

## **VIRUS PARTICLES WITH IMPROVED ENTRY INTO TUMOR CELLS**

### **CROSS REFERENCE TO RELATED APPLICATIONS**

[0001] The present application claims the benefit of priority of European Patent Application EP 23 194 741.7 filed on 31 August 2023, the content of which is hereby incorporated by reference in its entirety for all purposes.

### **FIELD OF THE INVENTION**

[0002] The invention relates to a virus particle comprising a mutated lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said GP, wherein the virus particle has an increased capacity to enter a tumor cell. The invention also relates to the mutated GP, nucleic acid molecules encoding the GP, host cells comprising said nucleic acid molecule or a cDNA of the genome of said virus particle, method of producing said virus particle, as well as medical uses.

### **BACKGROUND**

[0003] Oncolytic viruses (OVs) are potential therapeutic options for patients with cancer who fail to achieve durable responses with immune checkpoint inhibitors. OVs replicate preferentially in cancer cells and thereby have the ability to promote the immune response in the tumor. The reason for tumor specific propagation of OVs is currently intensively studied. The strongly enhanced anabolism makes cancer cells ideal hosts for viral replication. Further, cancer cells do not express a cell autonomous immunity because cellular antiviral mechanisms are actively suppressed by oncogenes. Specifically, overexpression of RAS can block expression of the anti-viral effector protein kinase R (PKR). These factors might explain the accelerated viral replication, translation of viral proteins and virion assembly in cancer cells. Whether additional factors including tumor-specific viral entry, additionally contribute to tumor specific propagation is insufficiently studied.

[0004] Viral tropism refers to the infectivity of a virus for a given cell type. It is partially determined by its entry receptor. Usually, viruses attach via its surface proteins to a receptor expressed on the target cell followed by entry. Hence, expression of the entry receptor on several cell types and tissues allows a broad tropism of the virus. In line, binding of the viral surface protein to a similar receptor in another species can allow viral replication. Although malignant transformation modulates expression and modification of several proteins, it remains unclear whether viral entry receptors are specifically overexpressed in the malignant cells. Whether OVs

can be modified to enhance their tumor tropism and reduce their tropism to healthy cells remains to be studied.

[0005] Arenaviruses are enveloped and pleiomorphic, with a diameter of 60–300 nm and two single-stranded ambisense RNA genomic segments. Several Old World Arenaviruses including Lymphocytic choriomeningitis virus (LCMV) and members of the clade C New World Arenaviruses bind to the ubiquitously expressed cellular receptor  $\alpha$ -Dystroglycan (DAG1). Proteoglycans can function as entry receptors in the presence of Heparan Sulfate. Recently CD164 was identified as additional co-receptor which accelerates entry of LCMV. Like other OV, LCMV propagates preferentially in tumor cells and thereby induces local immune activation. This immune activation modulates the tumor microenvironment and leads to infiltration of several immune cells, which then can activate anti-tumoral mechanisms. However, since the cellular entry receptor DAG1 is ubiquitously expressed, LCMV can replicate in healthy organs, limiting its use for cancer therapy.

[0006] However, there is a need in the art to provide arenaviruses, in particular LCMV, that have an improved properties for cancer therapy.

#### SUMMARY OF THE INVENTION

[0007] The invention relates to a virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said GP, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in

- (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
- (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
- (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;

- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha 3$  as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498;

wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

**[0008]** The invention also relates to a virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

**[0009]** The invention also relates to an LCMV glycoprotein, wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue as defined for the virus particle of the invention.

**[0010]** The invention also relates to a nucleic acid molecule encoding a LCMV GP of the invention.

[0011] The invention also relates to a virus particle comprising a glycoprotein (GP) of an arenavirus and/or a nucleic acid encoding said GP, wherein the glycoprotein comprises at least one of the following amino acid residues:

- (a) at the position corresponding to Ser 102 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Asn residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
- (b) at the position corresponding to Phe 122 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (c) at the position corresponding to Phe 129 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Ser residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (d) at the position corresponding to His 136 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Gln residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a His residue at said position;
- (e) at the position corresponding to Asn 152 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Tyr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (f) at the position corresponding to Ser 153 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Pro, Phe, or Tyr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
- (g) at the position corresponding to Asn 154 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Asp residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;



- (h) at the position corresponding to His 155 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu or Tyr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (i) at the position corresponding to Lys 156 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Glu residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (j) at the position corresponding to Ala 211 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Thr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises an Ala residue at said position;
- (k) at the position corresponding to Thr 217 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (l) at the position corresponding to Thr 218 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (m) at the position corresponding to Lys 256 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Arg residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (n) at the position corresponding to Leu 260 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Phe or Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Leu residue at said position;
- (o) at the position corresponding to Tyr 284 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a His residue,

wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Tyr residue at said position;

- (p) at the position corresponding to Ala 328 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Ser residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ala residue at said position;
- (q) at the position corresponding to Phe 332 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (r) at the position corresponding to Val 342 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ala residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Val residue at said position;
- (s) at the position corresponding to Arg 358 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Lys residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Arg residue at said position; and
- (t) at the position corresponding to Lys 492 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position.

**[0012]** The invention also relates to a host cell comprising a nucleic acid molecule of the invention or a cDNA of the genome of a virus particle of the invention.

**[0013]** The invention also relates to a method of producing a virus particle of the invention comprising cultivating the host cell of the invention under conditions suitable for virus particle formation.

**[0014]** The invention also relates to a pharmaceutical composition comprising a virus particle of the invention, a GP of the invention, a nucleic acid molecule of the invention, or an arenavirus particle of the invention.

[0015] The invention also relates to a virus particle of the invention, a GP of the invention, a nucleic acid molecule of the invention, or an arenavirus particle of the invention, for use in therapy, preferably for use in the treatment of cancer.

[0016] The invention also relates to a use of a virus particle of any one of the invention, a GP of the invention, a nucleic acid molecule of the invention, or an arenavirus particle of the invention, for the manufacture of a medicament, wherein the medicament is preferably for the treatment of cancer.

[0017] The invention also relates to a method of treating a disease comprising administering to a subject in need thereof an effective amount of a virus particle of the invention, a GP of the invention, a nucleic acid molecule of the invention, or an arenavirus particle of the invention, wherein the disease is preferably cancer.

[0018] The invention also relates to a method of producing a virus particle having an increased capacity to enter a tumor cell, comprising:

- (i) Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
  - (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
  - (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
  - (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
  - (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
  - (e) Helix  $\alpha$ 3 as defined by positions 187-199;
  - (f) Loop 3 as defined by positions 200-226;

- (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498; and
- (ii) Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
- (iii) Optionally assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell, preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a value, wherein the reference value is preferably at least as high or higher than the value that is obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

[0019] The invention also relates to a method of producing a virus particle having an increased tropism for a tumor cell, comprising:

- (i) Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
  - (a) Strand  $\beta 1$  N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
  - (b) Strands  $\beta 3$ ,  $\beta 4$ , and/or  $\beta 5$  as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
  - (c) Helix  $\alpha 1$  and/or  $\alpha 2$  as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;

- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha 3$  as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498; and
- (ii) Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
- (iii) Optionally assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell and/or a non-tumor cell, preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a reference value, wherein the reference value is preferably at least as high or higher than the value that is obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

### BRIEF DESCRIPTION OF THE DRAWINGS

**[0020] Figure 1: Amino acid positions in LCMV-GP, which are identified as tumor-tropic** LCMV-WE wildtype was passaged with or without 5-Flurouracil (5FU) in different human and murine tumor cell lines. After 10 – 12 passages the virus was sequenced. The newly gained mutations (MUT) and the original amino acid at this position (WT) are shown for each cell type. Each setup was done in 4-5 separate approaches. The number of approaches which do show the certain mutation is shown. The positions in Loop #2 were not included in the analysis. **A:** missense mutations in the stable signal peptide (SSP), **B:** missense mutations in GP1, **C:** missense mutations in GP2.

**[0021] Figure 2: LCMV-WE subtype P52 is stable and gained additional mutations.** The LCMV-WE subtype P52 (I181M, R185W) was passaged (23-55x) with or without 5-Flurouracil

(5FU). The virus derived after passaging was sequenced and the mutations are shown for each cell line.

**[0022] Figure 3: Mutations observed after propagation of LCMV-WE subtype YF13.**

**[0023] Figure 4: A. Tumor-tropic mutations accumulate in specific structural regions (structural hot spots).** Shown are the known structural domains of the LCMV glycoprotein (Hastie et al Nat Struct Mol Biol 23, 513-521 (2016) and RCSB protein data bank: <https://www.rcsb.org/structure/5INE> (release 2016-04-20)). The mutations in the according domain and the connecting sequence between the domains are shown. Loop#2 was omitted as it was not part of the analysis. The mutation frequency is given for each domain and their connecting sequence. **B.** Significance between low mutation frequency (n=2-13) and high mutation frequency (n=13-2 respectively) of the domains was calculated using the Mann Whitney Test. The cut-off was determined as the arithmetic mean (12,85%) of the two lowest significant values (p = 0,0003108) **C.** Mutation frequency of domains with low mutation frequency (n = 7) and high mutation frequency (n = 8) is illustrated and Mann Whitney Test was performed (0,0003108).

**[0024] Figure 5: Mutations within different domains of the LCMV-GP.** Shown are the total numbers of AS positions and the numbers of AS positions, which we identified as tumor tropic in the fast evolution platform sorted by structural regions. Loop#2 was not included in the analysis. \* shows a significant difference in the mutation frequency of the domain measured in the chi-square test.

**[0025] Figure 6: Tumor-tropic regions accumulate in specific functional regions (functional hot spots).** Shown are the known functional regions of LCMV-GP. Since Loop#2 was not involved in the analysis, it was omitted. The mutations in the according functional region are shown. The mutation frequency is given for each region.

**[0026] Figure 7: Mutations of the fast evolution platform accelerate entry into A549 cells: A:** Original FACS blots of entry assay in A549 cells of LCMV-WE wildtype. Time indicates the addition of Monensin, which will block virus entry. **B:** Entry assays of recombinant viruses which carry randomly chosen mutations from the fast evolution platform (n=6/mutation). The structural region where the mutation is located is given. Mutated viruses (dotted coloured line) compared to the recombinant WT control - WE-CL13(L)h2.r3 (solid black line). **C:** Entry assays of recombinant viruses which carry a mutation which was not identified within the fast evolution platform, but which is located in a structural region are shown (n=6/mutation). **D:** Entry assays of

a recombinant virus which carry a mutation at a position which was not identified within the fast evolution platform, but which is located in a postulated hotspot region are shown (n=2/mutation).

**[0027] Figure 8: Mutations lead to broad infectivity of cancer, but not healthy cells** **A:** Infection assays (MOI=0.1, 16 hours) of different human cancer (n=6) and primary neurons (n=4) and myotubes (n=2) cells with 10 different chimeric (WE-CL13-chim) viruses carrying 1 point mutation in the according position. To note infection of neurons and myotubes was not detectable. **B:** Infection ratios (Infectivity assay) from different tumor cell lines are blotted against the infection ratios of each other tumor cell lines. The contrast between the Melanoma and lung adenocarcinoma cell lines is visualized. The infection ratio of neurons is also plotted against the infection ratio of MaMel86a. The mean ratio for each mutated virus is given (n = 6). **C:** Spider blots showing the factor of acceleration in propagation of the mutations tested in various tumor cells and neurons. The mean ratio values for each mutated virus are given (n = 6). **D:** Infectivity assay of the mutant virus, carrying the point mutation F129S, was tested in the cell lines H1975, MaMel51, MaMel86a and A549. Infection rate is shown as bars. Infection rate for WT control virus is shown as dotted line (n=6). **E:** Infectivity assay of the mutant viruses carrying the mentioned point mutations was tested in H1975 and A549 cells (n=6/mutation). **F:** Infectivity assay of the mutant viruses, carrying the mentioned point mutations, was tested in the cell lines H1975, A549, Gist-T1, MaMel51, MaMel86a and Neurons. Infection rate is shown as bars. Infection rate for WT control virus is shown as dotted line (n=6/tumor cell lines; n=4 for neurons). **G:** Infectivity assay of LCMV-WE wildtype and a mutant virus strain, with the mutation 211T in the LCMV-GP was tested in B16F10 melanoma cells. Analysis of infected cells after 48 hours (n=6). **H:** Infectivity assay of LCMV-WE wildtype and a mutant virus strain, with the mutation 492I in the LCMV-GP was tested in MaMel51 melanoma cells. Analysis of infected cells after 48 hours (n=6). **I:** Immunofluorescence for LCMV-NP of the mentioned cell types, which were infected with the LCMV strains 8B10-D2 and A10D and control virus for 24 hours. One of three representative stainings is shown.

**[0028] Figure 9:** Infection assays (MOI = 0.1, 16 hours) of different human cancer and healthy cells with different recombinant viruses carrying optimized combinations. The mutations within the LCMV-GP are given for each virus strain. The selected human cancer cell lines for testing the infectivity were A549, H1975, MaMel86a and MaMel51. Tested murine cell lines were B16F10, TrampC2, MC-38 and MOPC (n=6-7).

**[0029] Figure 10: New mutations change the entry mechanism of the virus.** Randomly chosen recombinant viruses carrying mutations from the fast evolution platform were tested in entry

assay in A549 cells and A549 cells, which are defective of the known entry receptor of LCMV, alpha dystroglycan. The mutations within the LCMV-GP are given for each virus strain (n=6).

**[0030] Figure 11: Virus with combined mutations shows accelerated anti-tumoral activity.**

**A:** Infectivity assay of the LCMV-WE wildtype virus and the chimeric WE-CL13 virus, which carries the LCMV-WE wildtype glycoprotein, the LCMV-WE nucleoprotein and the L-segment from the LCMV clone 13 tested in primary human neurons and the mentioned tumor cell lines (n=3-6/virus strain). **B:** Infectivity assay of the WE-CL13 chimeric virus, which carries the LCMV-WE wildtype glycoprotein and a WE-CL13 chimeric virus, which carries the mentioned point mutations in the LCMV-GP, tested in the mentioned tumor cell lines (n=6/virus strain). **C:** Tumor growth in mice carrying an B16F10-OVA tumor which were treated with the LCMV-WE wildtype virus, a LCMV-WE strain, which carried the point mutation 211T in the LCMV-GP and a WE-CL13 chimeric virus, which carries the mentioned point mutations on day 0 (n=3-5/group). **D:** Tumor growth in mice carrying an MC38-OVA tumor which were treated with a WE-CL13 chimeric virus, which carries the mentioned point mutations on day 0 is shown. (n=3-5/group). Right panel shows tumor size after killing the mice on day 9 (n=5/group).

**[0031] Figure 12:** The mutations of the LCMV-GP positions 155, 156 and 256 were introduced into the glycoprotein of the arenavirus Lunk. It corresponded to the positions 152, 153 and 253. The capacity to replicate into different cell lines was analyzed in the infectivity assay. Data show the relative enhancement of infectivity when compared to the WT virus (n = 6-10).

**[0032] Figure 13:** The LCMV-GP expressing the mutation H155Y was expressed on the vesicular stomatitis virus (VSV). Infection rate of the wildtype chimeric virus (LCMV-GP/VSV) and the mutated chimeric virus (LCMV-GP-mut/VSV) was analyzed in the MC57 fibrosarcoma cells (n = 3).

#### DETAILED DESCRIPTION

**[0033]** The inventors of the present application have surprisingly found a method for identifying mutations to modulate the tropism of LCMV towards tumor cells. By using this method for primary and secondary cell cultures, at least 95 missense mutations have been identified. Production of recombinant LCMVs, carrying these mutations revealed that entry of LCMV into tumor cells was mainly affected by the mutations. By combining these mutations viruses with accelerated tumor-tropism, limited replication in healthy cells and beneficial anti-tumoral activity have been generated.



[0034] Virotherapy is one raising pillar in cancer therapy with clinical application in several cancer types. One major challenge in virotherapy is to design a virus which shows effective anti-tumoral activity in the absence of side effects. Enhancing tumor tropism without affecting replication of the virus in healthy tissue would solve this problem. By passaging the lymphocytic choriomeningitis virus (LCMV) in human and murine cancer cells, the inventors of the present application determined regions within the LCMV pre-glycoprotein polyprotein (GPC) which accelerate tumor cell specific entry. Combination of mutations in different GPC regions had synergistic and/or additive effects on tumor cell propagation. Consequently, modification of these regions in the LCMV-GPC increased the entry into tumor cells, limited replication in healthy cells and was therefore proprietary in a murine cancer mouse model. Mechanistically, it is believed that many of the selected recombinant viruses are not dependent on alpha-Dystroglycan (DAG-1) as main entry receptor. Consistently, introduction of mutated LCMV-GP on other viruses, such as a vesicular stomatitis virus vector system, likewise accelerated its entry into tumor cells, suggesting that this new and tumor-specific entry mechanism is suitable for other therapeutic viruses and not limited to LCMV. In conclusion, by using the biological principle of mutation and selection the inventors of the present application could identify functional LCMV-GPC regions, which shift the tropism of the virus towards cancer cells. Recombinant viruses carrying these mutations showed accelerated and more specific replication in tumor cells and induced a strong anti-tumoral immunity.

[0035] The use of mutated viruses for tumor therapy was proprietary due to accelerated site specific replication and immune activation but limited propagation in healthy tissue.

[0036] Accordingly, the present invention relates to a virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said GP, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or in comparison with the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87; (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113; (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions

selected from the group consisting of 126-130 and 136-147; (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157; (e) Helix  $\alpha 3$  as defined by positions 187-199; (f) Loop 3 as defined by positions 200-226; (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365; (i) the H1,H2 domain as defined by positions 1-58; and/or (j) the TM cytoplasmic domain as defined by positions 439-498. Preferably, the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred. Preferably, the reference virus particle only differs in the sequence of the glycoprotein.

**[0037]** The present invention also relates to a virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or in comparison with the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492. Preferably, the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild-type glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred. Preferably, the reference virus particle only differs in the sequence of the glycoprotein.

**[0038]** The virus particle of the disclosure is preferably an arenavirus particle, more preferably a lymphocytic choriomeningitis virus (LCMV) particle.

**[0039]** The wild-type arenavirus genomic segments and ORFs are known in the art. In particular, the wild type arenavirus genome typically consists of an S segment and an L segment. The S segment carries the ORFs encoding the GP and the NP. The L segment encodes the L protein and the Z protein. Both segments are flanked by the respective 5' and 3' UTRs.

**[0040]** The virus particles of the invention preferably comprise genomic segments that correspond to the genomic segments of a wild-type arenavirus. This means that the S segment carries the ORFs encoding the GP and the NP and that the L segment encodes the L protein and the Z protein. On the S segment, the ORF encoding the glycoprotein is under control of a 5' untranslated region (UTR) and the nucleoprotein is under control of a 3' UTR. On the L segment, the ORF encoding the L protein is under control of a 3' UTR and the ORF encoding the Z protein is under control of a 5' UTR. Accordingly, the genes of the virus particles of the disclosure are preferably located at their natural positions. The virus particle of the invention thus preferably has a bi-segmented genome. The genome of the virus particle of the invention preferably consists of one L segment and one S segment as described herein. Illustrative examples of LCMV S segments are shown in SEQ ID NOs: 1, 11, and 14. Illustrative examples of LCMV L segments are shown in SEQ ID NOs: 2 and 15.

**[0041]** Several strains of LCMV are part of the present disclosure. As used herein, LCMV "WE", "strain WE", "WE strain", or the like refers to an LCMV having the genomic segments as shown in SEQ ID NOs: 1 and 2. As used herein, LCMV "P52", "P52-WE", "strain P52", "P52 strain", or the like refers to a variant/derivative of strain WE, which has the genomic segments as shown in SEQ ID NOs: 11 and 2. As used herein, LCMV "Clone13", "Cl13", "strain Clone13", "Clone13 strain", or the like refers to an LCMV which has the genomic segments as shown in SEQ ID NOs: 14 and 15.

**[0042]** The terms "glycoprotein", "GP", "G protein", "glycoprotein complex", "GPC" which are used interchangeably, refer to an LCMV-derived glycoprotein, which is considered to mediate receptor binding and membrane fusion. Illustrative examples of glycoproteins are shown in SEQ ID NOs: 4, 13, and 17. Illustrative examples for genes that encode a glycoprotein are shown in SEQ ID NOs: 3, 12, and 16.

**[0043]** The terms "L protein", and "LP", which are used interchangeably, refer to an LCMV-derived RNA polymerase L. Illustrative examples of L proteins are shown in SEQ ID NOs: 10, and 23. Illustrative examples for genes that encode an L protein are shown in SEQ ID NOs: 9 and 22.

**[0044]** The terms "nucleoprotein", "N protein", and "NP", which are used interchangeably, refer to an LCMV-derived nucleoprotein. Illustrative examples of nucleoproteins are shown in SEQ ID NOs: 6 and 19. Illustrative examples for genes that encode a nucleoprotein are shown in SEQ ID NOs: 5 and 18.

