CLAIMS

1. A nucleic acid construct which comprises:

(1) a cDNA molecule encoding a full length antigenomic (+) RNA strand of a measles virus (MeV); and

(2) a first heterologous polynucleotide encoding at least one polypeptide, or an antigenic fragment thereof, of a Lassa virus (LASV), wherein one of said at least one polypeptide is the glycoprotein precursor (GPC); and another polypeptide being selected from the group consisting of the nucleoprotein (NP), a mutated nucleoprotein (mNP) and/or the zinc binding protein (Z),

wherein the first heterologous polynucleotide is operatively cloned within an additional transcription unit (ATU) inserted within the cDNA of the antigenomic (+) RNA, in particular an ATU localized between the P gene and the M gene of the MeV, in particular the ATU2 inserted between the P gene and the M gene of the MeV.

2. A nucleic acid construct which comprises:

(1) a cDNA molecule encoding a full length antigenomic (+) RNA strand of a measles virus (MeV);

(2) a first heterologous polynucleotide encoding at least one polypeptide, or an antigenic fragment thereof, of a Lassa virus (LASV), wherein one of said at least one polypeptide is the glycoprotein precursor (GPC); and

(3) a second heterologous polynucleotide encoding at least one polypeptide, or an antigenic fragment thereof, of the LASV, said at least one polypeptide being selected from the group consisting of the GPC protein, the nucleoprotein (NP), a mutated nucleoprotein (mNP) and/or the zinc binding protein (Z)

wherein the first heterologous polynucleotide is operatively cloned within an additional transcription unit (ATU) inserted within the cDNA of the antigenomic (+) RNA, in particular an ATU localized between the P gene

and the M gene of the MeV, in particular the ATU2 inserted between the P gene and the M gene of the MeV,
and wherein the second heterologous polynucleotide is operatively cloned within another ATU inserted within the cDNA of the antigenomic (+) RNA at a location distinct from the location of the first cloned heterologous polynucleotide.

3. The nucleic acid construct according to claim 2 wherein the first heterologous polynucleotide and the second heterologous polynucleotide are operatively cloned within ATUs located at different positions in the cDNA molecule of the MeV, in particular the first heterologous polynucleotide is operatively cloned with the ATU2 and the second heterologous polynucleotide is operatively cloned within the ATU1.

4. The nucleic acid construct according to any one of claims 1 to 3, wherein the heterologous polynucleotide(s) encoding the GPC protein, the NP protein, the mNP and/or the Z protein, or an antigenic fragment thereof, is(are) from the LASV strain *Josiah*, or is(are) derived from the LASV strain *Josiah*, in particular the heterologous polynucleotide(s) is(are) issued or derived from the sequence of Genbank J04324.1 and/or U73034.2.

5. The nucleic acid construct according to any one of claims 1 to 4, wherein the first and/or, when applicable, the second heterologous polynucleotide(s), encode(s) the mNP protein, or an antigenic fragment thereof , wherein the mNP protein has a mutated exonuclease domain, in particular wherein the amino acid sequence of the encoded mNP protein is mutated on amino acid residue 389 and/or 392, preferentially by substitution on amino acid residues 389 and 392, of SEQ ID No: 3, in particular the encoded mNP protein is the sequence of SEQ ID No: 5, in particular the heterologous polynucleotide encoding the mNP protein comprises SEQ ID No: 6.

6. The nucleic acid construct according to any one of claims 1 to 5, wherein the heterologous polynucleotide(s) encoding the GPC protein, the NP protein, the mNP protein and/or the Z protein, or an antigenic fragment thereof, has (have) codon-optimized open reading frame(s) (ORF), in particular, the heterologous polynucleotide(s) comprise(s) at least one of the following sequence:
   - SEQ ID No: 2 which encodes the GPC protein; and/or
   - SEQ ID No: 4 which encodes the NP protein; and/or
   - SEQ ID No: 6 which encodes the mNP protein; and/or
   - SEQ ID No: 8 which encodes the Z protein.

7. The nucleic acid construct according to any one of claims 1 to 6, wherein the heterologous polynucleotide(s) encode(s):
   - the GPC protein of SEQ ID No: 1 or an antigenic fragment thereof; and/or
   - the NP protein of SEQ ID No: 3 or an antigenic fragment thereof; and/or
   - the mNP protein of SEQ ID No: 5 or an antigenic fragment thereof; and/or
   - the Z protein of SEQ ID No: 7 or an antigenic fragment thereof.

