WHAT IS CLAIMED IS :

1. A replication-deficient pseudoinfectious virus of Flaviviridae family, comprising:

a deletion in the nucleotide sequence encoding capsid (C) protein such that the deletion does not disrupt the RNA sequence required for genome cyclization, the signal sequence for prM protein that is required for the proper maturation of prM/M or a combination thereof, wherein said replication-deficient pseudoinfectious virus replicate only in cells expressing C protein or C, prM, envelope protein, mutated C protein, mutated prM, mutated envelope protein or combinations thereof of a virus of the Flaviviridae family.

2. The replication-deficient pseudoinfectious virus of Flaviviridae family of claim 1, wherein said virus is a Flavivirus, Hepacivirus or Pestivirus or other chimeras of said viruses created by exchanging prM-E cassettes of other viruses with the prM-E cassettes of the pseudoinfectious virus.

3. The replication-deficient pseudoinfectious virus of Flaviviridae family of claim 2, wherein said Flavivirus is a yellow fever virus, a West Nile virus, a dengue virus, a tick-borne encephalitis virus, a Saint Louis encephalitis virus, a Japanese encephalitis virus or a Murray Valley encephalitis virus.

4. The replication-deficient pseudoinfectious virus of Flaviviridae family of claim 3, wherein nucleotide sequence encoding the C protein of said Flavivirus that is deleted encodes amino acids 26 to 100 or a combination of amino acids within amino acids 26 to 100 of the C protein.

5. The replication-deficient pseudoinfectious virus of Flaviviridae family of claim 2, wherein said Hepacivirus is a Hepatitis C virus.

6. The replication-deficient pseudoinfectious virus of Flaviviridae family of claim 2, wherein said Pestivirus is a Bovine virus diarrhea, a swine fever virus or a hog cholera virus.

7. The replication-deficient pseudoinfectious virus of Flaviviridae family of claim 1, wherein said deleted gene is replaced by a gene encoding a marker protein or an antigen.

8. A cell culture system expressing C protein or C, prM, envelope protein, mutated C protein, mutated prM, mutated envelope protein or combinations thereof of a virus of the Flaviviridae family, effective to enable propagation of the replication-deficient virus of claim 1 under suitable conditions.

9. The cell culture system of claim 8, wherein the cells expressing the wild type or mutated proteins of the virus are generated using genetically engineered replicons derived from viral vectors.

10. The cell culture system of claim 9, wherein the gene encoding the protein(s) of the virus of Flaviviridae family in the replicon is replaced by a codon-optimized version of the gene encoding the protein(s) of said virus ~~the~~ such that the replacement reduces the ability of the cell line-encoded genes to recombine with genome of the pseudoinfectious virus of the Flaviviridae family and/or increases the production of the pseudoinfectious virus of the Flaviviridae family.

11. The cell culture system of claim 10, wherein said replicon expresses a C protein that comprises mutations in at least 36 nucleotide positions of the gene encoding C protein of the virus belonging to the Flaviviridae family.

12. The cell culture of claim 10, wherein the replicon expresses a C protein in the replicon that comprises unnatural cyclization sequences such that presence of said cyclization sequences reduces the chances of productive recombination of the replication-deficient pseudoinfective virus with natural viruses.

13. The cell culture of claim 10, wherein said replicon expresses proteins comprising altered nucleotide sequences encoding truncated C-prM junction such that presence of such altered sequences enhances yield of the replication-deficient pseudoinfective virus in cell culture, prM/E containing SVP yield in vivo or a combination thereof.

14. The cell culture system of claim 9, wherein the replicons expressing the wild type or mutated proteins of the virus of the Flaviviridae family are introduced into the cells by transfection with in vitro synthesized replicon RNAs, by transfection with plasmid DNAs designed to synthesize functional alphaviral replicons from cellular RNA-polymerase II-specific promoters or by infection with alphaviral replicons packaged inside the alphaviral structural proteins.

15. The cell culture system of claim 9 wherein the viral vectors are alphaviruses.

16. The cell culture system of claim 15, wherein the alphavirus is Venezuelan Equine Encephalitis Virus (VEEV), Sindbis virus, Eastern Equine Encephalitis virus (EEEV), Western Equine Encephalitis virus (WEEV) or Ross River virus.