[0045] The terms “Z protein” or “ZP”, which are used interchangeably, refer to an LCMV-derived small RING finger protein Z. Illustrative examples of Z proteins are shown in SEQ ID NOs: 8 and 21. Illustrative examples for genes that encode a Z protein are shown in SEQ ID NOs: 7 and 20.

[0046] The term "amino acid" or "amino acid residue" typically refers to an amino acid having its art recognized definition such as an amino acid selected from the group consisting of: alanine (Ala or A); arginine (Arg or R); asparagine (Asn or N); aspartic acid (Asp or D); cysteine (Cys or C); glutamine (Gln or Q); glutamic acid (Glu or E); glycine (Gly or G); histidine (His or H); isoleucine (Ile or I); leucine (Leu or L); lysine (Lys or K); methionine (Met or M); phenylalanine (Phe or F); proline (Pro or P); serine (Ser or S); threonine (Thr or T); tryptophan (Trp or W); tyrosine (Tyr or Y); and valine (Val or V), although modified, synthetic, or rare amino acids may be used as desired. Naturally occurring residues are divided into groups based on common side-chain properties: (1) hydrophobic: methionine, alanine, valine, leucine, iso-leucine; (2) neutral hydrophilic: cysteine, serine, threonine, asparagine, glutamine; (3) acidic: aspartic acid, glutamic acid; (4) basic: histidine, lysine, arginine; (5) residues that influence chain orientation: glycine, proline; and (6) aromatic: tryptophan, tyrosine, phenylalanine. In some embodiments, substitutions may entail exchanging a member of one of these classes for another class.

[0047] As used herein, the term “mutation” in the context of proteins, polypeptides, peptides or amino acid sequences, or “mutated amino acid (residue)” or the like includes amino acid substitution(s), deletion(s), insertion(s), and/or one or more chemical modifications of an amino acid sequence or nucleotide sequence. Such substitutions may be conservative, i.e., an amino acid residue is replaced with a chemically similar amino acid residue. Examples of conservative substitutions are the replacements among the members of the following groups: 1) alanine, serine, and threonine; 2) aspartic acid and glutamic acid; 3) asparagine and glutamine; 4) arginine and lysine; 5) isoleucine, leucine, methionine, and valine; and 6) phenylalanine, tyrosine, and tryptophan. Mutations may also include substitutions by their respective D-stereoisomers or by amino acids other than the naturally occurring 20 amino acids, such as, for example, ornithine, hydroxyproline, citrulline, homoserine, hydroxylysine, norvaline. However, substitutions by naturally occurring amino acids are preferred.

[0048] The term “nucleic acid” as used herein may generally refer to DNA or RNA. DNA and RNA differ – among others – in their nucleobases. The complementary base to adenine in DNA is thymine, whereas in RNA, it is uracil. For the sake of simplification, the corresponding base to adenine is denoted as “t” throughout the application, which – depending on its context – may refer to thymine (in DNA) or uracil (in RNA).

[0049] The term “encoding” or “encode(s)” as used herein in the context of a nucleic acid, relates to a nucleic acid having a sequence that can be translated into a particular amino acid sequence that is encoded by the nucleic acid. The nucleic acid sequence may encompass the sequence of a coding strand and may also encompass the sequence of a strand that is complementary to the coding strand.

[0050] “Percent (%) sequence identity” with respect to sequences disclosed herein is defined as the percentage of amino acid residues or nucleotides in a candidate sequence that are pair-wise identical with the amino acid residues or nucleotides in a reference sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, ALIGN, or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximum alignment over the full length of the sequences being compared. The same is true for nucleotide sequences disclosed herein. For determining sequence identity, uracil (e.g. in RNA) may be considered to be identical to thymine (e.g. in DNA).

[0051] The term “attenuation” as used herein, relates to a reduced capacity of a virus to replicate within a given host (cell), a reduced capacity of replicating in a healthy organ, and/or a reduced capacity of inducing cytokines. A virus particle of the invention is preferably attenuated.

[0052] The term “infectious” as used herein, relates to a virus’ capacity to infect, i.e., enter, a given host cell. A virus particle of the invention is preferably infectious.

[0053] The term “replication competent” means that a virus has the ability to amplify and express its genetic material in infected cells and being able to produce further progeny in normal cells that are not genetically engineered. In particular, replication competent viruses do not require host cells that were engineered to express a viral gene for being capable of replication. A virus particle of the invention is preferably replication competent.

[0054] The term “pathogenic” as used herein, relates to a virus’ capacity to cause disease, i.e., harm to an organism.

[0055] The term “entry” relates to a virus’ capacity to enter a given target cell. Viral entry can be measured as essentially described in **Example 10 B**. The measurement preferably comprises the following steps: Target cells are preincubated with virus (multiplicity of infection of 0.1) at 4°C.

After the incubation of one hour, the cells are warmed up to 37°C. At different time points after heating up the cells to 37°C (i.e. 0min, 20min, 60min or 180min) Monensin is added to the cultures. Cells are then incubated for further 16 hours. After the incubation time, virus protein is determined in each cell by staining the cells with an anti-LCMV-NP antibody and analysis in the flow cytometer. The capacity to enter a cell is a direct correlate of the percentage of infected cells in this assay.

**[0056]** The term “infectivity” relates to a virus’ capacity to enter a cell, replicate in the cell and to produce viral proteins. Viral infectivity can be measured as essentially described in **Example 10 C**. The measurement preferably comprises the following steps: Target cells are incubated with virus (multiplicity of infection of 0.01 to 0.1) at 37°C for 16 hours. After the incubation time, virus protein is determined in each cell by staining the cells with an anti-LCMV-NP antibody and analysis in the flow cytometer. In this assay the percentage of infected cells is a direct correlate of the capacity of the virus to propagate in a certain target cell culture.

**[0057]** The term “RNA replication” relates to a virus’ capacity to replicate viral RNA within a cell.

**[0058]** The term “propagation” relates to the increase of viral particles.

**[0059]** The term “tropism” relates to the viral particle’s infectivity to a given cell type. Tropism is at least partially correlated with the virus’ capacity to enter a given cell type. The term “tumor tropism” relates to tropism in the context of a tumor cell.

**[0060]** A virus particle of the disclosure is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87; (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113; (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147; (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157; (e) Helix  $\alpha$ 3 as defined by positions 187-199; (f) Loop 3 as defined by

positions 200-226; (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; and/or (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365.

**[0061]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (a) Helix  $\alpha 1$  and/or  $\alpha 2$  as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;

**[0062]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (b) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;

**[0063]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (c) Strand  $\beta 1$  N terminal as defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;

**[0064]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;

**[0065]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (e) Strands  $\beta 3$ ,  $\beta 4$ ,

and/or  $\beta 5$  as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;

**[0066]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (f) Loop 3 as defined by positions 200-226;

**[0067]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (g) the H1,H2 domain as defined by positions 1-58;

**[0068]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (h) the TM cytoplasmic domain as defined by positions 439-498; and/or

**[0069]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (i) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258.

**[0070]** A virus particle of the disclosure, is preferably one wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in any one of the regions (a), (b), (c), (d), (e), (f), (g), (h), and/or (i) as defined supra as well as any combinations thereof.

**[0071]** A virus particle of the disclosure preferably comprise a glycoprotein and/or a nucleic acid encoding a glycoprotein, wherein the glycoprotein has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably



at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, to the glycoprotein sequence set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred.

**[0072]** In a virus particle of the disclosure, preferably, the one or more positions that comprise at least one mutated amino acid residue are selected from the group consisting of positions 102, 122, 129, 132, 136, 152, 153, 154, 155, 156, 211, 217, 218, 256, 260, 284, 328, 332, 342, 358, and 492. The at least one mutated amino acid residue is preferably in comparison with the linear polypeptide sequence of the wild type LCMV strain WE GP set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred.

**[0073]** In a virus particle of the disclosure, preferably, the at least one mutated amino acid residue is selected from the group consisting of Ser 102 → Asn, Phe 122 → Leu, Phe 129 → Ser, Lys 132 → Arg, His 136 → Gln, Asn 152 → Tyr, Ser 153 → Pro, Phe or Tyr, Asn 154 → Asp, His 155 → Leu or Tyr, Lys 156 → Glu, Ala 211 → Thr, Thr 217 → Ile, Thr 218 → Ile, Lys 256 → Arg, Leu 260 → Phe or Ile, Tyr 284 → His, Ala 328 → Ser, Phe 332 → Leu, Val 342 → Ala, Arg 358 → Lys, and Lys 492 → Ile, including combinations thereof. The at least one mutated amino acid residue is preferably in comparison with the linear polypeptide sequence of the wild type LCMV strain WE GP set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred.

**[0074]** In a virus particle of the disclosure, preferably, the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred:

- (a) Lys 492 → Ile;
- (b) Ala 211 → Thr;
- (c) Lys 260 → Phe and Lys 492 → Ile;
- (d) Ser 153 → Pro and Lys 492 → Ile;
- (e) Phe 122 → Leu, His 136 → Gln, and Ser 153 → Pro;
- (f) Phe 122 → Leu and Lys 492 → Ile;
- (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, and Lys 492 → Ile;
- (h) Glu 255 → Gly, Lys 492 → Ile;
- (i) Ser 153 → Pro and Arg 358 → Lys;

- (j) Ser 153 → Pro, Lys 256 → Arg, Leu 260 → Phe and Lys 492 → Ile;
- (k) Ser 153 → Phe, Glu 255 → Gly, and Leu 260 → Phe;
- (l) Ser 153 → Phe, Glu 255 → Gly, and Leu 260 → Phe;
- (m) Lys 156 → Glu and Lys 492 → Ile;
- (n) Ser 153 → Pro, Lys 256 → Arg, and Leu 260 → Phe;
- (o) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Lys 256 → Arg, and Lys 492 → Ile;  
or
- (p) Glu 379 → Asn and Lys 492 → Ile.

**[0075]** In a virus particle of the disclosure, preferably, the at least one mutated amino acid residue is selected from the group consisting of Ser 102 → Asn, Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro or Phe, Lys 156 → Glu, Ala 211 → Thr, Lys 256 → Arg, Leu 260 → Phe, Tyr 284 → His, Ala 328 → Ser, Phe 332 → Leu, Val 342 → Ala, Arg 358 → Lys, Lys 492 → Ile, including combinations thereof. The at least one mutated amino acid residue is preferably in comparison with the linear polypeptide sequence of the wild type LCMV strain WE GP set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred.

**[0076]** A virus particle of the disclosure may be equipped with additional modifications. Such modifications may comprise mutations at positions 181 and/or 185 of the GP, in particular Arg 185 → Trp and/or Ile 181 → Met. Such modified virus particles may result in a, compared to a strain having the WE wild-type amino acids at positions 181 and 185 (Ile 181 and Arg 185), stronger antitumoral activity, such as a stronger early LCMV directed T cell response. A preferred virus particle may comprise a glycoprotein, wherein the glycoprotein may at least one mutated amino acid residue at position 181 and/or 185 in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4. It is however preferred that the glycoprotein comprises a mutation at both positions in comparison with SEQ ID NO: 4. Preferred mutations at these positions are selected from Arg 185 → Trp and Ile 181 → Met or Val, more preferably selected from Arg 185 → Trp and Ile 181 → Met. Such mutations may be combined with other mutations disclosed herein, such as mutations that improve entry into a tumor cell.

**[0077]** In a virus particle of the disclosure, preferably, the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4

- (a) Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;

- (b) Ile 181 → Met, Arg 185 → Trp, and Ala 211 → Thr;
- (c) Ile 181 → Met, Arg 185 → Trp, Lys 260 → Phe, and Lys 492 → Ile;
- (d) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (e) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, and Arg 185 → Trp;
- (f) Phe 122 → Leu, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (h) Ile 181 → Met, Arg 185 → Trp, Glu 255 → Gly, and Lys 492 → Ile;
- (i) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Arg 358 → Lys;
- (j) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, Leu 260 → Phe, and Lys 492 → Ile;
- (k) Ser 153 → Phe, Arg 185 → Trp, Glu 255 → Gly, and Leu 260 → Phe;
- (l) Ser 153 → Phe, Glu 255 → Gly, and Leu 260 → Phe;
- (m) Lys 156 → Glu, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (n) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, and Leu 260 → Phe;
- (o) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, and Lys 492 → Ile; or
- (p) Ile 181 → Met, Arg 185 → Trp, Glu 379 → Asn, and Lys 492 → Ile.

**[0078]** In a virus particle of the disclosure, preferably, the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, a limited number of mutated amino acid residues. Said glycoprotein preferably comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutated amino acid residues, preferably mutated amino acid residues as defined herein. More preferably, said glycoprotein preferably comprises not more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutated amino acid residues, preferably mutated amino acid residues as defined herein.

**[0079]** In a virus particle of the disclosure, preferably, the glycoprotein has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in any one of SEQ ID NOs: 30-57.

**[0080]** In a virus particle of the disclosure, preferably, the virus particle comprises a nucleic acid encoding a glycoprotein, wherein said nucleic acid comprises a sequence that has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NOs: 58-85, or a respective complementary sequence.

**[0081]** In a virus particle of the disclosure, preferably, the virus particle comprises an LCMV L-protein (LP) and/or a nucleic acid encoding said LP, wherein said LP has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity to the L-protein sequence set forth in SEQ ID NO: 10 or 23.

**[0082]** In a virus particle of the disclosure, preferably, the virus particle comprises a nucleic acid encoding an LP, wherein said nucleic acid comprises a sequence that has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or that is preferably identical, to a sequence set forth in SEQ ID NO: 9 or 22, or a respective complementary sequence.

**[0083]** In a virus particle of the disclosure, preferably, the virus particle comprises an LCMV nucleoprotein (NP) and/or a nucleic acid encoding said NP, wherein said NP has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably

at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to the nucleoprotein sequence set forth in SEQ ID NO: 6.

**[0084]** In a virus particle of the disclosure, preferably, the virus particle comprises a nucleic acid encoding an NP, wherein said nucleic acid comprises a sequence that has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to the sequence set forth in SEQ ID NO: 5, or a respective complementary sequence.

**[0085]** In a virus particle of the disclosure, preferably, the virus particle comprises an LCMV Z-protein (ZP) and/or a nucleic acid encoding said ZP, wherein said ZP has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to the ZP sequence set forth in SEQ ID NOs: 8 or 21.

**[0086]** In a virus particle of the disclosure, preferably, the virus particle comprises a nucleic acid encoding a ZP, wherein said nucleic acid comprises a sequence that has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that

is identical, to the sequence set forth in SEQ ID NOs: 7 or 20, or a respective complementary sequence.

**[0087]** In a virus particle of the disclosure, preferably, the virus particle comprises an LCMV GP, and an LCMV NP, and/or one or more nucleic acids encoding said LCMV GP and LCMV NP, wherein said LCMV GP and LCMV NP have at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or are preferably identical to the following LCMV GP and LCMV NP sequences: (a) SEQ ID NOs: 30 and 6; (b) SEQ ID NOs: 31 and 6; (c) SEQ ID NOs: 32 and 6; (d) SEQ ID NOs: 33 and 6; (e) SEQ ID NOs: 34 and 6; (f) SEQ ID NOs: 35 and 6; (g) SEQ ID NOs: 36 and 6; (h) SEQ ID NOs: 37 and 6; (i) SEQ ID NOs: 38 and 6; (j) SEQ ID NOs: 39 and 6; (k) SEQ ID NOs: 40 and 6; (l) SEQ ID NOs: 41 and 6; (m) SEQ ID NOs: 42 and 6; (n) SEQ ID NOs: 43 and 6; (o) SEQ ID NOs: 44 and 6; (p) SEQ ID NOs: 45 and 6; (q) SEQ ID NOs: 46 and 6; (r) SEQ ID NOs: 47 and 6; (s) SEQ ID NOs: 48 and 6; (t) SEQ ID NOs: 49 and 6; (u) SEQ ID NOs: 50 and 6; (v) SEQ ID NOs: 51 and 6; (w) SEQ ID NOs: 52 and 6; (x) SEQ ID NOs: 53 and 6; (y) SEQ ID NOs: 54 and 6; (z) SEQ ID NOs: 55 and 6; (aa) SEQ ID NOs: 56 and 6; or (bb) SEQ ID NOs: 57 and 6.

**[0088]** In a virus particle of the disclosure, preferably, the virus particle comprises an LCMV GP, an LCMV LP, an LCMV NP, and an LCMV ZP, and/or one or more nucleic acids encoding said LCMV GP, LCMV LP, LCMV NP, and LCMV ZP, wherein said LCMV GP, LCMV LP, LCMV NP, and LCMV ZP have at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or are preferably identical to the following LCMV GP, LCMV LP, LCMV NP, and LCMV ZP sequences: (a) SEQ ID NOs: 30, 23, 6, and 21; (b) SEQ ID NOs: 31, 23, 6, and 21;

(c) SEQ ID NOs: 32, 23, 6, and 21; (d) SEQ ID NOs: 33, 23, 6, and 21; (e) SEQ ID NOs: 34, 23, 6, and 21; (f) SEQ ID NOs: 35, 23, 6, and 21; (g) SEQ ID NOs: 36, 23, 6, and 21; (h) SEQ ID NOs: 37, 23, 6, and 21; (i) SEQ ID NOs: 38, 23, 6, and 21; (j) SEQ ID NOs: 39, 23, 6, and 21; (k) SEQ ID NOs: 40, 23, 6, and 21; (l) SEQ ID NOs: 41, 23, 6, and 21; (m) SEQ ID NOs: 42, 23, 6, and 21; (n) SEQ ID NOs: 43, 23, 6, and 21; (o) SEQ ID NOs: 44, 23, 6, and 21; (p) SEQ ID NOs: 45, 23, 6, and 21; (q) SEQ ID NOs: 46, 23, 6, and 21; (r) SEQ ID NOs: 47, 23, 6, and 21; (s) SEQ ID NOs: 48, 23, 6, and 21; (t) SEQ ID NOs: 49, 23, 6, and 21; (u) SEQ ID NOs: 50, 23, 6, and 21; (v) SEQ ID NOs: 51, 23, 6, and 21; (w) SEQ ID NOs: 52, 23, 6, and 21; (x) SEQ ID NOs: 53, 23, 6, and 21; (y) SEQ ID NOs: 54, 23, 6, and 21; (z) SEQ ID NOs: 55, 23, 6, and 21; (aa) SEQ ID NOs: 56, 23, 6, and 21; or (bb) SEQ ID NOs: 57, 23, 6, and 21.

**[0089]** In a virus particle of the disclosure, preferably, the virus particle comprises an S segment comprising a 5' untranslated region (UTR) that has at least about 60%, preferably at least about 65%, preferably at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is identical, to a sequence set forth in SEQ ID NO: 24, or a respective complementary sequence.

**[0090]** In a virus particle of the disclosure, preferably, the virus particle comprises an L segment comprising a 5' untranslated region (UTR) that has at least about 60%, preferably at least about 65%, preferably at least about 70%, preferably has at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is identical, to a sequence set forth in SEQ ID NO: 26 or 28, or a respective complementary sequence.

**[0091]** In a preferred virus particle of the disclosure, the virus particle comprises an L segment comprising a 3' untranslated region (UTR) that has at least about 60%, preferably at least about 65%, preferably at least about 70%, preferably has at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is identical, to the sequence set forth in SEQ ID NO: 27 or 29, or a respective complementary sequence.

**[0092]** In a virus particle of the disclosure, preferably, the virus particle comprises an S segment comprising a nucleic acid sequence having at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity to the sequence set forth in SEQ ID NO: 1 or 11.

**[0093]** In a virus particle of the disclosure, preferably, the virus particle comprises an L segment comprising a nucleic acid sequence having at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or that is preferably identical to the sequence shown in SEQ ID NOs: 2 or 15.

**[0094]** In a virus particle of the disclosure, it is preferred that the virus particle comprises an S segment that is derived from a WE strain (or its derivatives, such as P52) and an L segment derived from the Clone 13 strain. Such chimeric, virus particles showed attenuated replication as described



in WO 2022/180203. Still, such virus particles typically retain or even enhance their strong anti-tumoral effects as compared to strains comprising an L segment derived from a WE strain (or one of its derivatives, such as P52) – despite their attenuation.

**[0095]** In a virus particle of the disclosure, preferably, the virus particle comprises an S segment comprising a nucleic acid sequence having at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity to the sequence set forth in SEQ ID NO: 1 or 11. It is also preferred, that said virus particle comprises an L segment comprising a nucleic acid sequence having at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or that is preferably identical to the sequence shown in SEQ ID NOs: 2 or 15, with the sequence shown in SEQ ID NO: 15 being preferred.

**[0096]** Several LCMV strains are part of the present disclosure. Such LCMV include the strains that are shown in Table A. These strains have a S segment derived from LCMV WE, which comprises mutations in the GP. The mutations in comparison with the glycoprotein set forth in SEQ ID NO: 4 are shown in Table A. Further said strains have the L segment of strain Clone 13 as shown in SEQ ID NO: 15. A preferred virus particle of the disclosure is an LCMV strain as shown in Table A.

