CLAIMS

1. A live-attenuated yellow fever virus strain adapted to grow on Vero cells from a parent yellow fever virus 17D substrain that is not adapted to grow on Vero cells, wherein said live-attenuated yellow fever virus strain is less neurovirulent than said parent yellow fever virus 17D substrain, wherein said parent yellow fever virus 17D substrain comprises an RNA sequence of SEQ ID NO. 2.

2. The live-attenuated yellow fever virus strain according to claim 1~~, wherein the parent yellow fever virus strain is a live-attenuated yellow fever virus strain adapted to grow on eggs.~~

~~3. The live-attenuated yellow fever virus strain according to claim 1 or 2, wherein the parent yellow fever virus strain is a yellow fever virus 17D-204 substrain.~~

~~4. The live-attenuated yellow fever virus strain according to any one of claims 1 to 3, wherein the parent yellow fever virus 17D substrain comprises an RNA sequence of SEQ ID NO. 2.~~

~~5. The live-attenuated yellow fever virus strain according to any one of claims 1 to 4~~, wherein said live-attenuated yellow fever virus strain is less neurovirulent than the parent yellow fever virus 17D-substrain in a mouse lethal dose 50 (MLD_{50}) test.

~~6~~

3. A live-attenuated yellow fever virus strain comprising a nucleic acid comprising:

i) a mutation in the codon for the amino acid at position 480 of the envelope protein (E) which results in an amino acid change from valine to leucine, or

ii) a mutation in the codon for the amino acid at position 65 of the non-structural protein 2A (NS2a) which results in an amino acid change from methionine to valine.

~~7~~

4. The live-attenuated yellow fever virus strain according to claim ~~6~~3 comprising a nucleic acid comprising:

i) a mutation in the codon for the amino acid at position 480 of the envelope protein (E) which results in an amino acid change from valine to leucine, and

ii) a mutation in the codon for the amino acid at position 65 of the non-structural protein 2A (NS2a) which results in an amino acid change from methionine to valine.

~~8~~

5. The live-attenuated yellow fever virus strain according to claim ~~6~~3 or ~~7~~4, wherein the nucleic acid further comprises a mutation in the codon for the amino acid at position 19 of the non-structural protein 4A (NS4a) which results in a codon change from AAA to AAG.

~~9~~

6. The live-attenuated yellow fever virus strain according to any one of claims ~~6~~3 to ~~8~~5, wherein the nucleic acid further comprises a mutation in the codon for the amino acid at position 145 of the envelope protein (E) which results in a codon change from GUA to GUU.

~~10~~

7. A live-attenuated yellow fever virus strain which comprises an envelope protein comprising a mutation at position 480 which results in an amino acid change from valine to leucine.

~~11~~

8. A live-attenuated yellow fever virus strain which comprises an envelope protein comprising a leucine residue at the position within the protein that corresponds to position 480 of SEQ ID NO. 15.

~~12. The live-attenuated yellow fever virus strain as claimed in claim 11, wherein said envelope protein comprises a sequence at least 90%, 95%, 98% or 100% identical to the sequence of SEQ ID NO. 15~~

~~13~~

9. A live-attenuated yellow fever virus strain comprising a nucleic acid molecule encoding:

(i) an envelope protein comprising a mutation at position 480 which results in an amino acid change from valine to leucine, and

(ii) a NS2a protein comprising a mutation at position 65 which results in an amino acid change from methionine to valine.

~~14~~

10. The live-attenuated yellow fever virus strain of claim ~~13~~9, wherein the nucleic acid further comprises a mutation in the codon for the amino acid at position 19 of the non-structural protein 4A (NS4a) which results in a codon change from AAA to AAG.

~~15~~

11. The live-attenuated yellow fever virus strain of claim ~~13~~9 or ~~14~~10, wherein the nucleic acid further comprises a mutation in the codon for the amino acid at position 145 of the envelope protein (E) which results in a codon change from GUA to GUU.

~~16~~

12. A live-attenuated yellow fever virus strain comprising a nucleic acid molecule encoding:

(i) an envelope protein which comprises a leucine residue at the position within the protein that corresponds to position 480 of SEQ ID NO. 15; and

(ii) an NS2a protein which comprises a valine residue at the position within the protein that corresponds to position 65 of SEQ ID NO. 16.

~~17~~

13. The live-attenuated yellow fever virus strain as claimed in claim ~~16, wherein said envelope protein comprises a sequence at least 90%, 95%, 98% or 100% identical to the sequence of SEQ ID NO. 15 and said NS2a protein comprises a sequence at least 90%, 95%, 98% or 100% identical to the sequence of SEQ ID NO. 16.~~

~~18. The live-attenuated yellow fever virus strain as claimed in claim 16 or 17~~12, wherein the nucleic acid further comprises a G nucleotide at position within the nucleic acid coding for the non-structural protein 4A (NS4a) that corresponds to position 57 of SEQ ID NO. 17.

~~19~~

14. The live-attenuated yellow fever virus strain according to any one of claims ~~16~~12 to ~~18~~13, wherein the nucleic acid further comprises a U nucleotide at position within the nucleic acid coding for the envelope protein (E) that corresponds to position 435 of SEQ ID NO. 18.

~~20~~

15. An immunogenic composition comprising a live-attenuated yellow fever virus strain according to any one of claims 1 to ~~19~~14 and a pharmaceutically acceptable vehicle.

~~21~~

16. A method for obtaining a live-attenuated yellow fever virus strain adapted to grow on Vero cells, comprising the steps of:

- a) purifying the viral genomic RNA of a parent live-attenuated yellow fever virus strain that is not adapted to grow on Vero cells, and that is optionally adapted to grow on eggs;

- b) transfecting Vero cells with the viral genomic RNA purified in step a), whereby transfected Vero cells are obtained;

- c) growing the transfected Vero cells obtained in step b) in a culture medium, whereby a first yellow fever virus population is obtained and further recovered;

- d) amplifying the recovered first yellow fever virus population obtained at the end of step c) 2 times or more on fresh Vero cells, whereby a second yellow fever virus population is obtained;

- e) cloning the second yellow fever virus population obtained in step d) by two or more successive plaque purifications on Vero cells whereby a plurality of yellow fever virus clones is obtained;

- f) amplifying separately each of the recovered yellow fever virus clones obtained at the end of step e) 2 times or more on fresh Vero cells, whereby a plurality of yellow fever virus strains is obtained; and

- g) selecting from the said plurality of yellow fever virus strains recovered in step f) one or more live-attenuated yellow fever virus strain that is less neurovirulent than the parent live-attenuated yellow fever virus strain, in a mouse lethal dose 50 (MLD_{50}) test.

~~22~~

17. The method according to claim ~~21~~16, wherein the said culture medium is serum-free, and is optionally free of any human or animal-derived substance.

~~23~~

18. A live-attenuated yellow fever virus strain obtainable by a method according to any one of claims ~~21~~16 or ~~22~~17.

~~24~~

19. A live-attenuated yellow fever virus strain according to any one of claims 1 to ~~19~~14 or claim ~~23~~18 for use in the preparation of a vaccine.

~~25~~

20. A vaccine comprising a live-attenuated yellow fever virus strain according to any one of claims 1 to ~~19~~14 or claim ~~23~~18 for use in preventing an infection by a yellow fever virus.