17. A method of producing a replication-deficient pseudoinfectious virus of Flaviviridae family, comprising;

generating a replication-deficient pseudoinfectious virus of Flaviviridae family that comprises a deletion in the capsid gene such that the deletion does not disrupt

the RNA sequence required for genome cyclization, the signal sequence for prM protein that is required for the proper maturation of prM/M or a combination thereof;

generating a cell line that expresses capsid protein or capsid, prM, E protein, mutated capsid protein, mutated prM, mutated E protein or combinations thereof of the virus of the Flaviviridae family, wherein the cell line provides high levels of the proteins of needed for propagation of the replication-deficient pseudoinfectious virus of Flaviviridae family; and

infecting the cell line with the pseudoinfectious virus of the Flaviviridae family, thereby producing the replication-deficient pseudoinfectious virus of the Flaviviridae family.

18. The method of claim 17, wherein said virus is a Flavivirus, Hepacivirus or Pestivirus or other chimeras of said viruses created by exchanging prM-E cassettes of other viruses with the prM-E cassettes of the pseudoinfectious virus.

19. The method of claim 18, wherein said Flavivirus is a yellow fever virus, a West Nile virus, a dengue virus, a tick-borne encephalitis virus, a Saint Louis encephalitis virus, a Japanese encephalitis virus or a Murray Valley encephalitis virus.

20. The method of claim 19, wherein nucleotide sequence encoding the C protein of said Flavivirus that is deleted encodes amino acids 26 to 100 or a combination of amino acids within amino acids 26 to 100 of the C protein.

21. The method of claim 18, wherein said Hepacivirus is a Hepatitis C virus.

22. The method of claim 18, wherein said Pestivirus is a Bovine virus diarrhea, a swine fever virus or a hog cholera virus.

23. The method of claim 17, wherein the cells expressing the wild type or mutated proteins of the virus are generated using genetically engineered replicons derived from viral vectors.

24. The method of claim 23, wherein the gene encoding the mutated protein(s) of virus of Flaviviridae family in the replicon is replaced by a codon-optimized version of the gene encoding the protein(s) of said virus such that the replacement reduces the ability of the cell line-encoded genes to recombine with the pseudoinfectious Flaviviridae genome and/or increases the production of the pseudoinfectious Flaviviridae.

25. The method of claim 24, wherein said replicon expresses a C protein that comprises mutations in at least 36 nucleotide positions of the gene encoding C protein of the virus belonging to the Flaviviridae family.

26. The method of claim 24, wherein the replicon expresses a C protein in the replicon that comprises unnatural cyclization sequences such that presence of said cyclization sequences reduces the chances of productive recombination of the replication-deficient pseudoinfective virus with natural viruses.

27. The method of claim 24, wherein said replicon expresses proteins comprising altered nucleotide sequences encoding truncated C-prM junction such that presence of such altered sequences enhances yield of the replication-deficient pseudoinfective virus in cell culture, prM/E containing SVP yield in vivo or a combination thereof.

28. The method of claim 23, wherein the replicons expressing the wild type or mutated proteins of the virus of the Flaviviridae family are introduced into the cells by transfection with in vitro synthesized replicon RNAs, by transfection with plasmid DNAs designed to synthesize functional alphaviral replicons from cellular RNA-polymerase II-specific promoters or by infection with alphaviral replicons packaged inside the alphaviral structural proteins.

29. The method of claim 23, wherein the viral vectors are alphaviruses.

30. The method of claim 29, wherein the alphavirus is Venezuelan Equine Encephalitis Virus (VEEV), Sindbis virus, Eastern Equine Encephalitis virus (EEEV), Western Equine Encephalitis virus (WEEV) or Ross River virus.

31. A pharmaceutical composition, comprising the replication-deficient pseudoinfectious virus of the Flaviviridae family produced by the method described in claim 17.

32. A method of protecting a subject from infections resulting from exposure to Flaviviridae, comprising administering to the subject an immunologically effective amount of the pharmaceutical composition of claim 31, wherein said composition elicits an immune response against the Flaviviridae in the subject, thereby protecting the subject from the infections.

33. The method of claim 32, wherein said administration is via intraperitoneal, intradermal, subcutaneous, intramuscular, oral, or intranasal route.

34. The method of claim 32, wherein said subject is a human, or an animal.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A replication-deficient pseudoinfectious flavivirus, wherein the genome of said flavivirus comprises a deletion in nucleotide sequences encoding capsid (C) protein, the deleted sequences encode amino acids 26-100 of said C protein or a combination of amino acids within amino acids 26-100 of said C protein, and the deletion does not disrupt RNA sequences required for genome cyclization or the signal sequence for prM protein that is required for the proper maturation of prM/M.