**Table A**

| <b>M</b> | <b>Strain</b> | <b>Mutations GP</b>                                                      |
|----------|---------------|--------------------------------------------------------------------------|
| M21      | 181h2         | Ile 181→ Met, Arg 185 → Trp, Lys 492→ Ile                                |
| M19      | 181h5         | Ile 181→ Met, Arg 185 → Trp, Ala 211→ Thr                                |
| M89      | 181h7         | Ile 181→ Met, Arg 185 → Trp, Lys 260→ Phe, Lys 492→ Ile                  |
| M90      | 153h7         | Ser 153 → Pro, Ile 181→ Met, Arg 185 → Trp, Lys 492→ Ile                 |
| M100     | 122h5         | Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181→ Met, Arg 185 → Trp |
| M94      | 122h2         | Phe 122 → Leu, Ile 181→ Met, Arg 185 → Trp, Lys 492→ Ile                 |

|      |       |                                                                                                         |
|------|-------|---------------------------------------------------------------------------------------------------------|
| M95  | 122h3 | Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 492 → Ile.               |
| M93  | 181h8 | Ile 181 → Met, Arg 185 → Trp, Glu 255 → Gly, Lys 492 → Ile                                              |
| M82  | 153h3 | Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Arg 358 → Lys                                              |
| M99  | 153h8 | Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, Leu 260 → Phe, Lys 492 → Ile                |
| M88  | 153h6 | Ser 153 → Phe, Arg 185 → Trp, Glu 255 → Gly, Leu 260 → Phe                                              |
| M87  | 153h5 | Ser 153 → Phe, Glu 255 → Gly, Leu 260 → Phe                                                             |
| M92  | 156h3 | Lys 156 → Glu, Ile 181 → Met, Arg 185 → Trp, Lys 492 → Ile                                              |
| M102 | 153h9 | Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, Leu 260 → Phe                               |
| M97  | 122h4 | Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, Lys 492 → Ile |
| M103 | 181h9 | Ile 181 → Met, Arg 185 → Trp, Glu 379 → Asn, Lys 492 → Ile                                              |
| M2   | 102h1 | Ser 102 → Asn                                                                                           |
| M3   | 122h1 | Phe 122 → Leu                                                                                           |
| M84  | 129h1 | Phe 129 → Ser                                                                                           |
| M17  | 136h1 | His 136 → Gln                                                                                           |
| M27  | 153h1 | Ser 153 → Pro                                                                                           |
| M59  | 154h1 | Asn 154 → Asp                                                                                           |
| M5   | 155h1 | His 155 → Leu                                                                                           |
| M10  | 217h1 | Thr 217 → Ile                                                                                           |
| M69  | 218h1 | Thr 218 → Ile                                                                                           |
| M25  | 260h1 | Leu 260 → Phe                                                                                           |
| M11  | 328h1 | Ala 328 → Ser                                                                                           |
| M78  | 332h1 | Phe 332 → Leu                                                                                           |

**[0097]** A virus particle of the disclosure preferably has an increased capacity to enter a tumor cell, preferably murine or human tumor cell, more preferably human tumor cell, as compared to a reference virus particle. The tumor cell is preferably a cell of one of the following tumors: lung tumor cells, such as H1975 or A549, LLC, TC-1, gastrointestinal tumor cells, such as Gist-T1, melanoma cells, such as MaMel86a, MaMel51, A375, B16F10, or RPMI-7951, pancreatic tumor cells, such as 511950, 60590, 511950R, or 60590R, thyroid tumor cells, such as 8305C or C643, sarcoma cells, such as Gist-T1, breast tumor cells, such as HCC1954, cervical tumor cells, such as HeLa, liver tumor cells, such as HepG2, colon tumor cells, such as MC38, Sw620, or Sw480, neuroblastoma cells, such as SK-N-BE(2), and/or prostate tumor cells, such as TrampC2. The capacity to enter a tumor cell can be determined using the assay as essentially described in **Example 10 B**. The assay preferably comprises the following steps: Target cells are preincubated with virus (multiplicity of infection of 0.1) at 4°C. After the incubation of one hour, the cells are warmed up to 37°C. At different time points after heating up the cells to 37°C (i.e. 0min, 20min, 60min or 180min) Monensin is added the cultures. Cells are then incubated for further 16 hours. After the incubation time, virus protein is determined in each cell by staining the cells with an anti-

LCMV-NP antibody and analysis in the flow cytometer. The capacity to enter a cell is a direct correlate of the percentage of infected cells in this assay. The reference virus particle is preferably a reference virus particle that comprises a LCMV GP of strain WE (SEQ ID NO: 4) or P52 (SEQ ID NO: 13), with a GP of strain WE being preferred. Except for the GP, the reference particle is preferably identical to the preferred virus particle that has an increased capacity to enter a tumor cell.

**[0098]** A virus particle of the disclosure preferably has an increased infectivity for a tumor cell, preferably murine or human tumor cell, more preferably human tumor cell, as compared to a reference virus particle. The tumor cell is preferably a cell of one of the following tumors: lung tumor cells, such as H1975 or A549, LLC, TC-1, gastrointestinal tumor cells, such as Gist-T1, melanoma cells, such as MaMel86a, MaMel51, A375, B16F10, or RPMI-7951, pancreatic tumor cells, such as 511950, 60590, 511950R, or 60590R, thyroid tumor cells, such as 8305C or C643, sarcoma cells, such as Gist-T1, breast tumor cells, such as HCC1954, cervical tumor cells, such as HeLa, liver tumor cells, such as HepG2, colon tumor cells, such as MC38, Sw620, or Sw480, neuroblastoma cells, such as SK-N-BE(2), and/or prostate tumor cells, such as TrampC2. The infectivity for a tumor cell can be determined using the assay as essentially described in **Example 10 C**. The assay preferably comprises the following steps: Target cells are incubated with virus (multiplicity of infection of 0.01 to 0.1) at 37°C for 16 hours. After the incubation time, virus protein is determined in each cell by staining the cells with an anti-LCMV-NP antibody and analysis in the flow cytometer. In this assay the percentage of infected cells is a direct correlate of the capacity of the virus to propagate in a certain target cell culture. The reference virus particle is preferably a reference virus particle that comprises a LCMV GP of strain WE (SEQ ID NO: 4) or P52 (SEQ ID NO: 13), with a GP of strain WE being preferred. Except for the GP, the reference particle is preferably identical to the preferred virus particle that has an increased capacity to enter a tumor cell.

**[0099]** A virus particle of the disclosure preferably has an increased tropism for a tumor cell. The tumor cell is preferably of a tumor described herein, preferably murine or human tumor cell, more preferably human tumor cell, as compared to said reference virus particle. A preferred virus particle of the disclosure may have increased tropism for a type of tumor selected from the group consisting of a cell of a tumor as disclosed herein, preferably lung tumor cells, such as H1975 or A549, LLC, TC-1, gastrointestinal tumor cells, such as Gist-T1, melanoma cells, such as MaMel86a, MaMel51, A375, B16F10, or RPMI-7951, pancreatic tumor cells, such as 511950, 60590, 511950R, or 60590R, thyroid tumor cells, such as 8305C or C643, sarcoma cells, such as

Gist-T1, breast tumor cells, such as HCC1954, cervical tumor cells, such as HeLa, liver tumor cells, such as HepG2, colon tumor cells, such as MC38, Sw620, or Sw480, neuroblastoma cells, such as SK-N-BE(2), and/or prostate tumor cells, such as TrampC2. A preferred virus particle of the disclosure may have increased tropism for more than one type of tumor, including all types of tumors selected from the aforementioned group. The reference virus particle is preferably a reference virus particle that comprises a LCMV GP of strain WE (SEQ ID NO: 4) or P52 (SEQ ID NO: 13), with a GP of strain WE being preferred. Except for the GP, the reference particle is preferably identical to the preferred virus particle that has an increased tropism for a human tumor cell.

**[0100]** A virus particle of the disclosure is preferably capable of entering a cell in an alpha dystroglycan-independent manner. A virus particle of the disclosure is thus preferably capable of entering a cell via a mechanism other than via alpha dystroglycan. A virus particle of the disclosure is preferably capable of entering a cell that does not or does not essentially express alpha dystroglycan. Preferably, the virus particle is capable of entering a cell that does not or does not essentially express alpha dystroglycan about as efficient as a cell that does express alpha dystroglycan. The capacity of entering a cell in an alpha dystroglycan-independent or dependent manner can be measured as essentially described in **Example 6**.

**[0101]** A virus particle of the disclosure may be an arenavirus particle other than an LCMV particle that is pseudotyped with an LCMV GP. “Pseudotyping” or “pseudotyped” or the like refers to virus, viral vectors, or virus particles that are combined with foreign envelope proteins, such as a non-LCMV viral particle combined with an LCMV GP. In this context, the foreign viral envelope protein can be used to alter host tropism or increase or decrease the stability of the virus particles. The virus particle may be a vesicular stomatitis virus (VSV) particle that is pseudotyped with an LCMV GP. The virus particle may be a Pichinde virus particle that is pseudotyped with an LCMV GP. The virus particle may be a particle of a virus other than an arenavirus that is preferably pseudotyped with an LCMV GP as defined herein. The virus particle may be a particle of a viral vaccination vector, that is preferably pseudotyped with an LCMV GP as defined herein.

**[0102]** A virus particle of the disclosure preferably does not comprise a heterologous ORF. A “heterologous ORF” in this context refers to an ORF from an organism other than an LCMV and/or a ORF encoding an artificial or synthetic protein.

[0103] A virus particle of the disclosure may be a virus particle comprising a glycoprotein (GP) of an arenavirus and/or a nucleic acid encoding said GP, wherein the glycoprotein comprises at least one of the following amino acid residues:

- (a) at the position corresponding to Ser 102 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Asn residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
- (b) at the position corresponding to Phe 122 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (c) at the position corresponding to Phe 129 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Ser residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (d) at the position corresponding to His 136 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Gln residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a His residue at said position;
- (e) at the position corresponding to Asn 152 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Tyr residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (f) at the position corresponding to Ser 153 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Pro, Phe, or Tyr residue, which is preferably not the wild-type residue of said GP at said position,

wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;

- (g) at the position corresponding to Asn 154 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Asp residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (h) at the position corresponding to His 155 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu or Tyr residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (i) at the position corresponding to Lys 156 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Glu residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (j) at the position corresponding to Ala 211 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Thr residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises an Ala residue at said position;
- (k) at the position corresponding to Thr 217 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ile residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (l) at the position corresponding to Thr 218 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ile residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;

- (m) at the position corresponding to Lys 256 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Arg residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (n) at the position corresponding to Leu 260 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Phe or Ile residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Leu residue at said position;
- (o) at the position corresponding to Tyr 284 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a His residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Tyr residue at said position;
- (p) at the position corresponding to Ala 328 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Ser residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ala residue at said position;
- (q) at the position corresponding to Phe 332 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (r) at the position corresponding to Val 342 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ala residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Val residue at said position;
- (s) at the position corresponding to Arg 358 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Lys residue,

which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Arg residue at said position; and

- (t) at the position corresponding to Lys 492 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ile residue, which is preferably not the wild-type residue of said GP at said position, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position.

Said virus particle is preferably a particle of an arenavirus, preferably an arenavirus other than LCMV, such as Lunk virus (LUNV). Preferably, said virus particle is an arenavirus particle and said GP is a GP of said arenavirus. Preferably, said at least one amino acid residue is at least one substitution of a native amino acid residue of the GP of said arenavirus. Said GP is preferably a GP other than an LCMV GP.

**[0104]** The present invention also relates to an LCMV GP as described herein. The glycoprotein preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred at least one mutated amino acid residue as defined herein in the context of a virus particle. The LCMV GP can be an isolated GP. The LCMV GP can also be comprised in a larger structure, such as being comprised in a virus particle.

**[0105]** A glycoprotein of the disclosure is preferably a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or in comparison with the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87; (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113; (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147; (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157; (e) Helix  $\alpha$ 3 as defined by positions 187-199; (f) Loop 3 as defined by positions 200-226; (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions



245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365; (i) the H1,H2 domain as defined by positions 1-58; and/or (j) the TM cytoplasmic domain as defined by positions 439-498.

**[0106]** A glycoprotein of the disclosure is preferably a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or in comparison with the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492.

**[0107]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions selected from the group consisting of comprised in (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87; (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113; (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147; (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157; (e) Helix  $\alpha$ 3 as defined by positions 187-199; (f) Loop 3 as defined by positions 200-226; (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; and/or (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365.

**[0108]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (a) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;

**[0109]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (b) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;

**[0110]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (c) Strand  $\beta$ 1 N terminal as defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;

**[0111]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue at one or more positions comprised in (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;

**[0112]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in at one or more positions comprised (e) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;

**[0113]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein

set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in at one or more positions comprised (f) Loop 3 as defined by positions 200-226;

**[0114]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in at one or more positions comprised (g) the H1,H2 domain as defined by positions f 1-58;

**[0115]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in at one or more positions comprised (h) the TM cytoplasmic domain as defined by positions 439-498; and/or

**[0116]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in at one or more positions comprised (i) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258.

**[0117]** A glycoprotein of the disclosure preferably comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, at least one mutated amino acid residue in any one of the regions (a), (b), (c), (d), (e), (f), (g), (h), and/or (i) as defined supra as well as any combinations thereof.

**[0118]** A glycoprotein of the disclosure preferably has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, to the glycoprotein sequence set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred.

**[0119]** In a glycoprotein of the disclosure, preferably, the one or more positions that comprise at least one mutated amino acid residue are selected from the group consisting of positions 102, 122,

129, 132, 136, 152, 153, 154, 155, 156, 211, 217, 218, 256, 260, 284, 328, 332, 342, 358, and 492. The at least one mutated amino acid residue is preferably in comparison with the linear polypeptide sequence of the wild type LCMV strain WE GP set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred.

**[0120]** In a glycoprotein of the disclosure, preferably, the at least one mutated amino acid residue is selected from the group consisting of Ser 102 → Asn, Phe 122 → Leu, Phe 129 → Ser, Lys 132 → Arg, His 136 → Gln, Asn 152 → Tyr, Ser 153 → Pro, Phe or Tyr, Asn 154 → Asp, His 155 → Leu or Tyr, Lys 156 → Glu, Ala 211 → Thr, Thr 217 → Ile, Thr 218 → Ile, Lys 256 → Arg, Leu 260 → Phe or Ile, Tyr 284 → His, Ala 328 → Ser, Phe 332 → Leu, Val 342 → Ala, Arg 358 → Lys, and Lys 492 → Ile, including combinations thereof. The at least one mutated amino acid residue is preferably in comparison with the linear polypeptide sequence of the wild type LCMV strain WE GP set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred.

**[0121]** In a glycoprotein of the disclosure, preferably, the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred:

- (a) Lys 492 → Ile;
  - (b) Ala 211 → Thr;
  - (c) Lys 260 → Phe and Lys 492 → Ile;
  - (d) Ser 153 → Pro and Lys 492 → Ile;
  - (e) Phe 122 → Leu, His 136 → Gln, and Ser 153 → Pro;
  - (f) Phe 122 → Leu and Lys 492 → Ile;
  - (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, and Lys 492 → Ile;
  - (h) Glu 255 → Gly and Lys 492 → Ile;
  - (i) Ser 153 → Pro and Arg 358 → Lys;
  - (j) Ser 153 → Pro, Lys 256 → Arg, Leu 260 → Phe and Lys 492 → Ile;
  - (k) Ser 153 → Phe, Glu 255 → Gly and Leu 260 → Phe;
  - (l) Ser 153 → Phe, Glu 255 → Gly, and Leu 260 → Phe;
  - (m) Lys 156 → Glu and Lys 492 → Ile;
  - (n) Ser 153 → Pro, Lys 256 → Arg, and Leu 260 → Phe;
  - (o) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Lys 256 → Arg and Lys 492 → Ile;
- or

(p) Glu 379 → Asn and Lys 492 → Ile.

**[0122]** In a glycoprotein of the disclosure, preferably, the at least one mutated amino acid residue is selected from the group consisting of Ser 102 → Asn, Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro or Phe, Lys 156 → Glu, Ala 211 → Thr, Lys 256 → Arg, Leu 260 → Phe, Tyr 284 → His, Ala 328 → Ser, Phe 332 → Leu, Val 342 → Ala, Arg 358 → Lys, and Lys 492 → Ile, including combinations thereof. The at least one mutated amino acid residue is preferably in comparison with the linear polypeptide sequence of the wild type LCMV strain WE GP set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred.

**[0123]** A glycoprotein of the disclosure may be equipped with additional modifications. Such modifications may comprise mutations at positions 181 and/or 185 of the GP, in particular Arg 185 → Trp and/or Ile 181 → Met. A virus particle comprising such a GP may have, compared to a strain having the WE wild type amino acids at positions 181 and 185 (Ile 181 and Arg 185), a stronger antitumoral activity, such as a stronger early LCMV directed T cell response. A preferred glycoprotein may comprise at least one mutated amino acid residue at position 181 and/or 185 in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4. It is however preferred that the glycoprotein comprises a mutation at both positions in comparison with SEQ ID NO: 4. Preferred mutations at these positions are selected from Arg 185 → Trp and Ile 181 → Met or Val, more preferably selected from Arg 185 → Trp and Ile 181 → Met. Such mutations may be combined with other mutations disclosed herein, such as mutations that improve entry into a tumor cell.

**[0124]** In a glycoprotein of the disclosure, preferably, the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4

- (a) Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (b) Ile 181 → Met, Arg 185 → Trp, and Ala 211 → Thr;
- (c) Ile 181 → Met, Arg 185 → Trp, Lys 260 → Phe, and Lys 492 → Ile;
- (d) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (e) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, and Arg 185 → Trp;
- (f) Phe 122 → Leu, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;

- (h) Ile 181 → Met, Arg 185 → Trp, Glu 255 → Gly, and Lys 492 → Ile;
- (i) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Arg 358 → Lys;
- (j) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, Leu 260 → Phe, and Lys 492 → Ile;
- (k) Ser 153 → Phe, Arg 185 → Trp, Glu 255 → Gly, and Leu 260 → Phe;
- (l) Ser 153 → Phe, Glu 255 → Gly, and Leu 260 → Phe;
- (m) Lys 156 → Glu, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
- (n) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, and Leu 260 → Phe;
- (o) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, and Lys 492 → Ile; or
- (p) Ile 181 → Met, Arg 185 → Trp, Glu 379 → Asn, and Lys 492 → Ile.

**[0125]** In a glycoprotein of the disclosure, preferably, the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or the LCMV strain P52 glycoprotein set forth in SEQ ID NO: 13, with SEQ ID NO: 4 being preferred, a limited number of mutated amino acid residues. Said glycoprotein preferably comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutated amino acid residues, preferably mutated amino acid residues as defined herein. More preferably, said glycoprotein preferably comprises not more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutated amino acid residues, preferably mutated amino acid residues as defined herein.

**[0126]** A glycoprotein of the disclosure preferably has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in any one of SEQ ID NOs: 30-57.

**[0127]** The present invention also relates to a nucleic acid molecule encoding a GP, preferably a LCMV GP, disclosed herein. Since the degeneracy of the genetic code permits substitutions of certain codons by other codons specifying the same amino acid, the disclosure is not limited to a specific nucleic acid molecule encoding a GP described herein, but rather encompasses all nucleic acid molecules that include nucleotide sequences encoding said GP.

[0128] The nucleic acid molecule may be DNA or RNA (e.g., mRNA, viral RNA). A nucleic acid molecule may be in the form of a molecule which is single-stranded or double-stranded. A nucleic acid molecule may be linear or covalently closed to form a circle.

[0129] A nucleic acid molecule, such as DNA, is referred to as “capable of expressing a nucleic acid molecule” or “able to allow expression of a nucleotide sequence” if it includes sequence elements that contain information regarding to transcriptional and/or translational regulation, and such sequences are “operably linked” to the nucleotide sequence encoding the protein. An operable linkage is a linkage in which the regulatory sequence elements and the sequence to be expressed are connected in a way that enables gene expression. The precise nature of the regulatory regions necessary for gene expression may vary among species, but in general these regions include a promoter, which, in prokaryotes, contains both the promoter per se, i.e., DNA elements directing the initiation of transcription, as well as DNA elements which, when transcribed into RNA, will signal the initiation of translation. Such promoter regions normally include 5' non-coding sequences involved in initiation of transcription and translation, such as the -35/-10 boxes and the Shine-Dalgarno element in prokaryotes or the TATA box, CAAT sequences, and 5'-capping elements in eukaryotes. These regions can also include enhancer or repressor elements as well as translated signal and leader sequences for targeting the native protein to a specific compartment of a host cell.

[0130] In addition, 3' non-coding sequences may contain regulatory elements involved in transcriptional termination, polyadenylation or the like. If, however, these termination sequences are not satisfactorily functional in a particular host cell, then they may be substituted with signals functional in that cell.