8. The nucleic acid construct according to any one of claims 1 to 7 comprising from 5' to 3' end the following polynucleotides:
   (a) a polynucleotide encoding the N protein of the MeV;
   (b) a polynucleotide encoding the P protein of the MeV;
   (c) the first heterologous polynucleotide encoding at least two polypeptides, which are the GPC protein or an antigenic fragment thereof and either the NP protein or the mNP protein, or an antigenic fragment thereof, in particular encoding the GPC protein and the mNP protein, wherein the first polynucleotide is in particular operatively cloned within an ATU, in particular ATU2;
   (d) a polynucleotide encoding the M protein of the MeV;
   (e) a polynucleotide encoding the F protein of the MeV;

(f) a polynucleotide encoding the H protein of the MeV; and
(g) a polynucleotide encoding the L protein of the MeV;
wherein said polynucleotides are operatively linked within the nucleic acid construct and under the control of a viral replication and transcriptional regulatory elements such as MeV leader and trailer sequence(s).

9. The nucleic acid construct according to any one of claims 2 to 7 comprising from 5' to 3' end the following polynucleotides:
(a) the second heterologous polynucleotide encoding at least one polypeptide selected from the group consisting of the GPC protein, the NP protein, the mNP protein and the Z protein of the LASV, or an antigenic fragment thereof, in particular encoding the Z protein, or an antigenic fragment thereof, wherein the second polynucleotide is operatively cloned within an ATU localized upstream the N gene of the MeV, in particular within the ATU1;
(b) a polynucleotide encoding the N protein of the MeV;
(c) a polynucleotide encoding the P protein of the MeV;
(d) the first heterologous polynucleotide encoding at least the GPC protein, or an antigenic fragment thereof, in particular encoding a single polypeptide which is the GPC protein or an antigenic fragment thereof, or encoding at least two polypeptides, which are the GPC protein or an antigenic fragment thereof and either the NP protein or the mNP protein, or an antigenic fragment thereof, in particular encoding the GPC protein and the mNP protein, wherein the first polynucleotide is in particular operatively cloned within an ATU, in particular ATU2;
(e) a polynucleotide encoding the M protein of the MeV;
(f) a polynucleotide encoding the F protein of the MeV;
(g) a polynucleotide encoding the H protein of the MeV; and
(h) a polynucleotide encoding the L protein of the MeV,
wherein said polynucleotides are operatively linked within the nucleic acid construct and under the control of a viral replication and

transcriptional regulatory elements such as MeV leader and trailer sequence(s).

10. The nucleic acid construct according to any one of claims 1 to 8, wherein the first heterologous polynucleotide comprises from 5' to 3' end:
(a) a nucleic acid encoding the NP protein or the mNP protein of the LASV, or an antigenic fragment thereof, in particular whose nucleic acid is SEQ ID No: 4 for the NP protein or SEQ ID No: 6 for the mNP protein; and
(b) a nucleic acid encoding the GPC protein of the LASV, or an antigenic fragment thereof, in particular whose nucleic acid is SEQ ID No: 2;
wherein the first heterologous polynucleotide is operatively cloned between the P gene and the M gene of the MeV, in particular within an ATU, in particular ATU2.

11. The nucleic acid construct according to any one of claims 1 to 9, wherein the first heterologous polynucleotide comprises from 5' to 3' end:
(a) the nucleic acid of SEQ ID No: 6 encoding the mNP protein; and
(b) the nucleic acid of SEQ ID No: 2 encoding the GPC protein;
wherein the first heterologous polynucleotide sequence is operatively cloned between the gene P and the gene M of the MeV, in particular within an ATU, in particular ATU2.

12. The nucleic acid construct according to any one of claims 2 to 11, wherein the second heterologous polynucleotide encodes the Z protein of the LASV, or an antigenic fragment thereof, and wherein the first heterologous polynucleotide encodes the GPC protein of the LASV, or an antigenic fragment thereof, in particular wherein the sequence of the second heterologous polynucleotide comprises the sequence of SEQ ID No: 8 and the sequence of the first heterologous polynucleotide comprises the sequence of SEQ ID No: 2.

13. The nucleic acid construct according to claim 12, wherein the first heterologous polynucleotide and the second heterologous polynucleotide are operatively cloned within ATUs located at different position in the cDNA molecule of the MeV, in particular the first heterologous polynucleotide is operatively cloned with the ATU2 and the second heterologous polynucleotide is operatively cloned within the ATU1.

14. The nucleic acid construct according to any one of claims 1 to 13, wherein the measles virus is an attenuated virus strain selected from the group consisting of the Schwarz strain, the Zagreb strain, the AIK-C strain, the Moraten strain, the Philips strain, the Beckenham 4A strain, the Beckenham 16 strain, the Edmonston seed A strain, the Edmonston seed B strain, the CAM-70 strain, the TD 97 strain, the Leningrad-16 strain, the Shanghai 191 strain and the Belgrade strain, in particular the Schwarz strain.

15. The nucleic acid construct according to any one of claims 1 to 14, wherein the sequence of the first heterologous polynucleotide comprises at least one of SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, and/or SEQ ID No: 8, and preferentially at least SEQ ID No: 2, in particular SEQ ID No: 2 and SEQ ID No: 6.

