a subject from infections resulting from exposure to an alphavirus.

21. The pharmaceutical composition of claim 18, wherein the subject is a human, a horse or other domestic animal.

22. A method of generating attenuated, recombinant alphavirus incapable of infecting mosquitoes, comprising: cloning an internal ribosomal entry site (IRES) wherein the IRES is capable of expression in mammalian cells but not insect cells; and a capsid gene downstream of envelope glycoprotein genes with the capsid gene at the 3' end of the subgenomic region just upstream of the 3' UTR, wherein the capsid is expressed in an IRES-dependent manner and the envelope protein genes are expressed in a cap-dependent.

23. A method of generating an attenuated, recombinant alphavirus incapable of infecting mosquitoes, comprising: (i) inactivating the subgenomic promoter of an alphavirus; and (ii) cloning an internal ribosomal entry site (IRES) between the end of nonstructural protein 4 (nsP4) coding sequence and initiating AUG of a subgenomic RNA coding sequence of the alphavirus wherein the IRES is capable of expression in mammalian cells but not insect cells; and generating the live, attenuated, recombinant alphavirus.

24. The method of claim 23, wherein inactivating the subgenomic promoter comprises introducing clustered point mutations to the nucleic acid sequence of the subgenomic promoter.

25. The method of claim 24, wherein the clustered point mutations include two or more mutations at positions 5, 8, 11, 12, 14, 17, 20, 22, 24, 25, 26, 27, 28 of SEQ ID NO:1, 5' ccccuauaacucucuacggcuaaccugaauggacuacg 3'.

26. The method of claim 24 or 25, wherein the clustered point mutations do not modify the amino acid sequence of the carboxy terminus of non-structural protein 4.

27. The method of any of the preceding claims, wherein the IRES is an encephalomyelocarditis virus (EMCV) IRES.

SEQUENCE LISTING

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