[0131] Therefore, a nucleic acid molecule of the disclosure may be “operably linked” to one or more regulatory sequences, such as a promoter sequence, to allow expression of this nucleic acid molecule. In some embodiments, a nucleic acid molecule of the disclosure includes a promoter sequence and a transcriptional termination sequence.

[0132] A nucleic acid of the disclosure preferably comprises a nucleic acid sequence that has at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93% preferably at least about 94, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%,

preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NOs: 58-85, or a respective complementary sequence.

**[0133]** Provided nucleic acid molecules can also be part of a vector or any other kind of cloning vehicle, such as a plasmid, a phagemid, a phage, a baculovirus, a cosmid or an artificial chromosome. A provided nucleic acid molecule can be comprised in an expression vector. Cloning vehicles can include, aside from the regulatory sequences described above and a nucleotide sequence encoding a glycoprotein as described herein, replication and control sequences derived from a species compatible with the host cell that is used for expression as well as selection markers conferring a selectable phenotype on transformed or transfected cells. Large numbers of suitable cloning vectors are known in the art and are commercially available.

**[0134]** The present invention also relates to a host cell comprising a nucleic acid molecule disclosed herein, and/or nucleic acid molecules comprising nucleic acid sequences encoding proteins of the virus particle described herein. A host cell of the disclosure may comprise a cDNA of the genome of the virus particle. The cDNA of the genome may be comprised in one or more nucleic acid molecules. A host cell of the disclosure is preferably an isolated host cell. A host cell of the disclosure is preferably not part of a human or animal body. A host cell of the disclosure is preferably not part of an entire plant. A host cell of the disclosure is preferably a non-human host cell.

**[0135]** The present invention also relates to a host cell comprising cDNA of an ORF encoding a glycoprotein as described herein, an ORF encoding an L protein as described for the virus particle of the disclosure, an ORF encoding a nucleoprotein as described for the virus particle of the disclosure, and an ORF encoding a Z protein as described for the virus particle of the disclosure.

**[0136]** The present invention also relates to a host cell comprising cDNA of an LCMV S segment and an LCMV L segment as described for the virus particle of the disclosure.

**[0137]** Techniques for the production of a cDNA are routine and conventional techniques of molecular biology and DNA manipulation and production. Any cloning technique known to the skilled artisan can be used. Such as techniques are well known and are available to the skilled artisan in laboratory manuals such as, Sambrook and Russell, *Molecular Cloning: A laboratory Manual*, 3rd edition, Cold Spring Harbor Laboratory N.Y. (2001).

**[0138]** A cDNA described herein can be incorporated into a plasmid. The cDNA described herein can be part of or can be incorporated into a DNA expression vector and optionally introduced into



a host cell. A cDNA described herein or plasmid or vector comprising the cDNA preferably comprises a promoter. Specific examples of promoters include an RNA polymerase I promoter, an RNA polymerase II promoter, an RNA polymerase III promoter, a T7 promoter, an SP6 promoter or a T3 promoter.

**[0139]** A host cell can be any host cell suitable for cloning, expression, propagation, or production of the virus particle. A host cell can be prokaryotic, such as *Escherichia coli* (*E. coli*) or *Bacillus subtilis*, or eukaryotic, such as *Saccharomyces cerevisiae*, *Pichia pastoris*, SF9 or High5 insect cells, immortalized mammalian cell lines (e.g., HEK cells, BHK cells, HeLa cells or CHO cells) or primary mammalian cells. Preferred host cells include HEK cells, in particular HEK293 cells, such as HEK293T (CVCL\_0063) or FreeStyle 293-F (CVCL\_D603). FreeStyle 293-F cells are commercially available, e.g., from Thermo Fisher Scientific Inc. (Catalogue number 12338026). Preferred host cells also include BHK cells, such as BHK-21 cells (CVCL\_1914). Preferred host cells also include WHO Vero RCB 10-87 cells (ATCC CCL 81).

**[0140]** The present invention also relates to a method of producing a virus particle of the disclosure. The method comprises cultivating a host cell of the disclosure under conditions suitable for virus particle formation.

**[0141]** The method of producing the virus particle can further comprise introducing into a host cell the cDNA described herein. The method of producing the virus particle can also comprise recovery and/or purification of the virus particle. Such recovery and/or purification methods are well-known to those skilled in the art.

**[0142]** The present invention also relates to a pharmaceutical composition comprising a virus particle, such as an arenavirus particle, disclosed herein. The virus particle preferably comprises a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein as described herein for the virus particle. The present invention also relates to a pharmaceutical composition comprising a glycoprotein disclosed herein, a nucleic acid molecule disclosed herein, and/or a host cell disclosed herein. The pharmaceutical composition may further comprise a pharmaceutically acceptable excipient or carrier. A carrier may be e.g., be selected from the group consisting of water, aqueous saline solution, aqueous buffer solution, cell culture medium and combinations of at least two of the foregoing carriers.

**[0143]** The present invention also relates to a virus particle, such as an arenavirus particle, disclosed herein, a glycoprotein disclosed herein, a nucleic acid molecule disclosed herein, and/or a host cell disclosed herein for use in therapy. The virus particle preferably comprises a

lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein as described herein for the virus particle. The virus particle disclosed herein may be for use in the treatment of a cancer or tumor.

[0144] The present invention also relates to a use of a virus particle, such as an arenavirus particle, disclosed herein, a glycoprotein disclosed herein, a nucleic acid molecule disclosed herein, and/or a host cell disclosed herein for the manufacture of a medicament. The virus particle preferably comprises a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein as described herein for the virus particle. The medicament is preferably for the treatment of a cancer or tumor.

[0145] The present invention also relates to a method of treating a disease comprising administering to a subject a virus particle, such as an arenavirus particle, disclosed herein, a glycoprotein disclosed herein, a nucleic acid molecule disclosed herein, and/or a host cell disclosed herein. The subject is preferably in need thereof. The virus particle, glycoprotein, nucleic acid molecule, and/or host cell is preferably administered in an effective amount. The virus particle preferably comprises a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein as described herein for the virus particle. The disease is preferably a cancer or tumor.

[0146] A "subject" is a vertebrate, preferably a mammal, more preferably a human. The term "mammal" is used herein to refer to any animal classified as a mammal, including, without limitation, humans, domestic and farm animals, and zoo, sports, or pet animals, such as mice, sheep, dogs, horses, cats, cows, rats, pigs, apes such as cynomolgus monkeys and etc., to name only a few illustrative examples. Preferably, the mammal herein is human. The cancer or tumor may be a human or murine cancer or tumor, with a human cancer or tumor being preferred.

[0147] An "effective amount" is an amount sufficient to effect beneficial or desired results. An effective amount can be administered in one or more administrations.

[0148] A "cancer" or "tumor" may be any cancer or tumor disclosed herein. Generally, the cancer or tumor can be selected from the group consisting of carcinoma, melanoma, blastoma, lymphoma and sarcoma.

[0149] The term "carcinoma" in the context of the present disclosure should be understood to mean a malignant neoplasia of epithelial origin. A carcinoma is preferably selected from the group consisting of anal carcinoma, bronchial carcinoma, lung carcinoma, endometrial carcinoma, gallbladder carcinoma, bladder carcinoma, hepatocellular carcinoma, testicular carcinoma, colon

carcinoma, colorectal carcinoma, rectal carcinoma, laryngeal carcinoma, esophageal carcinoma, gastric carcinoma, breast carcinoma, renal carcinoma, ovarian carcinoma, pancreatic carcinoma, pharyngeal carcinoma, oropharyngeal carcinoma, prostate carcinoma, thyroid carcinoma and cervical carcinoma.

[0150] The term "sarcoma" in the context of the present disclosure should be understood to mean a malignant neoplasia of mesodermal origin. A sarcoma can be selected from the group consisting of angiosarcoma, chondrosarcoma, Ewing sarcoma, fibrosarcoma, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant fibrous histiocytoma, neurogenic sarcoma, osteosarcoma and rhabdomyosarcoma.

[0151] The term "melanoma" in the context of the present disclosure should be understood to mean a malignant neoplasia of melanocytic origin.

[0152] The term "lymphoma" in the context of the present disclosure should be understood to mean a malignant neoplasia of lymphocytic origin.

[0153] The term "blastoma" in the context of the present disclosure should be understood to mean a malignant neoplasia of embryonic origin.

[0154] The cancer or tumor to be treated may be a cold tumor. Preferred cold tumors include breast cancer, ovarian cancer, prostate cancer, pancreatic cancer, and glioblastoma.

[0155] The cancer or tumor to be treated may be a hot tumor. Preferred hot tumors include melanoma, bladder cancer, kidney cancer, head and neck cancer, and non-small cell lung cancer.

[0156] Preferred cancers or tumors to be treated include melanoma, colon carcinoma, fibrosarcoma, pancreas cancer, thyroid carcinoma, lung cancer, adenocarcinoma, and gastrointestinal cancer.

[0157] Generally, the virus particle, glycoprotein, nucleic acid molecule, and/or host cell disclosed herein can be administered via any suitable route that is known to the skilled person. Administration generally includes enteral and parenteral administration. Parenteral administration can include local administration, such as intramuscular, intraperitoneal, subcutaneous, or intratumoral administration. Alternatively, parenteral administration can include systemic administration, in particular intravenous administration, such as via injection or infusion.

[0158] The present invention also relates to a method of producing a virus particle having an increased capacity to enter a tumor cell, comprising

- a. Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein described herein.
- b. Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
- c. Optionally assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell.

**[0159]** The nucleic acid preferably encodes a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred at least one mutated amino acid residue at one or more positions selected from the group consisting of comprised in (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87; (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113; (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147; (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157; (e) Helix  $\alpha$ 3 as defined by positions 187-199; (f) Loop 3 as defined by positions 200-226; (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365; (i) the H1,H2 domain as defined by positions 1-58; and/or (j) the TM cytoplasmic domain as defined by positions 439-498; or at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492. The mutated LCMV strain WE glycoprotein may be any mutated LCMV strain WE glycoprotein disclosed herein.

**[0160]** In step b, the mutated LCMV strain WE glycoprotein is preferably expressed with further viral proteins that are required for the production of a virus particle. Such further viral proteins

may include a NP disclosed herein, a LP disclosed herein, and/or a ZP disclosed herein, preferably a NP, an LP, and/or ZP disclosed in the context of the virus particle of the invention.

**[0161]** Assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell can e.g. be carried out by means of a signal transduction assay, e.g. an assay which measures the activation of NF-kB and/or IRF3/7 in a tumor cell after infection with the virus particle. Assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a reference virus particle or a reference value. The reference virus particle preferably comprises the wild type glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred. Preferably, the reference virus particle only differs in the sequence of the glycoprotein. A reference value is preferably a reference value that is derived from a reference virus particle. A reference value is preferably at least as high or higher than the value that is or would be obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred. Preferably, the reference virus particle only differs in the sequence of the glycoprotein. The tumor cell is preferably a tumor cell line, such as a lung carcinoma cell line.

**[0162]** The method may also comprise isolating the virus particle, preferably if the virus particle has a capacity of entering a tumor cell that is higher than the capacity of the reference virus particle and/or the reference value. The method may also comprise providing the virus particle, preferably if the virus particle has a capacity of entering a tumor cell that is higher than the capacity of the reference virus particle and/or the reference value. The method may also comprise selecting the virus particle, preferably if the virus particle has a capacity of entering a tumor cell that is higher than the capacity of the reference virus particle and/or the reference value.

**[0163]** The present invention also relates to a method of producing a virus particle having an increased tropism for a tumor cell, comprising:

- a. Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein described herein.
- b. Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
- c. Optionally assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell.

**[0164]** Preferably, the virus particle has an increased tropism for one of the following tumor and/or tumor cells: lung tumor (cells), such as H1975 or A549, LLC, TC-1, gastrointestinal tumor (cells), such as Gist-T1, melanoma (cells), such as MaMel86a, MaMel51, A375, B16F10, or RPMI-7951, pancreatic tumor (cells), such as 511950, 60590, 511950R, or 60590R, thyroid tumor (cells), such as 8305C or C643, sarcoma (cells), such as Gist-T1, breast tumor (cells), such as HCC1954, cervical tumor (cells), such as HeLa, liver tumor (cells), such as HepG2, colon tumor (cells), such as MC38, Sw620, or Sw480, neuroblastoma (cells), such as SK-N-BE(2), and/or prostate tumor (cells), such as TrampC2.

**[0165]** The nucleic acid preferably encodes a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred at least one mutated amino acid residue at one or more positions comprised in (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87; (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113; (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147; (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157; (e) Helix  $\alpha$ 3 as defined by positions 187-199; (f) Loop 3 as defined by positions 200-226; (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365; (i) the H1,H2 domain as defined by positions 1-58; and/or (j) the TM cytoplasmic domain as defined by positions 439-498; or at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492. The mutated LCMV strain WE glycoprotein may be any mutated LCMV strain WE glycoprotein disclosed herein.

[0166] In step b, the mutated LCMV strain WE glycoprotein is preferably expressed with further viral proteins that are required for the production of a virus particle. Such further viral proteins may include a NP disclosed herein, a LP disclosed herein, and/or a ZP disclosed herein, preferably a NP, an LP, and/or ZP disclosed in the context of the virus particle of the invention.

[0167] Assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell can e.g., be carried out by means of a signal transduction assay, e.g. an assay which measures the activation of NF-kB and/or IRF3/7 in a tumor cell after infection with the virus particle. Assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a reference virus particle or a reference value. The reference virus particle preferably comprises the wild type glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred. Preferably, the reference virus particle only differs in the sequence of the glycoprotein. A reference value is preferably a reference value that is derived from a reference virus particle. A reference value is preferably at least as high or higher than the value that is or would be obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4 or 13, with SEQ ID NO: 4 being preferred. Preferably, the reference virus particle only differs in the sequence of the glycoprotein. The tumor cell is preferably a tumor cell line, such as a lung carcinoma cell line.

[0168] The method may also comprise isolating the virus particle, preferably if the virus particle has a capacity of entering a tumor cell that is higher than the capacity of the reference virus particle and/or the reference value. The method may also comprise providing the virus particle, preferably if the virus particle has a capacity of entering a tumor cell that is higher than the capacity of the reference virus particle and/or the reference value. The method may also comprise selecting the virus particle, preferably if the virus particle has a capacity of entering a tumor cell that is higher than the capacity of the reference virus particle and/or the reference value.

[0169] The present invention also relates to a virus particle having an increased capacity to enter a tumor cell or having an increased tropism for a tumor cell obtainable by a method of producing a virus particle having an increased capacity to enter a tumor cell disclosed herein and/or obtainable by a method of comprising of producing a virus particle having an increased tropism for a tumor cell disclosed herein.

[0170] It must be noted that as used herein, the singular forms “a”, “an” and “the” include plural references and *vice versa* unless the context clearly indicates otherwise.

[0171] Unless otherwise indicated, the term "at least" preceding a series of elements is to be understood to refer to every element in the series.

[0172] Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the present invention.

[0173] The term "and/or" wherever used herein includes the meaning of "and", "or" and "all or any other combination of the elements connected by said term".

[0174] The term "about" or "approximately" as used herein preferably means within 20%, preferably within 10%, and more preferably within 5% of a given value or range. It includes, however, also the concrete number, e.g., about 20 includes 20.

[0175] Throughout this specification and the claims, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integer or step. When used herein the term "comprising" can be substituted with the term "containing" or "including" or sometimes when used herein with the term "having".

[0176] When used herein "consisting of" excludes any element, step, or ingredient not specified in the claim element. When used herein, "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim.

[0177] In each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. E.g., the term "comprising" is meant to provide explicit support also for "consisting essentially of" and "consisting of", the term "consisting essentially of" is meant to provide explicit support also for "comprising" and "consisting of", the term "consisting of" is meant to provide explicit support also for "consisting essentially of" and "comprising". The possibility to replace terms with each other is not to be understood that these terms are synonymous.

[0178] The invention is further characterized by the following items.

Item 1. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said GP, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE



glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in

- (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
- (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
- (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha$ 3 as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498;

wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

Item 2. The virus particle of item 1, wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in

- (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;

- (b) Strands  $\beta 3$ ,  $\beta 4$ , and/or  $\beta 5$  as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
- (c) Helix  $\alpha 1$  and/or  $\alpha 2$  as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha 3$  as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258; and/or
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365.

Item 3. The virus particle of item 1, wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in

- (a) Helix  $\alpha 1$  and/or  $\alpha 2$  as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
- (b) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (c) Strand  $\beta 1$  N terminal as defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;

- (e) Strands  $\beta 3$ ,  $\beta 4$ , and/or  $\beta 5$  as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
- (f) Loop 3 as defined by positions 200-226;
- (g) the H1,H2 domain as defined by positions 1-58;
- (h) the TM cytoplasmic domain as defined by positions 439-498; and/or
- (i) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258.

Item 4. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

Item 5. The virus particle of any one of the preceding items, wherein the glycoprotein has at least 95% sequence identity to SEQ ID NO: 4.

Item 6. The virus particle of any one of the preceding items, wherein the one or more positions are selected from the group consisting of positions 102, 122, 129, 132, 136, 152, 153, 154, 155, 156, 211, 217, 218, 256, 260, 284, 328, 332, 342, 358, and 492.

Item 7. The virus particle of any one of the preceding items, wherein the at least one mutated amino acid residue is selected from the group consisting of Ser 102  $\rightarrow$  Asn, Phe 122  $\rightarrow$  Leu, Phe 129  $\rightarrow$  Ser, Lys 132  $\rightarrow$  Arg, His 136  $\rightarrow$  Gln, Asn 152  $\rightarrow$  Tyr, Ser 153  $\rightarrow$  Pro, Phe or Tyr, Asn 154  $\rightarrow$  Asp, His 155  $\rightarrow$  Leu or Tyr, Lys 156  $\rightarrow$  Glu, Ala 211  $\rightarrow$  Thr, Thr 217  $\rightarrow$  Ile, Thr 218  $\rightarrow$  Ile, Lys 256  $\rightarrow$  Arg, Leu 260  $\rightarrow$  Phe or Ile, Tyr 284  $\rightarrow$  His, Ala 328  $\rightarrow$  Ser, Phe 332  $\rightarrow$  Leu, Val 342  $\rightarrow$  Ala, Arg 358  $\rightarrow$  Lys, and Lys 492  $\rightarrow$  Ile.

Item 8. The virus particle of any one of the preceding items, wherein the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4:

- (a) Lys 492→ Ile;
  - (b) Ala 211→ Thr;
  - (c) Lys 260→ Phe and Lys 492→ Ile;
  - (d) Ser 153 → Pro and Lys 492→ Ile,;
  - (e) Phe 122 → Leu, His 136 → Gln, and Ser 153 → Pro;
  - (f) Phe 122 → Leu, and Lys 492→ Ile,;
  - (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, and Lys 492→ Ile,;
  - (h) Glu 255 →Gly and Lys 492→ Ile,;
  - (i) Ser 153 → Pro and Arg 358→ Lys;
  - (j) Ser 153 → Pro, Lys 256 →Arg, Leu 260 → Phe and Lys 492→ Ile,;
  - (k) Ser 153 → Phe, Glu 255 →Gly, and Leu 260 → Phe;
  - (l) Lys 156 → Glu and Lys 492→ Ile,;
  - (m) Ser 153 → Pro, Lys 256 →Arg, and Leu 260 → Phe;
  - (n) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Lys 256 →Arg and Lys 492→ Ile,;
- or
- (o) Glu 379 → Asn and Lys 492→ Ile.

Item 9. The virus particle of any one of the preceding items, wherein the glycoprotein further comprises a mutation at position 181 and/or 185 in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4, wherein the mutation is preferably selected from the group consisting of Ile 181 → Met or Val and Arg 185 → Trp.

Item 10. The virus particle of any one of the preceding items, wherein the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4

- (a) Ile 181 → Met, Arg 185 → Trp, and Lys 492→ Ile;
- (b) Ile 181 → Met, Arg 185 → Trp, and Ala 211→ Thr;
- (c) Ile 181 → Met, Arg 185 → Trp, Lys 260→ Phe, and Lys 492→ Ile;
- (d) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Lys 492→ Ile;
- (e) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, and Arg 185 → Trp;
- (f) Phe 122 → Leu, Ile 181 → Met, Arg 185 → Trp, and Lys 492→ Ile;

- (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
  - (h) Ile 181 → Met, Arg 185 → Trp, Glu 255 → Gly, and Lys 492 → Ile;
  - (i) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, and Arg 358 → Lys;
  - (j) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, Leu 260 → Phe, and Lys 492 → Ile;
  - (k) Ser 153 → Phe, Arg 185 → Trp, Glu 255 → Gly, and Leu 260 → Phe;
  - (l) Ser 153 → Phe, Glu 255 → Gly, and Leu 260 → Phe;
  - (m) Lys 156 → Glu, Ile 181 → Met, Arg 185 → Trp, and Lys 492 → Ile;
  - (n) Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, and Leu 260 → Phe;
  - (o) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Ile 181 → Met, Arg 185 → Trp, Lys 256 → Arg, and Lys 492 → Ile; or
  - (p) Ile 181 → Met, Arg 185 → Trp, Glu 379 → Asn, and Lys 492 → Ile.
- Item 11. The virus particle of any one of the preceding items, wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutated amino acid residues as defined in any one of items 1-10.
- Item 12. The virus particle any one of the preceding items, wherein said GP has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in any one of SEQ ID NOs: 30-57.
- Item 13. The virus particle of any one of the preceding items, wherein the virus particle comprises a nucleic acid encoding a glycoprotein, wherein said nucleic acid comprises a sequence that has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NOs: 58-85, or a respective complementary sequence.
- Item 14. The virus particle any one of the preceding items, wherein the virus particle comprises an LCMV L-protein (LP) and/or a nucleic acid encoding said LP, wherein said

LP has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity to the L-protein sequence set forth in SEQ ID NO: 10 or 23.