16. The nucleic acid construct according to any one of claims 1 to 15, or a transfer plasmid vector comprising the nucleic acid construct according to any one of claims 1 to 15, whose recombinant cDNA sequence is selected from the group consisting of:
    - SEQ ID No: 9 (construct MeV-GPC);
    - SEQ ID No: 10 (construct MeV-NP-GPC);
    - SEQ ID No: 11 (construct MeV-mNP-GPC);
    - SED ID No: 12 (construct Z-MeV-GPC);
    - SEQ ID No: 13 (construct Z-MeV-NP-GPC); and
    - SEQ ID No: 14 (construct Z-MeV-mNP-GPC).

17. A recombinant measles virus in which the genome comprises or consists of a nucleic acid construct according to any one of claims 1 to 16, or a transfer plasmid vector according to claim 16.

18. The recombinant measles virus according to claim 17 expressing at least two polypeptides, one being the GPC protein, the other being selected from the group consisting of the NP protein or the mNP protein or the Z protein of the LASV, or an antigenic fragment thereof; or in particular expressing the GPC protein and the Z protein of the LASV, or an antigenic fragments thereof, or in particular expressing the GPC protein and the mNP protein of the LASV, or antigenic fragments thereof.

19. The recombinant measles virus according to claim 17 or 18 further expressing at least one of the N protein, the P protein, the M protein, the F protein, the H protein and the L protein of the MeV.

20. The recombinant measles virus according to any one of claims 17 to 19 , which elicits a cellular and/or humoral and cellular response, in particular after a single immunization, against the antigenic fragment(s) of the GPC protein, the NP protein, the mNP protein and/or the Z protein of LASV, in particular against the antigenic fragments of the N protein, the P protein, the M protein, the F protein, the H protein and/or the L protein of MeV, in particular a T cell response, in particular a CD4+ and CD8+ T cell response.

21. A host cell transfected with the nucleic acid construct according to any one of claims 1 to 16 or with the transfer plasmid vector according to claim 16, or infected with the recombinant measles virus according to any one of claims 17 to 20, in particular a mammalian cell, a VERO NK cell, CEF cell, human embryonic kidney cell line 293 or MRC5 cell.

22. A method for producing recombinant virus like particles (VLPs) comprising a Z protein and a GPC protein, and optionally a NP protein and/or a mNP protein, or an antigenic fragment thereof, of the LASV, wherein the protein(s) or antigenic fragments thereof is(are) the result of

the expression of the first, and when applicable the second, heterologous polynucleotide(s) of the nucleic acid construct according to claims 1 to 16, or of the transfer plasmid vector of claim 16, or the recombinant measles virus according to any one of claims 17 to 20, or produced within the host cell of claim 21.

23. An immunogenic composition, especially a virus vaccine composition, comprising the recombinant VLPs produced according to claim 22, or the recombinant measles virus according to any one of claims 17 to 20 , or the recombinant VLPs produced according to claim 22 and the recombinant measles virus according to any one of claims 17 to 20, and a pharmaceutically acceptable vehicle.

24. The composition according to claim 23 for use in the elicitation of a protective, and preferentially prophylactic, immune response against the Lassa virus and/or Measles virus by the elicitation of antibodies directed against LASV protein(s) and/or Measles virus protein(s), or antigenic fragment(s) thereof, and/or a cellular and/or humoral and cellular response against the Lassa virus and/or the Measles virus, in a host in need thereof, in particular a human host, in particular a child.

25. A process for rescuing recombinant Lassa virus like particles (VLPs) and/or recombinant measles virus expressing at least the GPC protein of LASV, or an antigenic fragment thereof, and one of polypeptide of LASV, or an antigenic fragment thereof, selected from the group consisting of the NP protein, the mNP protein and the Z protein, comprising:
    (a) transfecting cells, in particular helper cells, in particular HEK293 helper cells, stably expressing T7 RNA polymerase and measles virus N and P proteins with the nucleic acid construct according to any one of claims 1 to 16 or with the transfer plasmid vector according to claim 16;
    (b) maintaining the transfected cells in conditions suitable for the production of recombinant measles virus and/or LASV VLPs;

(c) infecting cells enabling propagation of the recombinant measles virus and/or the LASV VLPs by co-cultivating them with the transfected cells of step (b);

(d) harvesting the recombinant measles virus expressing at least the GPC protein and the mNP protein and/or the NP protein and/or the Z protein, and/or the LASV VLPs expressing at least the Z protein and the GPC protein, and optionally the NP protein and/or the mNP protein of LASV.

26. Use of recombinant Lassa VLPs produced according to claim 22, and/or a measles virus according to any one of claims 17 to 20 in the manufacture of a medicament for preventing a Lassa virus related disease.

27. Use of recombinant Lassa VLPs produced according to claim 22, and/or a measles virus according to any one of claims 17 to 20 in the manufacture of a medicament for treating a Lassa virus related disease.