2. The replication-deficient pseudoinfectious flavivirus of claim 1, wherein said flavivirus is a chimeric flavivirus created by exchanging a prM-E cassette of another flavivirus with the prM-E cassette of the flavivirus.

3. The replication-deficient pseudoinfectious flavivirus of claim 1 or claim 2, wherein said flavivirus is, or said chimeric flavivirus comprises sequences of, a yellow fever virus, a West Nile virus, a dengue virus, a tick-borne encephalitis virus, a Saint Louis encephalitis virus, a Japanese encephalitis virus or a Murray Valley encephalitis virus.

4. The replication-deficient pseudoinfectious flavivirus of claim 1, wherein the nucleotide sequence encoding the C protein of said flavivirus that is deleted encodes amino acids 26 to 100, 26 to 93, or 31 to 100.

5. The replication-deficient pseudoinfectious flavivirus of claim 1, wherein said deleted gene is replaced by a gene encoding a marker protein or an antigen.

6. The replication-deficient pseudoinfectious flavivirus of claim 5, wherein the marker protein is a green fluorescent protein.

7. A cell culture system comprising one or more cells expressing C protein of a flavivirus, wherein said expression is effective to enable propagation of the replication-deficient pseudoinfectious flavivirus of claim 1 under suitable conditions, and wherein the nucleic acid sequence encoding the C protein is codon optimized such that the codon optimization reduces the ability of the C protein nucleic acid sequence of the cell to

recombine with genome of the pseudoinfectious flavivirus and/or increases the production of the pseudoinfectious flavivirus.

8. The cell culture system according to claim 7, wherein the cells express C protein, but not prM protein or envelope protein of a flavivirus, effective to enable propagation of the replication-deficient flavivirus of claim 1 under suitable conditions.

9. The cell culture system of claim 7 or claim 8, wherein the cells expressing the C protein are generated using genetically engineered replicons derived from viral vectors.

10. The cell culture system of claim 9, wherein

(a) said replicon expresses a C protein that comprises mutations in at least 36 nucleotide positions of the gene encoding C protein of the flavivirus;

(b) said replicon expresses a C protein in the replicon that comprises unnatural cyclization sequences such that presence of said cyclization sequences reduces the chances of productive recombination of the replication-deficient pseudoinfective flavivirus with natural viruses; or

(c) said replicon expresses proteins comprising altered nucleotide sequences encoding truncated C-prM junction such that presence of such altered sequences enhances yield of the replication-deficient pseudoinfective flavivirus in cell culture, prM/E containing SVP yield in vivo or a combination thereof.

11. The cell culture system of claim 9, wherein the replicons expressing the C protein of the flavivirus are introduced into the cells by transfection with in vitro synthesized replicon RNAs, by transfection with plasmid DNAs designed to synthesize functional alphaviral replicons from cellular RNA-polymerase II-specific promoters or by infection with alphaviral replicons packaged inside the alphaviral structural proteins.

12. The cell culture system of claim 9, wherein the viral vectors are alphaviruses.

13. The cell culture system of claim 12, wherein the alphavirus is Venezuelan Equine Encephalitis Virus (VEEV), Sindbis virus, Eastern Equine Encephalitis virus (EEEV), Western Equine Encephalitis virus (WEEV) or Ross River virus.

14. A method of producing a replication-deficient pseudoinfectious flavivirus, comprising:

(a) generating the replication-deficient pseudoinfectious flavivirus of claim 1;

(b) generating one or more cells expressing C protein of a flavivirus, wherein the cells provide high levels of the proteins of needed for propagation of the replication-deficient pseudoinfectious flavivirus; and

(c) infecting the cells with the pseudoinfectious flavivirus, thereby producing the replication-deficient pseudoinfectious flavivirus.

15. The method of claim 14, wherein said flavivirus is as defined in any one of claims 2 to 6.

16. The method of claim 14, wherein the cells expressing the C protein are as defined in any one of claims 7 to 13.

17. The method of any one of claims 14 to 16 further comprising a step of formulating said flavivirus in a pharmaceutical composition.

18. A pharmaceutical composition, comprising the replication-deficient pseudoinfectious flavivirus of any one of claims 1 to 6.