Item 15. The virus particle of any one of the preceding items, wherein the virus particle comprises a nucleic acid encoding an LP, wherein said nucleic acid comprises a sequence that has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or that is preferably identical, to a sequence set forth in SEQ ID NO: 9 or 22, or a respective complementary sequence.

Item 16. The virus particle of any one of the preceding items, wherein the virus particle comprises an LCMV nucleoprotein (NP) and/or a nucleic acid encoding said NP, wherein said NP has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to the nucleoprotein sequence set forth in SEQ ID NO: 6.

Item 17. The virus particle any one of the preceding items, wherein the virus particle comprises a nucleic acid encoding an NP, wherein said nucleic acid comprises a sequence that has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to the sequence set forth in SEQ ID NO: 5, or a respective complementary sequence.

Item 18. The virus particle of any one of the preceding items, wherein the virus particle comprises an LCMV Z-protein (ZP) and/or a nucleic acid encoding said ZP, wherein said ZP has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%,

preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to the ZP sequence set forth in SEQ ID NOs: 8 or 21.

Item 19. The virus particle of any one of the preceding items, wherein the virus particle comprises a nucleic acid encoding a ZP, wherein said nucleic acid comprises a sequence that has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is identical, to the sequence set forth in SEQ ID NOs: 7 or 20, or a respective complementary sequence.

Item 20. The virus particle of any one of the preceding items, wherein the virus particle comprises an LCMV GP, and an LCMV NP, and/or one or more nucleic acids encoding said LCMV GP and LCMV NP, wherein said LCMV GP and LCMV NP have at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or are preferably identical to the following LCMV GP and LCMV NP sequences:

- (a) SEQ ID NOs: 30 and 6;
- (b) SEQ ID NOs: 31 and 6;
- (c) SEQ ID NOs: 32 and 6;
- (d) SEQ ID NOs: 33 and 6;
- (e) SEQ ID NOs: 34 and 6;
- (f) SEQ ID NOs: 35 and 6;
- (g) SEQ ID NOs: 36 and 6;
- (h) SEQ ID NOs: 37 and 6;
- (i) SEQ ID NOs: 38 and 6;
- (j) SEQ ID NOs: 39 and 6;
- (k) SEQ ID NOs: 40 and 6;
- (l) SEQ ID NOs: 41 and 6;
- (m) SEQ ID NOs: 42 and 6;

- (n) SEQ ID NOs: 43 and 6;
- (o) SEQ ID NOs: 44 and 6;
- (p) SEQ ID NOs: 45 and 6;
- (q) SEQ ID NOs: 46 and 6;
- (r) SEQ ID NOs: 47 and 6;
- (s) SEQ ID NOs: 48 and 6;
- (t) SEQ ID NOs: 49 and 6;
- (u) SEQ ID NOs: 50 and 6;
- (v) SEQ ID NOs: 51 and 6;
- (w) SEQ ID NOs: 52 and 6;
- (x) SEQ ID NOs: 53 and 6;
- (y) SEQ ID NOs: 54 and 6;
- (z) SEQ ID NOs: 55 and 6;
- (aa) SEQ ID NOs: 56 and 6; or
- (bb) SEQ ID NOs: 57 and 6.

Item 21. The virus particle of any one of the preceding items, wherein the virus particle comprises an LCMV GP, an LCMV LP, an LCMV NP, and an LCMV ZP, and/or one or more nucleic acids encoding said LCMV GP, LCMV LP, LCMV NP, and LCMV ZP, wherein said LCMV GP, LCMV LP, LCMV NP, and LCMV ZP have at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or are preferably identical to the following LCMV GP, LCMV LP, LCMV NP, and LCMV ZP sequences:

- (a) SEQ ID NOs: 30, 23, 6, and 21;
- (b) SEQ ID NOs: 31, 23, 6, and 21;
- (c) SEQ ID NOs: 32, 23, 6, and 21;
- (d) SEQ ID NOs: 33, 23, 6, and 21;
- (e) SEQ ID NOs: 34, 23, 6, and 21;
- (f) SEQ ID NOs: 35, 23, 6, and 21;
- (g) SEQ ID NOs: 36, 23, 6, and 21;
- (h) SEQ ID NOs: 37, 23, 6, and 21;
- (i) SEQ ID NOs: 38, 23, 6, and 21;



- (j) SEQ ID NOs: 39, 23, 6, and 21;
- (k) SEQ ID NOs: 40, 23, 6, and 21;
- (l) SEQ ID NOs: 41, 23, 6, and 21;
- (m) SEQ ID NOs: 42, 23, 6, and 21;
- (n) SEQ ID NOs: 43, 23, 6, and 21;
- (o) SEQ ID NOs: 44, 23, 6, and 21;
- (p) SEQ ID NOs: 45, 23, 6, and 21;
- (q) SEQ ID NOs: 46, 23, 6, and 21;
- (r) SEQ ID NOs: 47, 23, 6, and 21;
- (s) SEQ ID NOs: 48, 23, 6, and 21;
- (t) SEQ ID NOs: 49, 23, 6, and 21;
- (u) SEQ ID NOs: 50, 23, 6, and 21;
- (v) SEQ ID NOs: 51, 23, 6, and 21;
- (w) SEQ ID NOs: 52, 23, 6, and 21;
- (x) SEQ ID NOs: 53, 23, 6, and 21;
- (y) SEQ ID NOs: 54, 23, 6, and 21;
- (z) SEQ ID NOs: 55, 23, 6, and 21;
- (aa) SEQ ID NOs: 56, 23, 6, and 21; or
- (bb) SEQ ID NOs: 57, 23, 6, and 21.

Item 22. The virus particle of any one of the preceding items, wherein the virus particle comprises an S segment comprising a 5' untranslated region (UTR) that has at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, or that is preferably identical, to a sequence set forth in SEQ ID NO: 24, or a respective complementary sequence.

Item 23. The virus particle of any one of the preceding items, wherein the virus particle comprises an S segment comprising a 3' untranslated region (UTR) that has at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about

98% preferably at least about 99%, or that is preferably identical, to a sequence set forth in SEQ ID NO: 25, or a respective complementary sequence.

Item 24. The virus particle of any one of the preceding items, wherein the virus particle comprises an L segment comprising a 5' untranslated region (UTR) that has at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is identical, to a sequence set forth in SEQ ID NO: 26 or 28, or a respective complementary sequence.

Item 25. The virus particle of any one of the preceding items, wherein the virus particle comprises an L segment comprising a 3' untranslated region (UTR) that has at least about 70%, preferably at least about 75%, preferably at least about 80%, preferably at least about 85%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, sequence identity, or that is preferably identical, to the sequence set forth in SEQ ID NO: 27 or 29, or a respective complementary sequence.

Item 26. The virus particle of any one of the preceding items, wherein the virus particle comprises an S segment comprising a nucleic acid sequence having at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity to the sequence set forth in SEQ ID NO: 1 or 11.

Item 27. The virus particle of any one of the preceding items, wherein the virus particle comprises an L segment comprising a nucleic acid sequence having at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least

about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or that is preferably identical to the sequence shown in SEQ ID NOs: 2 or 15.

- Item 28. The virus particle of any one of the preceding items, wherein the virus particle has an increased capacity to enter a human tumor cell as compared to said reference virus particle.
- Item 29. The virus particle of any one of the preceding items, wherein the virus particle has an increased tropism for a human tumor cell as compared to said reference virus particle.
- Item 30. The virus particle of any one of the preceding items, wherein the virus particle is capable of entering a cell in an alpha dystroglycan-independent manner.
- Item 31. The virus particle of any one of the preceding items, wherein the virus particle is infectious.
- Item 32. The virus particle of any one of the preceding items, wherein the virus particle is replication competent.
- Item 33. The virus particle of any one of the preceding items, wherein the virus particle has a bi-segmented genome.
- Item 34. The virus particle of any one of the preceding items, wherein the virus particle is an arenavirus particle.
- Item 35. The virus particle of any one of the preceding items, wherein the virus particle is an LCMV particle.
- Item 36. The virus particle of any one of the item 1-34, wherein the virus particle is an arenavirus particle other than an LCMV particle that is pseudotyped with an LCMV GP.
- Item 37. The virus particle of any one of items 1-32, wherein the virus particle is a vesicular stomatitis virus (VSV) particle that is pseudotyped with an LCMV GP.
- Item 38. The virus particle of any one of items 1-32, wherein the virus particle is a Pichinde virus particle that is pseudotyped with an LCMV GP.
- Item 39. The virus particle of any one of items 1-32, wherein the virus particle is a particle of a virus other than an arenavirus.
- Item 40. The virus particle of any one of items 1-32, wherein the virus particle is a particle of a viral vaccination vector.
- Item 41. The virus particle of any one of items 1-34, wherein the virus particle does not comprise an ORF from an organism other than an LCMV.

- Item 42. An LCMV GP, wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue as defined in any one of items 1-12.
- Item 43. A nucleic acid molecule encoding a LCMV GP of item 42.
- Item 44. The nucleic acid molecule of item 43, wherein the nucleic acid molecule comprises a sequence that has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NOs: 58-85, or a respective complementary sequence.
- Item 45. A virus particle comprising a glycoprotein (GP) of an arenavirus and/or a nucleic acid encoding said GP, wherein the glycoprotein comprises at least one of the following amino acid residues:
- (a) at the position corresponding to Ser 102 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Asn residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
  - (b) at the position corresponding to Phe 122 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
  - (c) at the position corresponding to Phe 129 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Ser residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
  - (d) at the position corresponding to His 136 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Gln residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a His residue at said position;
  - (e) at the position corresponding to Asn 152 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Tyr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;

- (f) at the position corresponding to Ser 153 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Pro, Phe, or Tyr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
- (g) at the position corresponding to Asn 154 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Asp residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (h) at the position corresponding to His 155 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu or Tyr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (i) at the position corresponding to Lys 156 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Glu residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (j) at the position corresponding to Ala 211 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Thr residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises an Ala residue at said position;
- (k) at the position corresponding to Thr 217 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (l) at the position corresponding to Thr 218 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (m) at the position corresponding to Lys 256 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Arg residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;

- (n) at the position corresponding to Leu 260 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Phe or Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Leu residue at said position;
  - (o) at the position corresponding to Tyr 284 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a His residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Tyr residue at said position;
  - (p) at the position corresponding to Ala 328 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Ser residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ala residue at said position;
  - (q) at the position corresponding to Phe 332 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Leu residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
  - (r) at the position corresponding to Val 342 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably an Ala residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Val residue at said position;
  - (s) at the position corresponding to Arg 358 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a mutated amino acid residue, or preferably a Lys residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Arg residue at said position; and
  - (t) at the position corresponding to Lys 492 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ile residue, wherein the virus particle preferably has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position.
- Item 46. The virus particle of item 45, wherein said GP is a GP other than an LCMV GP.
- Item 47. The virus particle of item 45, wherein said at least one amino acid residue is at least one substitution of a native amino acid residue of the GP of said arenavirus.

- Item 48. A host cell comprising the nucleic acid molecule of item 43 or 44 or a cDNA of the genome of a virus particle of any one of items 1-41 and 45-47.
- Item 49. A method of producing a virus particle of any one of items 1-41 and 45-47 comprising cultivating the host cell of item 48 under conditions suitable for virus particle formation.
- Item 50. A pharmaceutical composition comprising a virus particle of any one of items 1-41, a GP of item 42, a nucleic acid molecule of item 43 or 44, or an arenavirus particle of any one of items 45-47.
- Item 51. A virus particle of any one of items 1-41, a GP of item 42, a nucleic acid molecule of item 43 or 44, or an arenavirus particle of any one of items 45-47, for use in therapy, preferably for use in the treatment of cancer.
- Item 52. A use of a virus particle of any one of items 1-41, a GP of item 42, a nucleic acid molecule of item 43 or 44, or an arenavirus particle of any one of items 45-47, for the manufacture of a medicament, wherein the medicament is preferably for the treatment of cancer.
- Item 53. A method of treating a disease comprising administering to a subject in need thereof an effective amount of a virus particle of any one of items 1-41, a GP of item 42, a nucleic acid molecule of item 43 or 44, or an arenavirus particle of any one of items 45-47, wherein the disease is preferably cancer.
- Item 54. A method of producing a virus particle having an increased capacity to enter a tumor cell, comprising
- (i) Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
    - (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
    - (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;

- (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha$ 3 as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498; and
- (ii) Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
- (iii) Optionally assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell, preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a value, wherein the reference value is preferably at least as high or higher than the value that is obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

Item 55. A method of producing a virus particle having an increased tropism for a tumor cell, comprising

- (i) Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
  - (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;



- (b) Strands  $\beta 3$ ,  $\beta 4$ , and/or  $\beta 5$  as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
- (c) Helix  $\alpha 1$  and/or  $\alpha 2$  as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha 3$  as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha 4$ ,  $\alpha 5$  domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498; and
- (ii) Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
- (iii) Optionally assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell and/or a non-tumor cell, preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a reference value, wherein the reference value is preferably at least as high or higher than the value that is obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

Item 56. The method of items 54 or 55, wherein the virus particle has an increased tropism for at least one of the following tumor cells: lung tumor cells, such as H1975 or A549, LLC, TC-1, gastrointestinal tumor cells, such as Gist-T1, melanoma cells, such as MaMel86a, MaMel51, A375, B16F10, or RPMI-7951, pancreatic tumor cells, such as 511950, 60590, 511950R, or 60590R, thyroid tumor cells, such as 8305C or C643, sarcoma cells, such as Gist-T1, breast tumor cells, such as HCC1954, cervical tumor cells, such as HeLa, liver

tumor cells, such as HepG2, colon tumor cells, such as MC38, Sw620, or Sw480, neuroblastoma cells, such as SK-N-BE(2), and/or prostate tumor cells, such as TrampC2.

Item 57. The method of any one of items 54-56, wherein the mutated LCMV strain WE glycoprotein is a GP as defined in any one of items 1-12.

Item 58. A virus particle having an increased capacity to enter a tumor cell or having an increased tropism for a tumor cell obtainable by the method of any one of items 54-57.

## EXAMPLES

### **Example 1: The fast evolution platform identifies missense mutations promoting tumor tropism**

[0179] The ambisense RNA genome of arenaviruses consists of an approximately 3.5kb S-segment encoding the pre-glycoprotein polyprotein complex (GPC) and the nucleoprotein (NP), and a 7.2kb L-segment encoding the RNA-dependent RNA polymerase (RdRP) and the Z-protein. During replication, the viral polymerase will generate, with a failure rate of  $10^{-5}$ , a variety of genetically closely related progeny called quasispecies. These quasispecies will only prevail if they are replication competent and outcompete their counterparts. Usually, viral strains fitting best to their environment will exhibit best replication ('survival of the fittest'). Therefore, we hypothesized that passaging of the arenavirus LCMV-WE on tumor cells will lead to enrichment of mutations, which accelerate their propagation in cancer cells.

[0180] In an initial approach, LCMV-WE was propagated for 7, 13, 42 or 52 passages on human or mouse cancer cells with or without 5-Fluorouracil (5-FU). We then standardized the process by passaging the virus 10-12 times on 7 human and 8 mouse tumor cell lines, each in the presence or absence of the anti-viral mutagen 5FU, which limits viral replication by further enhancing the mutation rate. Each combination was set up in 4 to 5 parallel cultures to test, if mutations occur completely at random with low selection bias (different mutants in parallel cultures) or selection occurs, with specific mutants preferentially in one or several specific tumor cell lines (identical mutations in parallel cultures). Virus obtained from the so-called "fast-evolution platform (FEP)" was reverse transcribed and the cDNA of the S-Segment was sequenced. We identified 6 missense mutations (5 AA positions) in the stable signal peptide (SSP), 44 missense mutations (40 AA positions) in GP1 and 19 missense mutations (18 AA positions) in GP2 (Table 1). The location of these 65 AA positions (74 missense mutations) of LCMV-GPC might have impact on virus propagation in cancer cells. Several of these mutations occurred more than one time in the same

tumor cell line, or in several other tumor cell lines, indicating that missense mutations of certain amino acids are more, critical than others, for viral entry and propagation (Fig 1A-C).

**[0181]** Next, we tested whether virus of primary tumor cell cultures will keep the acquired mutation when further passaged in other tumor cell lines. Accordingly, a long-term passaged (52 passages) mutant virus, LCMV-WE subtype P52 (I181M, R185W) was further propagated on different tumor cell lines for 23-55 additional passages. Both mutations remained stable in the p52 viral subtype (Figure 2). On one occasion, in the presence of 5-FU, the codon of amino acid 181 changed by a single nucleotide polymorphism to M181V, a forward rather than a back mutation (M181I). During the course of 23 to 55 passages, the p52 viruses gained additional mutations on the five different tumor cell lines. Of 16 viral mutations observed, 13 seem to be “private”, since they established only in one tumor cell line, while the virus gathered an additional “public” mutation on each of the five tumor cell lines either in the absence and/or presence of 5-FU. In the A375 tumor cell line the p52 virus carrying a genetic background (H136, S153, L260, H155), known to be poorly DAG binding, gained the mutation H155Y, which converts the P52 mutant to a subtype, binding  $\alpha$ -DG with high affinity. When the p52 virus was propagated on HCC1954, A549 and SW620 tumor cells, P52 gained the mutation S153P, indicating that the genotype (H136, S153, L260, H155) with poorly DAG binding capacity may further reduce DAG binding by switching from S153 to P153. In the SW620 cell line and absence of 5-FU the P52 virus gained two mutations, S153P and H155Y resulting in the genotype (H136, P153, L260, Y155), in this case Y155 (high DAG-binding) is not expected to compensate the loss of S153 to bind  $\alpha$ -DG with high affinity. The mutants T217I in the tumor cell line RPMI-7951 and T217S together with S153P in the cell line SW620 are, expected to be of poor or diminished DAG binding, since T217I is not known to directly contribute to DAG binding.

**[0182]** Next, we compared the accumulation of viral mutations of LCMV-WE (A211) to the subtype YF13 (T211). The acquired mutation T211 in YF13 was stably expressed in 4/4 parallel cultures, each with or without 5-FU (Figure 3). Upon passaging YF13 gained further mutations (Figure 3). The mutation repertoire of 211T positive virus was more selective than the LCMV-WE 211A virus, especially in the presence of 5-FU. When a mixture of six different viruses (WE, p42, p52, Y18, YF13, FP7) were, passaged on the C643 cell line, the virus (211T carrier) outcompetes the 211T non-carrier and gained additional mutations (Figure 3).

**Example 2: The fast evolution platform identifies mutational hot spots for tumor-tropism**

[0183] Next, we evaluated which regions in the LCMV-GPC show the highest mutation frequency and might therefore be of special importance for the tumor tropism. 15 domains within the LCMV-GP were analyzed (Figure 4A). In the Strand  $\beta 7$  domain we identified only one mutated out of 18 AS positions while in huge contrast the Loop 1 showed 6 mutated AS out of 10 AS (Figure 4A and Figure 5). This clearly demonstrates that some regions within the LCMV-GP are more important to determine the tumor tropism than other regions. To identify highly mutated areas, we compared the mutation frequencies of different domains and found that 10.3% and 15.4% as the highest value of the low mutation domain group were most significant, suggesting a threshold between low and high mutation rates at 12.85% (Figure 4B+C). Moreover, the significance of the mutation frequency was analyzed (Figure 5). Beside the Loop1 and Loop 3 the domains Strand  $\beta 1$  N terminal, Strand  $\beta 3$   $\beta 4$   $\beta 5$ , the N-Helix, Helix  $\alpha 1$   $\alpha 2$ , the  $\alpha 4$ ,  $\alpha 5$  domain, the TM cytoplasmic domain, the H1,H2 domain showed a significant enhancement of mutations (Figure 1a). In conclusion, we identified several structural domains which show significant mutation frequencies upon propagation in tumor cells. Several of the identified regions are believed to interact with the host membrane and thereby determine entry of the LCMV.

**Example 3: LCMV GP mutants trigger enhanced viral entry into tumor cells**

[0184] Viral entry is triggered by the interaction of the LCMV glycoprotein with host cell proteins and membranes. While LCMV-GP utilize glycosylated  $\alpha$ -Dystroglycan (DAG) as an entry receptor, other receptors have been described. Several tumor cells (including those of the FEP) do not necessarily express high levels of DAG. Therefore, it is tempting to speculate that viral mutants, selected in the FEP improve entry of virus into cancer cells. Consistently, amino acid positions, which are known to trigger binding to DAG and dimerization of LCMV-GP are heavily mutated in viruses from the FEP (Figure 6). In turn, amino acids from the fusion peptide/loop region were not mutated (Figure 6). To validate our hypothesis that the mutated regions affect viral entry into tumor cells we quantified entry of LCMV in A549 cells. Since, recombinant chimeric virus exhibit attenuated viral replication we used a recombinant system carrying the S segment of the WE strain and the L segment of the LCMV clone13 strain. 14 positions in 7 regions were selected and recombinant chimeric viruses, which carry the mutated S segment (carrying the LCMV-GP and NP), and the L-segment from LCMV strain clone 13 were generated. A549 cells were exposed to rec LCMV-mutants and entry was stopped at different time points using Monensin. All mutants tested showed accelerated entry into the human tumor cell line A549 (Figure 7 A&B). Next, we wondered whether other amino acids in a mutated position similarly

can accelerate entry into tumor cells. In the fast evolution platform, the polar and neutral serine was mutated to a hydrophobic proline. To analyze this position further we generated mutations which expressed the hydrophobic phenylalanine or the neutral and polar tyrosine. Both amino acids accelerated the entry into A459 cells (Figure 7 C). The neutral and polar amino acid tyrosine at position 155 accelerated entry into A549 cells similar to the hydrophobic leucine (in exchange to the basic histidine, Figure 7C). From these data we conclude that also other amino acids than the mutated one identified in the FEP can accelerate entry into tumor cells. Next, we wondered whether also other positions within the identified regions, which were not detected in the FEP could similarly enhance tumor cell entry. To do so, we have chosen 1 mutation in the Loop 1 region and analyzed the virus carrying this mutation in the entry assay. Indeed, the virus showed significantly enhanced entry in the A549 tumor cells (Figure 7D). Together we concluded that entry of virus into cancer cells was one major mechanism which led to selection of mutant viruses in the fast evolution platform.

**Example 4: FEP identified mutations include mutations promoting specific tumor cell replication**

[0185] While we identified 19 mutations that showed accelerated entry into A549 cells, only the mutations 102, 153 and 260 initially occurred in A549 cell passages. The other mutations were obtained from passaging of different cell lines. This suggests that a proportion of the identified mutations accelerate entry of virus in several cancer cells. To investigate whether these mutations exhibit tumor cell tropism, 20 recombinant LCMV strains carrying single mutations were generated. The viral entry was tested on six very diverse human cancer cell types and three healthy cell types. As cancer cells we selected cell lines from sarcoma, lung cancer and melanoma. As healthy cells we have chosen neurons, myotubes and human myoblasts. Almost all of the tested mutations showed accelerated propagation in at least one of the tested cell lines (Figure 8a). Several of the tested mutations showed accelerated propagation in a range of cancer cells (Figure 8a), while some of the mutations showed only enhanced replication in one tumor cell line (Figure 8a). To get insights into the broadness of viral propagation we plotted the infection rate of H1975 and MaMel86a cells against the other tested tumor cell lines (Figure 8b). Interestingly most of the mutations accelerated propagation in several cell types (Figure 8b).

[0186] As expected, the two lung cell lines showed a very similar pattern of mutations which accelerated virus propagation (A459 versus H1975, Figure 8b). But also non-related tumor cell lines showed a similar sensitivity to mutations (Figure 8b). Spider blots showing the factor of acceleration revealed that most of the mutations tested are from a public type, meaning that they

accelerate propagation in most of the tested tumor cell lines (Figure 8c). Interestingly, some of the tested mutations reduced the propagation in tumor and healthy cells. We consider two possible explanations. First, these mutations might still accelerate the entry into tumor cells, but then limited the virus replication. Second, the mutations might give another selection advantage to the virus. In conclusion, our data indicate that mutations in different regions within the LCMV-GP can modulate tumor cell entry, without affecting entry into healthy cells.

#### **Example 5: Combination of mutations can act synergistically**

[0187] To investigate whether mutations from different regions could be combined, we generated recombinant viruses carrying several mutations in combination. The combination of the mutations I181M, R185W and K492I exhibited strong infection of several tumor cell lines (Figure 9A). Next, we wondered whether further combination of mutations, which were identified with the FEP or already reported to affect cell tropism, could improve tumor cell specific tropism. We generated 15 recombinant LCMV with combinations of mutations and tested them on a panel of four human and four murine cancer cell lines. As expected, most of the viruses showed accelerated replication on the human cancer cell line A549 (Figure 9A&B). Notably, a proportion of viruses appeared to have a broad replication capacity, while others showed a specific tropism (Figure 9A&B). Accordingly, we identified the different mutations into four groups: broad type, human type, murine type and cell-specific type. The broad type viruses showed accelerated replication in all eight tested cell types (Figure 9B). The 'human cancer type' showed accelerated replication only in human, but not in murine cancer cells (Figure 9B). The 'murine cancer cell type' showed stronger replication in murine cancer cells than in human cancer cells (Figure 9B) and the cell type specific viruses show very diverse propagation in different cell types (Figure 9B). While we did not do a site by site comparison of different mutations we consider by these data that the mutations 256R and 358K correlate with a higher human specific tropism while the mutation 153F correlates with more murine specific appearance. The mutation 156E appears to trigger a cell type specific tropism. The mutations 122L, 129S, 136Q 260F and 490E amplify tumor cell specific propagation. In conclusion, we identified mutations, which can be combined for additional effects. Depending on the type of combination the virus shows a tropism to human cancer, murine cancer or specific cell types.

#### **Example 6: Entry into tumor cells is independent from aDG**

[0188] We found that the identified mutations accelerate entry of virus in several tumor cells, including A549 cells. Since LCMV-GP can bind glycosylated aDG as entry receptor, we next

analyzed entry in A549 cells WT and aDG knockout cells. Recombinant chimeric viruses with absence (WT) or presence (MUT) of mutations GP-F122L, GP-S153P and GP-I181M-R185W-K492I were incubated with aDG deficient or competent cells. As expected, all viruses showed accelerated entry in A549 cells (Figure 10). While virus GP-F122L entry was in part dependent aDG, GP-S153P and GP-I181M-R185W-K492I entered A549 cells independently of aDG (Figure 10). Notably, the WT virus strain used (155H) did show little aDG dependent entry into tumor cells, which is consistent with reports showing that 155Y is mediating high affinity towards aDG (Figure 10). This suggests that tumor cell specific entry is not mediated by affinity towards aDG.

#### **Example 7: Virus with combined mutations shows accelerated antitumoral activity**

[0189] Next, we aim to analyze whether the specific entry into tumor cells can be beneficial for tumor therapy. First, we analyzed the viral distribution of different tumor-tropic strains. The strains comprised the following mutations in the GP:

G122h3.r1 = 122L, 136Q, 153P, 181M, 185W, 492I  
 G122h5.r1 = 122L, 136Q, 153P, 181M, 185W  
 G153h7 = 122F, 136H, 153P, 181M, 185W, 492I  
 G181h7 = 122F, 136H, 153S, 181M, 185W, 492I  
 G153h3.r2 = 153P, 181M, 185W, 260L, 492I  
 G181h2.r3 = 153S, 181M, 185W, 260L, 492I  
 G181h7.r2 = 153S, 181M, 185W, 260F, 492I  
 G122h3.r1 = 122L, 136Q, 153P, 181M, 185W, 260L, 492I  
 G153h7.r1 = 122F, 136H, 153P, 181M, 185W, 260L, 492I

[0190] As expected, the new strains showed hardly replication in healthy mouse tissue. Replication in tumor cells was enhanced. Next, we analyzed whether this superior viral distribution influenced antitumoral activity of LCMV. To do so we infected MC38-OVA carrying mice with different tumor-tropic strains and then analyzed tumor growth. Indeed, all tested tumor tropic strains showed strong antitumoral activity (Figure 11A-B). Mechanistically, we suggested an enhanced inflammatory response within the tumor, as we detected accelerated levels of cytokines seven days after treatment (Figure 11A). In conclusion, the mutated viruses are proprietary over the WT strain, which makes them potentially good candidates for further development.

**Example 8: Mutations identified with LCMV-WE are similarly active in other viruses expressing the LCMV-GP**

[0191] We found that the LCMV-GP with our detected tumor-tropic mutations shows highly enhanced tumor cell entry and is therefore superior for tumor therapy. Next, we wondered whether these mutations can be also translated to other arenaviruses. To do so we introduced some of the identified mutations on the glycoprotein of the Lunk virus (LUNV) and these glycoproteins were expressed on the LCMV-chimeric background virus (the viruses comprised the L segment of LCMV clone 13 and a S segment comprising GP from Lunk virus and NP from LCMV strain WE). The Mutations of the LCMV-GP positions 155, 156 and 256 were introduced into the glycoprotein of the arenavirus Lunk. These corresponded to the positions 152, 153 and 253. Mutations there were introduced were Y152H, K153E, and K253R. The capacity to replicate into different cell lines was analyzed in the infectivity assay. These viruses were analyzed in the entry assay in A549 cells. Indeed, the mutations in these glycoproteins similarly enhanced entry into A549 cells (Fig 12). In conclusion, we found that the mutations can be transferred to other arenavirus glycoproteins. Additionally, a mutated glycoprotein can enhance tumor entry also if it is expressed on other backbone viruses.

**Example 9: Discussion**

[0192] In this study the inventors of the present application show by using a fast evolution platform, that mutations can be identified to induce tumor cell specific tropism. Several point mutations and structural regions within the LCMV-GP were identified, which trigger tumor cell specific entry. The mutations can be combined and act synergistically in terms of propagation in tumor cells. The use of mutated viruses for tumor therapy was proprietary due to accelerated site specific replication and immune activation but limited propagation in healthy tissue.

[0193] While it was found that the increased entry into tumor cells was not dependent on aDG, the exact molecular entry mechanism has not been identified. Interestingly, it was found that several mutations accelerated propagation not only in human, but also in murine cancer cells. Propagation of virus in human healthy cells or murine healthy tissue (*in vivo*) was limited. This suggests that tumors in both species must overexpress this receptor.

[0194] In conclusion the inventors of the present application adapted the LCMV towards tumor. This led to viruses with accelerated replication in cancer cells, limited replication in healthy organs and enhanced antitumoral activity.



**Example 10: Material and Methods**

**[0195] A. Mice:** All used mice were maintained on the C57BL/6 background. All mice were maintained in single ventilated cages, with the authorization of the Veterinärämte Nordrhein Westfalen (Düsseldorf, Germany) in accordance with the German law for animal protection or institutional guidelines of the Ontario Cancer Institute.

**[0196] B. Entry assay:** To determine the capacity of a certain virus to enter the cells, an entry assay was performed. In this assay cells (i.e., A459 cells, directly after harvesting) are preincubated with virus (multiplicity of infection of 0.1) at 4°C (in 96 well plates flat bottom in 200µL of the according cell culture medium) so that the virus can bind to the membrane of the cells. Because entry of LCMV is an active process virus cannot enter the cells at these conditions. After the incubation of one hour most of the virus is supposed to bind to the cells and the cells are warmed up to 37°C. At different time points after heating up the cells to 37°C (i.e., 0min, 20min, 60min or 180min) Monensin is added the cultures, which inhibits the further entry process of the virus. Cells are then incubated for further 16 hours. This incubation time gives the virus enough time to replicate its RNA and to produce virus proteins. After the incubation time, virus protein is determined in each cell by staining the cells with an anti-LCMV-NP antibody (Clon VL4) and analysis in the flow cytometer. To do so, cells are harvested with Trypsin/EDTA and then fixed for 10minutes with 2%Formalin and then washed two times with FACS Buffer (PBS, 1%FCS, 5mM EDTA and 0,1% Sodium acid) with 0,01% Saponin added. After washing cells are stained with anti-LCMV-NP (VL4 house made) for 30minutes. After additional two washes the primary antibody is detected with a fluorescently labeled anti-rat antibody. In this assay replication and protein production will only happen in cells, which were infected before Monensin was added. Cells in which entry process did not happen before the addition of Monensin, are not infected and therefore will not produce virus RNA and proteins. Therefore, the capacity to enter a cell is a direct correlate of the percentage of infected cells in this assay.

**[0197] C. Infectivity assay:** The infectivity assay determines the capacity of a virus to enter the cell, replicate in the cell and produce virus proteins. In this assay, cells (i.e., A459 cells, MaMel86a cells, MaMel51 cells, directly after harvesting) are incubated with virus (multiplicity of infection of 0.01 to 0.1) at 37°C for 16 hours (in 96 well plates flat bottom in 200µL of the according cell culture medium). In this incubation time the virus is propagating in the cell culture. Virus particles, which are produced within the cell culture can infect new cells. After the incubation time, virus protein is determined in each cell by staining the cells with an anti-LCMV-NP antibody (Clone VL4) and analysis in the flow cytometer. To do so, cells are harvested with Trypsin/EDTA

and then fixed for 10 minutes with 2% Formalin and then washed two times with FACS Buffer (PBS, 1% FCS, 5mM EDTA and 0,1% Sodium acid) with 0,01% Saponin added. After washing cells are stained with anti-LCMV-NP (VL4 house made) for 30 minutes. After additional two washes the primary antibody is detected with a fluorescently labeled anti-rat antibody. In this assay, the percentage of infected cells is a direct correlate of the capacity of the virus to propagate in a certain cell culture. If assuming that the entry into a cell is a rate limiting step, then it might also be a correlate with entry capacity.

**[0198] D. Tumor growth experiment:** For transplantation of tumors  $10^6$  murine colon carcinoma MC38-OVA (MC38-OVA) cells were injected in 100  $\mu$ l PBS subcutaneous. Tumor growth was monitored every second day.

**[0199] E. Statistical Analysis:** Mean values were compared using an unpaired Student's two-tailed t-test. Data are expressed as means  $\pm$  SEM. Student's t-test was used to detect significant differences between groups. Chi-Quadrat test was additionally used. Survival was compared with log-rank (Mantel-Cox) tests. The level of statistical significance was set at  $P < 0.05$ .

**[0200] F. Cells:** 511950 and 60590 are primary tumor cells isolated from a transgenic murine pancreatic carcinoma. 511950R and 60590R originate from 511950 and 60590 under treatment of trametinib. 8305C (CVCL\_1053) is anaplastic thyroid carcinoma derived. A549 (CVCL\_0023) is a human lung adenocarcinoma cell line. A375 (CRL-1619) malignant melanoma cells. B16F10 (CVCL\_0159) is a murine melanoma cell line. C643 (CVCL\_5969) is a human anaplastic thyroid carcinoma cell line. Gist-T1 cells are primary sarcoma cells. HCC1954 (CVCL\_1259) is a breast ductal carcinoma cell line. H1975 CVCL\_1511, ATCC, CRL-5908) is a human lung carcinoma cell line. HeLa (CVCL\_0030) is derived from a papillomavirus-related endocervical adenocarcinoma. HepG2 (CVCL\_0027) is derived from a hepatoblastoma. HEK293FT human embryonic kidney cells. LLC (CVCL\_4358) Lewis lung carcinoma (mouse). MC38 (CVCL\_B288) is a murine mouse colon adenocarcinoma cell line. MOPC cells are murine oropharyngeal cells. MC57 (CVCL\_4985) is a murine fibroblast cell line in which the arenavirus LCMV can replicate well. RPMI-7951 cells (CVCL\_1666) are human melanoma cells. SK-N-BE(2) (CRL-2271) neuroblastoma cell line. Sw620 (CVCL\_0547) are human colon adenocarcinoma cells. Sw480 (CVCL\_0546) is derived from a colon adenocarcinoma. TC-1 (CVCL-4699) mouse lung cancer. TrampC2 is a murine adenocarcinoma cell line (CVCL\_3615). UKE-Mel-51 (=MaMel51), Mel-86a (=MaMel86a), 118b, 118c are primary tumor cells isolated from a metastasis of a human melanoma.

[0201] Embodiments illustratively described herein may suitably be practiced in the absence of any element or elements, limitation or limitations, not specifically disclosed herein. Thus, the terms and expressions employed herein have been used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present embodiments have been specifically disclosed by preferred embodiments and optional features, modification and variations thereof may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention. Each of the narrower species and subgeneric groupings falling within the generic disclosure also forms part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. In addition, where features are described in terms of Markush groups, those skilled in the art will recognize that the disclosure is also thereby described in terms of any individual member or subgroup of members of the Markush group.

[0202] Equivalents: Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

[0203] It should be understood that this invention is not limited to the particular methodology, protocols, material, reagents, and substances, etc., described herein and as such can vary. The terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention, which is defined solely by the claims.

[0204] All publications cited throughout the text of this specification (including all patents, patent applications, scientific publications, manufacturer's specifications, instructions, etc.) are hereby incorporated by reference in their entirety. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention. To the extent the material incorporated by reference contradicts or is inconsistent with this specification, the specification will supersede any such material.

[0205] Further embodiments will become apparent from the following claims.

## SEQUENCES

SEQ ID NO: 1: LCMV WE S-Segment.

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SEQ ID NO: 2: LCMV WE L-Segment.

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SEQ ID NO: 3: LCMV WE GPC.

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ACAACAGTAAATTCTCTGATTTCCGATCAGCTGTTGATGAGGAATCATCTAAGAGATCTAATGGGGGTACCATACTGTAATTACTC  
AAAGTCTGTGATCTGGAACATGCTAAGACTGGTGAAGTGTACCCAGTGTGCTGCTACTAATGGCTCCTACTTGAATG  
AGACCACTTTAGTGATCAAATCGAACAAGAAGCAGATAACATGATCACAGAGATGTTGAGGAAGGACTACATAAAAAGACAAGGG  
AGTACTCCTTTAGCCTTAATGGATCTTTTGTATGTTTTCAACATCAGCATATCTAATCAGCATCTTTCTGCATCTTTGTGAAGATACC  
AACACATAGACACATAAAGGGCGGTTCATGTCCAAAGCCACACCGCTTGACCAACAAGGGGATCTGTAGTTGTTGGTGCATTCAAGG  
TGCCTGGTGTAAAACTATCTGGAAAAGACGCTGA

SEQ ID NO: 4: LCMV WE GPC.

MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSANNSHHYISMSSGLELFTTNDISILNHNFCNLTSAFNKKTFDHTLMSIVSSHLHSIRGNSNHNKAVSCDFNNGITIQYNL  
SFDQPSAISQCRTPRGRVLDMFRFAFGGKYMRSGWGWAGSDGKTTWCSSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRLAGTFMTLSDSSGVENPGGYCLTKWMLAAELKCFGNTAVAKCNVNHDEEFCMDRLRIDYNKAALSFKQDVESALHVPK  
TTVNSLISDQLLMRNLRLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSDQIEQEADNMI TEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRIKGGSCPKPHRLTNKGICSCGAFKVPVKTWKRR

SEQ ID NO: 5: LCMV WE NP.

ATGTCTTTGTCCAAAGAAGTCAAAAGCTTTTCAGTGGACACAGGCCTTGAGGAGGGAGTTGCAGAGTTTTACATCAGATGTAAAGGC  
TGCCGTCATCAAGGACGCAACCAGTCTTCTAAATGGGTGGACTTTTCTGAAGTCAGCAACGTTTCAGAGGATCATGAGAAAGGAAA  
GGAGGGATGATAAAGACTTGCAGAGACTCAGGAGTCTTAACSDGKTTWCSSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
AATGTTCTGAAAGTGGGAAGACTTAGTGCAGAGGAATGATGACCTTGCAGCTGATCTTGAGAAGCTGAAGGCCAAAATTTATGAG  
AACTGAGAGGCCCTCAAGCTTCTGGAGTCTACATGGGAAATTTGACAGCACAACAACCTTGATCAAAGATCCCAAATCTGCAAATGG  
TTGGGATGAGAAGACCTCAGCAGGGTGCAAGTGGTGTAGTAAGGGTTTGGGATGTGAAGGACTCATCACTTCTGAACAATCAGTTC  
GGCACAATGCAAGCTGACAATGGCTTGCATGGCAAAACAGTCACAGACCCCACTCAATGATGTTGTGCAGGCCTCACAGACCT  
TGGCTTACTTTACACAGTCAAATACCCGAATCTCAGTGATCTTGAAGGCTAAAGGATAAACACCCAGTCTTGGGGGTCACTACTG  
AACAGCAATCTAGTATCAATATCTCTGGTTATAATTTTCAGTCTTGGTGCAGCTGTGAAAGCGGGGGCAGCTCTGCTAGATGGAGGG  
AACATGCTGGAATCTATCTTGATCAAACCGAGCAACAGTGAGGATCTCTCTAAAAGCAGTCTCGGGGCCAAGAAGAACTCAACAT  
GTTTGTCTCAGATCAAGTTGGAGATAGAAATCCCTATGAAAACATCCTTTATAAAGTCTGTCTTTCAGGTGAAGGATGGCCATACA  
TAGCCTGTAGAACGTCAGTTGTGGGGAGAGCATGGGAGAACACACAATGATCTCACAAATGAAAACTTGTGCCAACTCATCT  
AGGCCAGTGCTGGAGCAGCAGGCCCACTCAGGTGGGCTTGAGTTACAGTCAGACAATGCTGTGAAAGACTTGATGGAGGGAT  
TGATCCCAATGCTCCACATGGATTGACATTGAGGGCAGGTTCAATGATCCAGTGGAGATAGCAATATTTCAACCACAAAATGGGC  
AATTACATATTTTACAGGGAACCTACGGACCAGAAGCAATTCAGCAGGACTCAAAGTATTCACACGGCATGGATCTTGCTGAT  
CTCTTCAATGCACAGCCTGGGCTGACCTCATCAGTTATAGGTGCTCTCCACAAAGGGATGGTTTTGAGCTGTCAAGGTTCTGATGA  
CATCAGAAAGCTTCTGGACTCACAAAATAGAAGGGACATAAACTCATTGATGTGAGATGACCAAGGAGGCCTCAAGAGAATATG  
AAGATAAAGTGTGGGACAAATATGGCTGGCTATGCAAAATGCACACTGGGGTAGTGAGAGACAAAAGAAGAAAGAGATCACCCCA  
CACTGTGCACTCATGGACTGCATCATTTTTTGAGAGTGCTTCCAAGGCAAGACTCCCTGATCTAAAAACCGTTCAACATCCTGCC  
ACATGATTTAATCTTCAGAGGACCAATGTTGTGACACTCTAA

SEQ ID NO: 6: LCMV WE NP.

MSLSKEVKSFWTQALRRELQSFTSDVKAIVIKDATSLNLGLDFSEVSNVQIRIMRKERRDDKDLQRLRLSNQTVHSLVDLKDSTSKK  
NVLKVGRLSAEELMTLAADLEKLKAKIMRTERPQASGVYMGNLTAQQLDQRSQILQVMGMRPQQGASGVVRVWDVKDSSLNNQF  
GTMPSLTMACMAKQSTPLNDVVQALTDLGLLYTVKYPNLSDLERLKDHPVLGVI TEQQSSINISGYNFSLGAAVKAGAAALLDGG  
NMLESILIKPSNSEDLLKAVLGAKKKLNMFVSDQVGRNYPENILYKVLCSGEGWPYIACRTSVVGRAWENTTIDLTNEKLVANSS  
RPVPGAAGPPQVGLSYSQTMLLKDLMGGIDPNAPTWIDIEGRFNDPVEIAIFQPQNGQFIHFYREPTDQKQKQDSKYSHGMDLAD  
LFNAQPGLTSSVIGALPQGMVLSQGSDDIRKLLDSQNRDIKLIDVEMTKEASREYEDKVWDKYGWLCMKMTGVVRDKKKKEITP  
HCALMDCIIFESASKARLPDLKTVHNI LPHDLIFRPNVVTL

SEQ ID NO: 7: LCMV WE ZP.

ATGGGCCAAGGCAAGTCCAAAGAAGAAAGGGACACCAGCAATACAGGCAGAGCAGAGCTTTTGCCAGACACCACCTATCTTGGTCC  
TCTAAATTGTAAATCATGTTGGCAGAAATTTGACAGCTTGGTTAGATGCCATGACCACTATCTTTGCAGACACTGCTGTAATCTCT  
TGCTGTCACTTTCCGACAGATGCTCTCTGTAAGTATCCACTGCCAACCAAACCTGAAGGTGTCAACAGTCCCAAGCTCCCCACCT  
CCCTATGAGGAGTGA

SEQ ID NO: 8: LCMV WE ZP.

MGQGKSKEERDTSNTGRAELLPDITYLGPLNCKSCWQKFDLSVRCHDHYLCRHCLNLLSVSDRCP LCKYPLPTKLKVSTVPSSPP  
PYEE

SEQ ID NO: 9: LCMV WE LP.

ATGGATGAACTATTTCAGATTTGAGAGAGTTGTGTCTAAATTACATAGAACAGGACGAGAGGCTGTCAAGGCAAAACCTCAACTT  
CCTGGGACAAAAGAGAACCCAGAATGGTGTCTAATTGAGGGACTCAAATTGTTATCACGCTGTATAGAGATAGACAGTGCAGACAAAA  
GTGGTGCATACACAAACCAGATGACAAATCTGTTGAAACAATCTAATAGACTCTGGGATTGTGTGTCAGGACTGCCACTCATC  
ATCCCTGATGGTTATAAGTTGATTGACAAATCCCTTATCTTCTGTAATGTTTTGTTAGAAAGCACAGCTAGTTTGAAGAGAA  
GTTTCATTGAGGACCAACAACCTAGCATCAAGAGAGATCTGCTGTGCAAGGCATCACAGTGGTCCAAATAGTGATGGTTC  
GTTGTGATTATGATAACAGTTTCATGCCAGAATGGGTGAATTTTAAAGTTCAGAGACCTCCTATTTAAACCTCCTGGAGTATCTAGT

CAAGATGAGAAAGTTTTTGAGGAGTCTGAATACTTCAGGCTCTGTGAGTCTCTTAAGACCACTGTTGACAAACGTTCCGGCATGGA  
CTCAATGAAAATTTTGAAAGACGCAAGATCATTTTCATAACGATGAGATTATGAAAATGTGCCACGATGGTGTCAACCCCAACATGA  
GTTGCGATGATGTGCTCTTTGGCATAAATTCCTTTTGGCAGGTTTAGGAGGGACCTGTTAAATGGGAACTCAAAGGAATTTTC  
CAAAGGTCAGCCCTGGGGGCTTAATCAAGGAATCTCTGAACCTTATGAAACCTTACTGATAATGATGACATATTAATGTTGAG  
CAAAGAGGCAGTTGAATCCTGCCCCCTTAATGAGGTTCAATACAGCAGAGACCCATGGGCATGAGAGAGGAAGCGATGCTAACACTG  
AGTATGAAAGGCTACTCTCTATGTTGAACAAGGTGAAAAGTTTAAATTTATTAACACTAGAAGGAGACAGCTGCTGAACCTTAGAT  
GTCTTATGTCTTTCTTCACTTATTAAGCAGTCAATTTCCAAAGGTTTGGAAAATGATAAACATTGGGTTGGTTGTGTCTACAGTAG  
TGTGAATGATAGGCTTGTGAGCCTTCAAAGTACCAAGAAGAATTCATGAGACTTTTGAAGAACAAGAAAATCAAGAGTGCACA  
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AGTTTTGAGCATTACGGACTATCAGAATGCCCTCGTGCAAGAATGCCATATACCATTGTCTGAATTTGAGAAGCTTTATGAGAGCCGG  
GACTCATCCTGTAATGCATTACACAAAATTTGAAGATTACACTTTCCAGCCTAACATAGAGCAATTGAGGGGTTTACAGAGTTTGA  
GAAAAGTGTCACTGTTTGGTCTTAACAAACAGCATCAAAACAAGCTCAGTTGCAAGGTTGAGACAGAACCCTGGGCTGCT  
GTGAGATATCAAGTGGTGGAGTGCAAGAGGTGTTTGGCCAGATAATAAACTGGATTCCGAAGAGTATCATCTACTATATCAGAA  
AACTGGAGAATCATCGAGGTGTTATTCATACAAGGTCCGGATGTCTGATTGCTTTTACGAGATCCAAAAGGTTCTTTT  
TACCAATTTTTTCAGATGAGGTGTTGCACAAACATGATAGACACAATGATTTCATGGATTAGGTCATGCCCTGACTTAAAGATCTT  
CTTATTGACATTGAGACTGCATAAGGACATTGATCCTACTGATGCTCAGCAACCAACAAAGAGAAAATCAAAGCAGGTTCAA  
TATTAGGTATTAGTGATGCCATCGTCTCAGACTTTTCATCGACCTCATTAATGGATAAGTTGAAGGAGGATCTAATCACACCTG  
CCGAGAAAGTGGTGACAGGCTGCTTCGGTTTTGATTAGGACAATTTTTGGTACTGGTGAAAAGGTGTTATTGAGTGCAAAAATTC  
AAGTTTATGTTGAATGTGTACATCTGTGTCATTTGATCACAAGGAGACCCCTGATAGATTGACAGATCAGATAAAATGTTTGA  
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GTCTCAAAGCTGTCTCTAGATTAGTCATCGGTTCCAGGAAAACAGAAGTAGACAAAATGGAAGATGATCCGGTAGATGTGTGTTT  
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TAGTTTCTTTTCAGGATCTTGTTTAAACAATGACAAAGAGTTTGAATGCAATCTGTCAATGACTATCAATGTGAGAGAAGGT  
TGTTGAAAGGCAAGTATGATCAGCAAAATGGGGACCAATGAGAGTGGCCATTCTTATCTTAATGCTTCTCAAAGAATCTGTGTT  
GGTGATGATCAGTACGTGCGTTCTGGAAAAGATCATGTTAGCACCTTGTGACTTGGCATATGCATAAATCTGTTGAAGTCCCTTT  
CCCTGTTGTGAATGAATGATGAAATCATATGTTAAATCAAACTCAAGCTTCTCAAAGGTGAGGAACGACTGTTACGGAGAGAA  
TCTTTAGAGGATATTTTGAATGGGGTGGTGCCATCTCACATATCTAGTCTCATTGACATGGGACAGGGGATCCTACACAATGCT  
TCTGATTTTTACGGTTTTAATGAGTAAAGGTTTATCAATTTAGTATGTTGTTGTCATTTTTTGGAGAGAGGCCAGGCTATACATC  
AAGTGATGATCAGATCACTTTATTTGACAAGAGATTGAGTGACTTAGTTGATAGTGACCCAGAAGAAGTCTTGTCTTGTGGAAT  
TCCACTCTCACTTAAGTGGTTGTTGAACAGGTTTCATCAGTCCAAAAGTGTGGTTGGGCGGTTTGCAGCGGAATTCAAATCCAGA  
TTTTATGTGTGGGGGAGGAGGTCCCTCTCTCACGAAATTTGTGTCTGCGGCACTACACAATGTTAAGTGTAAGAACCAGCATCA  
ACTTTGTGAGCAATGATACGATTGCTGATCAAGCTATGAGCAAGGATGAGTTCCAGTTTTTTTAGTAAATGTTTCCAGTGGAG  
CACTGGATCTCTTGAATATGCTAATTTCCCTTTAGATCCATTCTTGTAAACACTCACACTGATGTAAGGATTGGTTAGATGGT  
TCTAGAGGTTATAGAAATCCAAAGACTCATTGAAGAATTGTTGCCAGTGAACAAAGATCATGAGAAAATCTGTAAGAAGACTACA  
TCACAACTCAAGAACGGTGAATGTAACGAGGAATTTTTCTAGACCTCTTCAACAGGGAAAAGAAAGAGGCCATCTTCAATTTG  
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GCTTTGTAGTAAGTTCAAGAGGTGCACAGAAGCTGTTGTGAGAGGCAATCAACAAATCAGCTTTTTCAGAGTTGTGTCTCATCCG  
GCTTTATAGGTCTCTGTAAGACTTTAGGAAGTAGGTGTGTGAGAAATAAAACAGGGAAAATATGTATATCAGAAAGGTGCTTGAA  
GATCTGACCATGGATGAACATGTCACAAGGTTTCAACAAAGATGGTGTGATGTTGTACATTTGCGACAAAGCAGAGACACCAGA  
GGCTCACCGTGACCACATCAACCTTTTGGGCCCTCTCTGGGACTACATTGCATCTCATTGAGCAACTCTTTTGTGAGTGGGTG  
TTTGGGTTTTAGCAGAACCTGTGAAAGGAAAGAACGAGAGTAATTCGGCTGTTAGGCACTTAAATCCATGTGATTATGTAGCAAGA  
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TGAGATCATTTGCTCCCATTCATGCTGTGATGTGAGCTCAAAAATATGAGATGGAGTCCAGGATTAATTCCTTGACCTTTGTG  
TGCTGATTGACATCAACTCAGAGTCTTTGTCACTCATTCTCATGTTGTCAAATGGAAGAGGACGAACATTACACTGTGCTGTTT  
TCTGATCTCGTCAACTCTCACAACGGTCAAGCTCAAGTTTGTGATGTAATTTGTTGTGAGCACAAGGGATGTCTGCAAGAATCT  
TTTGAAGCAAGTGTATTTGAATCATTGTGACGAGGTTTGTGCAACAGCTAGGACCTTAGGTAACTTTTCATGGTTCCCCCATA  
AGGACATGATGCAATCTGAAGATGGCGCTGAAGCACTGGGACCTTCCAATCATTATTTTGAAGTGGTGAACAAGAAAATAGAG  
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AATTAAGCAGGGTTTACAGATCCAAAAGCATTTAAATCTTTAAGAGATTGTGGGATTACATGCTCAGCAGCACAGAGGGGATAT  
TGGAGTTCTCAATCAGATGGATTTACACACAACCAAGCAACACTGACTGCTTGAAGAAATTTTCAATGATCTTTGTGTTAA  
TGCCAAATTACAGAGTCCAGGTGTAGCTGATTACTTATCGTCTCATTTCTTCAAAGGTGAGGTTGACAGGAGATTATAGATGA  
GTGTCTCAATCTGTTGAGGACAGACCCATCTTTAAGCGAATGATGGAGTCTTTGACATTAGGTCTGAAGAGTTTGAAGATTACA  
TGAAGACCCCTTTGACACTTGGTGATTCACTAGAAGTGAACATAAGGTTCTAGAAGGATCTGAATGAGATCAAATCTACTGAC  
TTTGAGAGGATAGGGCTGAGTGGGAACCTGTGCCCTTGACCATAAGGAAGGGTCCCTCTTTGAGGGGAGGAACTTTGGTTAGAA  
TATCTCTGTGAAATTTGAGACAAAGGACATGAGGGTCTTTCTGGCAGAGCTCAGGGCTGTGGAATAATTTGGTGATGTCTCGGCA

GCCTCCTCCTGCACCGATTGAGAACTGGTGAGCACTTGATGGAGTCAGAAATAAGTACAGTTCTTCAGGAGCTCTGCATGGACAGA  
TCCGTCATGCTGACACCATTATCTTTTGTGCCAGATTGGTTCACCTTCAGAGATTGTAGGCTCTGCTTCAGCAGGTCAAAGAACAC  
TGTAATGTATGAGACAACTGGGGGCAGGTTGAGACTCAAGGGGAAATCCTGTGACGATTGGCTGGCGGAGCGGGTGGCCGAGGAGA  
TCGACTAG

SEQ ID NO: 10: LCMV WE LP.

MDETIADLRELCLNYIEQDERLSRQKLNFLGQREPRMVLIEGLKLLSRCIEIDSADKSGCIHNHDDKSVETILIDSGIVCPGLPLI  
IPDGYKLIDNSLILLECFVRSTPASFEKKFIEDTNKLACIKEDLAVAGITLVPIVDGRCDYDNSFMPPEWVNFKFRDLLFKLLEYSS  
QDEKVFEESEYFRCLCESLKTTVDKRSGMDSMKILKDARSFHNDIMKCMCHDGVNPNMSCDDVVGINSFFGRFRDRDLLNGKLRNF  
QKVPSPGLIKEFSELYETLTDNDIIMLSKEAVESCLPMRFITAETHGHERGSDANTEYERLLSMLNKVSKLKLNTRRRQLLNLD  
VLCSSSLIKQSI SKGLENDKHVWGCCYSSVNDRLVSLQSTKEEFMRLKNRRKSRVHKASLDELFRVS INEFIAKIQKCLSTVGL  
SFEHYLSECLVQECHIPFAEFENFMRACTHPVMHYTKFEDYTFQPNIEQLRGLQSLRKLSSVCLATNSMKTSSVARLRQNLG  
VRYQVVECKEVFCQIKLDSSEYHLLYQKTGESSRCYSIQGPDGHLISFYADPKRFFLPIFSDEVLHNIMDTMISWRSCPDLDKDS  
LIDIEITALRLTILLMLTNPTRKNQKQVQNI RYLVMAIVSDFSSTSLMDKLKEDLITPAEKVVYRLRLRFLIRTI FGTGEKVLLSAKF  
KFMLNVSYLCHLITKETPDRLDQIKCFEKFEPKSEFGFVNPKETITPEEECVFYEQMKKFTGKDIDCQHSTPGVNLEIFSMVM  
SSFNNGTLIILKGEKALNNLDPMTNSGCATALDLASNKSVVNMKHLNGERLLEYDFNKLKLVSAVSQITTEGEMARINQKYLHNDYEV  
VSKLVSRVLIGSRKTEVDKLEDDPVDVCFEGEEETSFFRSLEDKVSSTITRYNRGTRLNEGQGEFKNKGLHHLQIILSGKRAY  
LRKVLILSEISFHLVDFDPSCLTNDDMRFICEAVEGSTELSPLYFTSAVKEQCGLDEMARNLCRKFSEGDWVFCMKMILLQMNAN  
AYSGKYRHMQRQSLNFKFDWDKLEEDVRI SERESNSESLKALSITKCMSAALKNLFCYSEESPTS YTSVGPDSGRKLFALS YKEQ  
VDLNVSHQRSDSSSLVDFEVVSTRDVCKNFKLVQVYFESFVREVFATARTLGNFSWFPKDMMPSEDEGAELGPFQSFILKVVNKKIE  
GDDQVYRSGKDHVSTLLTWHMHKLVVEPFPVNVAMKSYVSKLKLKLGSGTTVTERIFREYFEMGVVPSHISLIDMGQGLHNA  
SDFYGLISERFINYICGVI FGERPEAYTSDDQITLFDKRLSDLVSDPEEVLVLEFHSLSGLLNKFI SPKSVVGRFAAEFKSR  
FYVWGEVPLLTKFVSAALHNKCKEPHQLCETIDTADQAIANGVPVFLVNCIQRRTLDLLKYANFPLDPFLNTHTDVKDWLDG  
SRGYRIQRLIEELCPSETKIMRKLVRRLHHKLKNGECNEEFFLDLFNREKKEAILQLGEILGLEDDLNELASINWLNLMEMFPLRM  
VLRQKVVPVSVMTFQEEKI PSLIKTLQNKLC SKFTRGAQKLLSEAINKSAFQSCVSSSGFGLCKTLGSRVNRKNRENMYIRKVL  
DLTMDHEVTRVHKQDGVMLYICDKQRHPEAHRDHINLLRPLLDWYICISLSNSFELGVVLAEPVKGKNESNSAVRHLNCPDYVAR  
KPESRRLLEDKVS LNHIQSVRRLYPKIFEDQLLPFMSDVSSKNMRWSPRIKFLDLCLVIDINSESLSHVVKWKRDEHYTVLF  
SDLVNSHQRSDDSSSLVDFEVVSTRDVCKNFKLVQVYFESFVREVFATARTLGNFSWFPKDMMPSEDEGAELGPFQSFILKVVNKKIE  
RPMFRNDLQFGFGWFSYRVGDVVCNAAMLKQGLTDPKAFKSLRDLWDYMLSSTEGILEFSITVDFTHNQNTDCLRKFSLIFVVK  
CQLQSPGVADYLSCHFFKGEVDRLLDCLNLLRTDPIFKANDGVFDIRSEEFEDYMEDPLTLGDSLELELIGSRRIILNEIKSTD  
FERIGPEWEPVPLTIRKGFALFEGRFVQNISVKLETKDMRVFLAELEGCGKIGDVLGSLLLHFRFTGEHLMSEISTVLQELCMDR  
SVMLTPLSFVPDWFTRDCRLCFRSKNTVMYETTGGRFLKKGSCDDWLAERVAEEID

SEQ ID NO: 11: LCMV variant S-Segmentt

GCGCACCGGGGATCTAGGCTTTTGGATTGCGCTTTCCCTTTAGGACAATTGGGTGCTGGATTCTATCCAATAAAAGGATGGGTCA  
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TCAAAGCTGTGTACAATTTCCGCCACCTGTGGGATATTAGCACTGGTCAGCTTCCCTTTTTTGGCTGGTAGGTCCTGTGGCATGTAC  
GGCCTTAATGGTCCCACATCTATAAAGGGGTTTACCAGTTCAAATCAGTGGAGTTTGATATGTCTCACTAAATCTGACGATGCC  
CAATGCGTGTCTAGCCAACTCTCATCTACATCAGTATGGGAAGCTCTGGACTGGAGCTAACTTTCACTAACGATCCATCC  
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GTAATCAAGCCACCTGAGGTGGGCTGTGCTCCAGGCACTGGCCTAGATGAGTTGGCAACAAGTTTTTCATTGTGAGATCAA  
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GAGATPCTCTACTGTTGCTCGTTTTGATCAAGATAGATTCAGCATGTTCCCTCCATCAGCAGAGCTGCCCCCGTTTTACAGCTG  
CACCAGACTGAAATATAACCAGAGATATTGATACTAGATTGCTGTTTCAAGTAAAGACCCAGAACTGGGTGTTTATCTTTAGC  
CTTTCAAGATCACTGAGATTCGGGTATTTGACTGTGTAAGTAAGCCAGGTCTGTGAGTGCCTGCACACATCATGAGTGGGT  
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GCTGTCAAATTTCCCATGTAGACTCCAGAAGCTTGAGGCCTCTCAGTTCTCATAATTTTGGCCTTCAGCTTCTCAAGATCAGCTGC  
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CAGTCTGGTTAAGACTCCTGAGTCTCTGCAAGCTTTATCATCCCTCCTTTCCTTCTCATGATCCTCTGAACGTGCTGACTTCA  
GAAAAGTCCAACCCATTTAGAAGACTGGTTGCGTCTTGTATGACGGCAGCCTTTACATCTGATGTAAACTCTGCAACTCCCTCCT  
CAACGCTGTGTCCACTGAAAGCTTTTGACTTCTTTGGACAAAGACATTTTGTGCACACAATGAATTTCCAAATAAAGCGCAATTA  
AATGCCTAGGATCCACTGTGCG

SEQ ID NO: 12: LCMV variant GPC.

ATGGGTCAGATTGTGACAAATGTTTGGAGCTTTGCCTCACATCATTGATGAGGTCATCAACATTGTCATTATTGTGCTCATTATAAT  
CACGAGCATCAAAGCTGTGTACAATTTGCCACCTGTGGGATATTAGCACTGGTCAGCTTCTTTTTTTGGCTGGTAGGTCCTGTG  
GCATGTACGGCTTAATGGTCCCGACATCTATAAAGGGGTTACCAGTTCAAATCAGTGGAGTTTGATATGTCTCACTTAAATCTG  
ACGATGCCCAATGCGTGAATCAGCCAACTCTCATCACTACATCAGTATGGGAAGCTCTGGACTGGAGCTAACTTTCACTAACGA  
CTCCATCCTTAATCACAATTTTGAACCTTAACCTCCGCTTTCAACAAAAGACTTTTGACCATACACTCATGATATAGTCTCGA  
GTCTGCACCTCAGTATTAGAGGGAATTCCAACCACAAAGCAGTGTCTTGTGATTTAACAATGGCATCACCATTCAATACAACCTG  
TCATTTTTCGGACCCACAGAGCGCTATGAGCCAGTGTGGACTTTGAGAGGTAGAGTCTTGGACATGTTTGAAGTGCCTTTGGAGG  
AAAATACATGAGAAGTGGCTGGGGCTGGGCAGGTTAGATGGCAAGACCCTTGGTGCAGCCAAACAAGCTATCAGTACCTAATCA  
TACAAAACAGGACTTGGGAAAACCACTGTAGATATGCAGGCCCTTTGGGATGTCTAGAATCCTCTTGTCTCAGGAAAAGACAAG  
TTTCTCACTAGGAGACTTGACGGCATTACCTGGACCTGTGACACTCCTCAGGAGTAGAAAATCAGGTGGTTATTGCCTGAC  
CAAATGGATGATCCTTGTGCGAGCTCAAATGTTTGGGAATACAGCTGTTGCAAAATGTAATGTCAATCATGATGAAGAGTTCT  
GTGATCAGCAAGTGTACAGTACAGCAAGGCCGCCCTGAGTAAGTTCAAGCAAGATGTAGAGTCTGCCTTGCATGTATTCAAA  
ACAACAGTAAATCTCTGATTTCCGATCAGCTGTTGATGAGGAATCATCTAAGAGATCTAATGGGGGTACCATACTGTAATTACTC  
AAAGTCTGTGATCTGGAACATGCTAAGACTGGTGAGACTAGTGACCCAAAGTGTGGCTGTGCTAATGGCTCCTACTTGAATG  
AGACCCACTTTAGTGATCAAATCGAACAAGAAGCAGATAACATGATCACAGAGATGTTGAGGAAGGACTACATAAAAAGACAAGG  
AGTATCCTTTAGCCTTAATGGATCTTTTGTGTTTCAACATCAGCATATCTAATCAGCATCTTCTGCACTCTGTGAAGATACC  
AACACATAGACACATAAAGGGCGGTTTATGTCCAAAGCCACACCGCTTGACCAACAAGGGGATCTGTAGTTGTGGTGCATTCAAGG  
TGCTGGTGTAAAACCTATCTGAAAAGACGCTGA

SEQ ID NO: 13: LCMV variant GPC.

MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQKFSVEFDMSHLNL  
TMPNACSANNSHHYLSMGSGLLELFTNDSILNHNFCNLTSAFNKTDFDHTLMSIVSSHLHSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDLMTAFGGKYMRSWGWSGSDGKTTWCSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKT  
FLTRRLAGTTFTWTLSDSSGVENPGGYCLTKWMILAAELKCFGNATAVAKCNVNHDEEFCDMLRLIDYNKAALSFKQDVEALHVF  
TTVNSLISDQLLMRNLRLDMGVPCYNYSKFWYLEHAKTGETSVPKWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLIMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPVKT IWKR

SEQ ID NO: 14: LCMV Clone13 S-Segment.

GCGCACCGGGGATCCTAGGCTTTTGGATTGCGCTTTCTCTAGATCAACTGGGTGTGAGGCCCTATCCTACAGAAGGATGGGTCA  
GATTGTGACAAATGTTTGAGGCTCTGCCATCATATCGATGAGGTGATCAACATTGTCTATTATTGTGCTTATCGTGATCACGGGTA  
TCAAGGCTGTCTACAATTTTGCCACCTGTGGGATATTGCGATTGATCAGTTTCTTACTTCTGGCTGGCAGGTCCTGTGGCATGTAC  
GGTCTTAAGGACCCGACATTACAAAGGAGTTTACCAATTTAAGTCAGTGGAGTTTGATATGTACATCTGAACCTGACCATGCC  
CAACGCATGTTTCAGCCAACAACCTCCACCATTACATCAGTATGGGACTTCTGGACTAGAATTGACCTTCACCAATGATTCCATCA  
TCAGTCACAACCTTTTGCAATCTGACCTCTGCCCTCAACAAAAGACCTTTGACCACACACTCATGAGTATAGTTTCGAGCCTACAC  
CTCAGTATCAGAGGGAACCTCAACTATAAGGCAGTATCTGCGACTTCAACAATGGCATAACCATCCAATACAACCTTGACATTCTC  
AGATGCACAAAGTGTCTCAGAGCCAGTGTAGAACCCTTCAGAGGTAGAGTCTCAGAAATGCAATGTAATCATGATGAAGAATTTCTGACAT  
TGAGGAGTGGCTGGGGCTGGACAGGCTCAGATGGCAAGACCCTGGTGTAGCCAGACGAGTTACCAATACCTGATTATACAAAAT  
AGAACCTGGGAAAACCACTGCACATATGCAGGTCTTTTGGGATGTCAGGATTCTCCTTCCCAAGAGAAGACTAAGTCTCTCAC  
TAGGAGACTAGCGGGCACATTACCTGGACTTTGTGAGCTCTTCAGGGGTGGAGAATCCAGGTGGTTATTGCCTGACCAAAATGGA  
TGATTCCTTGCTGCAGAGCTTAAGTGTTCGGGAACACAGCAGTTCGAAATGCAATGTAATCATGATGAAGAATTTCTGACAT  
CTGCGACTAATTGACTACAACAAGGCTGCTTTGAGTAAGTTCAAGAGGACGTAGAATCTGCCTTGCACTTATTCAAACAACAGT  
GAATTCCTTTGATTTAGATCAACTACTGATGAGGAACCACTTGAGAGATCTGATGGGGGTGCCATATTGCAATTACTCAAAGTTT  
GGTACCTAGAACATGCAAGACCGGCGAACTAGTGTCCCAAGTGTGGCTTGTACCAATGGTTCTTACTTAAATGAGACCCAC  
TTCAGTGACCAAAATCGAACAGGAAGCCGATAACATGATTACAGAGATGTTGAGGAAGGATTACATAAAGAGGCGAGGGAGTACCCC  
CCTAGCATTGATGGACCTTCTGATGTTTCCACATCTGCATATCTAGTCAGCATCTTCTGCACCTTGTCAAATACCAACACACA  
GGCACATAAAGGTGGCTCATGTCCAAAGCCACACCGATTAAACCAACAAAGGAATTTGTAGTTGTGGTGCATTTAAGGTGCTGGT  
GTAAAACCGTCTGGAAAAGACGCTGAAGAACAGCGCCTCCTGACTCTCCACCTCGAAAGAGGTGGAGAGTCAGGGAGGCCCAGA  
GGGTCTTAGAGTGTCAACAACATTTGGGCCCTTAAAAATTAGGTGATGTGGCAGAATGTTGTGAACAGTTTTCAGATCTGGGAGCCT  
TGCTTTGGAGGCGCTTTCAAATGATGCAGTCCATGAGTGCACAGTGCAGGGGTGATCTCTTTCTCTTTTGTCCCTTACTATT  
CAGTATGCATCTTACACAACCCAGCCATATTGTCCACACTTTGTCTTCACTCCTCGAAGCTTCCCTGGTCATTTCAACATCG  
ATAAGCTTAATGTCCTTCTTATTCTGTGAGTCCAGAAGCTTTCTGATGTATCGGAGCCTTGACAGCTTAGAACCATCCCTGCGG  
AAGAGCACCTATAACTGACGAGGTCAACCCGGGTTGCGCATTTGAAGAGGTGCGCAAGATCCATGCCGTGTGAGTACTTGAATCTT  
GCTTGAATTTGTTTTGATCAACGGGTTCCCTGTAAAGTGTATGAACTGCCCCTTCTGTGGTTGGAATAATGCTATTTCCTGGA  
TCATTAATCTACCTCAATGTCAATCCATGTAGGAGCGTTGGGGTCAATTCCTCCCATGAGGTCTTTTAAAGCATTTGTCTGGCT  
GTAGCTTAAGCCACCTGAGGTGGACCTGCTGCTCAGGCGCTGGCCTGGGTGAATGACTGCAGGTTTCTCGTGTGTGAGATCAA  
TTGTTGTGTTTTTCCATGCTCTCCCAACATCGATGTTTCTACAAGCTATGTATGCCATCCTTCACTGAAAGGCAAACTTTATAG  
AGGATGTTTTATAGGGTTCTGTCCCAACTTGGTCTGAAACAACATGTTGAGTTTTCTCTTGGCCCGGAGAACTGCCTTCAA  
GAGGTCTCTGCTGTTGCTTGGCTTGTATCAAATGACTCTAACATGTTTACCCCATCCACAGGGGTGCCCTGCTCTACGGCAG  
CACCAGACTAAAGTTATAGCCAGAATGTTGATCTGAGCTGCTGTTTCAAGTGTGACCCCGAAGCTGGGTGCTGTCTTTCAGC  
CTTTCAAGATCATTAAGATTGGATACCTGACTGTGTAAGCAAGCCAGGTCTGTGAGCGCTTGACACAGCTCATTGAGCGGAGT

CTGTGACTGTTTGGCCATACAAGCCATAGTTAGACTTGGCATTGTGCCAAATTGATTGTTCAAAGTGATGAGTCTTTCACATCCC  
AAACTCTTACCACACCACTTGCACCCTGCTGAGGCTTTCTCATCCCACTATCTGTAGGATCTGAGATCTTTGGTCTAGTTGCTGT  
GTTGTTAAGTTCCCCATATATACCCTGAAGCCTGGGGCTTTTCAGACCTCATGATCTTGGCCTTCAGCTTCTCAAGGTGAGCCGC  
AAGAGACATCAGTTCTTCTGCACTGAGCCTCCCCACTTTCAAACATTCTTCTTTGATGTTGACTTTAAATCCACAAGAGAATGTA  
CAGTCTGGTTGAGACTTCTGAGTCTCTGTAGGCTTTGTGCATCTCTCTTTTCTCCTCATGATCCTCTGAACATTGCTGACCTCA  
GAGAAGTCCAACCCATTGAGAAGTTGGTTGCATCCTTAATGACAGCAGCCTTCACATCTGATGTGAAGCTCTGCAATTCTTCTCT  
CAATGCTTGGTCCATTGGAAGCTCTTAACCTCCTTAGACAAGGACATCTGTTGCTCAATGTTTCTCAAGACAATGCGCAATC  
AATGCTTAGGATCCACTGTGCG

SEQ ID NO: 15: LCMV Clone13 L-Segment.

GCGCACCGGGGATCTTAGGCGTTTGTGTCGCTGTTTGGTTGCACAACCTTTCTTCGTGAGGCTGTGAGAAGTGGACCTGGCTGATA  
GCGATGGGTCAAGCAACCAAGAGAGGAGAAAGGCACCAATAGTACAAACAGGGCCGAAATCCTACAGATACACCTATCTTGG  
CCCTTTAAGCTGCAAACTTGTCTGGCAGAAATTTGACAGCTTGGTAAGATGCCATGACCACTACCTTTGAGGCACTGTTTAAACC  
TTCTGCTGTGATATCCGACAGGTGCTCTTTGTAAATATCATTACCAACAGATTGAAGATATCAACAGCCCCAAGCTCTCCA  
CCTCCTACGAAGAGTAACACCGTCCGGCCCCGGCCCCGACAAACAGCCAGCACAAGGGAACCGCAGCTCACCCACGCACACAG  
ACACAGCACCCCAACACAGAACACGACACACACACACACACACACACACACACACACACACACACACACACACACACACACAC  
GGGGGGCGGGCCCCGGGAGCCCGGGCGGAGCCCCACGGAGATGCCATCAGTCTGATGTCTCGGCCACCGACCCGCCAGCCCAAT  
CGTCCGAGGACCTCCCTTGTAGTCTAAACCTGCCCCCCAGTGTTCATACATCAAAGTGCTCCTAGATTGTCTAAACAAAGTCTG  
CAATCCTTAAAGGCGAACCACTGTGGCAAAAGCGACAGTGAATCAGCAGAATAGATCTGTCTATACATAGTTCTCTGGAGGATTAC  
ACTTATCTCTGAAGCAACCAATGTTCCAGCTTCTGAACCTGACAGTTCGACGGAAGAGGTTCCCAAGGACATCTCTATCTATCTCAGAC  
CCTCAAGTCTGTGATAGAAAGACTTTTCATGTCTTGGTCTCCAGCTTCACAATGATATTTTGGACAAGGTTCTTCTCTCAAAAAGG  
GCACCCATCTTTACAGTCACTGGCAGAGGCTCCCACTCAGTCCAACTCTCTCAAAGTCAATAGATCTAATCCCATCCAGTATTCT  
TTTGGAGCCCAACAACTCAAGCTCAAGAGAATCACCAGTATCAAGGGATCTTCCATGTAATCCTCAAACCTCTCAGATCTGATAT  
CAAGACACCATCGTTACCTTGAAGACAGAGTCTGTCTCAGTAAGTGGAGGCATTCATCCAACATTCTCTATCTATCTCAGAC  
TTAAAGAGGTGAGAGCATGATAAAAGTTTACGCCACACCTGGATTCTGTAATTGGCACCTAACCAAGAATATCAATGAAATTTCTCT  
TAAACAGTCACTATTATCTGATTGTGCGTAAAGTCCACTGAAATGAAACTCCAATACCCCTTTTGTGTAGTTGAGCATGTAGT  
CCCACAGATCCTTTAAGGATTTAAATGCCCTTTGGGTTTGTGAGGCCCTGCCTAATCAACATGGCAGCATTACACACAACATCTCCC  
ATTCCGTAAGAGAACCACCCAAACCAAACTGCAAACTCATTCCTAAACATAGGCTCTCCACATTTTGTTCACCACTTTGAGAC  
AAATGATTGAAAGGGGCCAGTGCCTCAGCACCATCTTCAGATGGCATCATTTCTTTATGAGGGAACCATGAAAAATTGCCATATG  
TCCTGGTTGTGCAACAAATTTCTGAACAAATGATTCAAATACACCTGTTTAAAGAGTTCTTGCAGACATCCCTCGTCTAACA  
ACAAATTCATCAACCAGACTGGAGTCAGATCGCTGATGAGAATTGGCAAGGTGAGAAAACAGAACAGTGAATGTTTATCCCTTTT  
CCACTTAACAAACATGAGAAATGAGTGACAAGGATTTCTGATGTAATATCAATTAAACACAGAGGTCAAGGAATTAATTTCTGGGAC  
TCCACCTCATGTTTTTTGAGCTCATGTGACACATAAATGGAAGAAGCTGATCCTCAAAGATCTTGGGATATAGCCGCTCACAGAT  
TGAATCACTTGGTTCAAATTCACCTTGTCTCAGTAGCCTTGTGCTCAGGCTTCTTGTCTACATAATCACATGGGTTAAGTG  
CTTAAGAGTTAGGTTCTCACTGTTATTCTTCCCTTTGGTCTGTTCTGCTAGGACCCAAACACCCAACTCAAAGAGTTGCTCAATG  
AAATACAAATGATAGTCCAAAGAAAGAGGCTTAAAGGCATATATGATCAGGTGGGCTTCTGGATGAGACTGTTGTCTACAAATG  
TACAGCGTTATACCATCCCGATTGCAAACTCTTGTACATGATCATCTGTGGTTAGATCCTCAAGCAGCTTTTGTATATACAGATT  
TTCCCTATTTTGTCTCTCACACCTGCTTCTAGAGTTTGTCAAAGGCTATAAAGCCAGATGAGATACAACCTCTGGAAGGCTG  
ACTTGTGATTGCTTCTGACAGCAGCTTCTGTGCACCCCTTGTGAATTTACTACAAAGTTTGTCTGGAGTGTCTTGATCAATGAT  
GGGATCTTCTCTCTCTGGAAGTCACTACCTGATGGATAAACCACTTTTGTCTTAAACACCATCTTATAGGCACTCTGTTCAAA  
ATTCAACCAAGTTAATATCTGCTAACTGATTGATCTTCTTCAAGACCGAGGAGGTCTCCAATTGAAGAATGGCTCTCTTTTAT  
CTCTGTTAAATAGGTCTAAGAAAAATCTTTCATTAAATTCACATTTTGTGAGCTTATGATGCAGTTTCTTACAGCTTCTTAC  
ACCTTTGTTTTCATTAGGACACAGTTCCCTCAATGAGTCTTGTATTCTGTAACCTCTAGAACCATCCAGCAATCTTTCACATCAGT  
GTTGTATTACAACAGGTCTCAGCCTCTATCAATAAAGTATGATCTGATCAGGTGAGGCTTCTCTCTTGGATGAGACTGTTGTCTACAAATG  
AGACTGGGACGCCATTTGCGATGGCTTGATCTGCAATTGTATCTATTGTTTCAAAAGTTGATGTGGCTCTTTACACTTGACATTG  
TGTAAGCCTCGAGATACAACTTTGTGAGAAGAGGAGCTTCTTCCCCCATACATAGAATCTAGATTAAATTTGCAAGCAACCT  
CCCAGCCACACTTTTGGGCTGATAAATTTGTTTAAACAGCCGCTCAGATGAGATTGGAATCCAACAGGACAAGGACTTCTCTCCG  
GATCACTTACAACAGGTCTCAGCCTCTATCAATAAAGTATGATCTGATCATCACTTGATGTGTAAGCCTCTGGTCTTTCCGCA  
AAGATAACCAATGCAGTAGTTGATGAACCTCTCGCTAAGCAACCATAGAAGTCAGAAGCATTATGCAAGATTCCCTGCCCAT  
ATCAATAAGGCTGGATATATGGGATGGCACTATCCCATTTCAAATATTGTCTGAAATTTCTCTCAGTAACAGTTGTTCTGAAC  
CCCTGAGAAGTTTGTGCTTGCATATGATTTTCATCATTTGCATTCACAACAGGAAAGGGGACCTCGACAAGCTTATGCATG  
TGCCAAGTTAACAAGTGAACATGATCTTTCCGGAACGCACATCTGGTCTACACCTAGTTTGAAGATTTTGTAGAACAATTA  
GAACAAAAATGGGCACATCATTGGTCCCCATTGTGTGTATCTACTATAGTTTAAAGACCCTTCCCGCACATTGATAGTCATTG  
ACAAGATTGCATTTTCAAATTCCTATCATGTTTAAACAGGAGCTGAAAAGAACTTGAAGAAAGACTCAAATAATCTCTATT  
AACCTTGTGAACATTTTGTCTCAAATCTCAATATAGAGTTCTCTATTTCCTCCCAACCTGCTCTTTATAAGATAGTGCAAAATTT  
CAGCCTTCCAGAGTACAGGCTTACTGAGGTGATGATGTTGGTGATTTCTCTGAGTAGAAGCACAGATTTTCAAAGCAGCACTCA  
TACATTGTGTCAACGACAGAGCTTTACTAAGGGACTCAGAATTACTTTCCCTCTCACTGATTCTCAGCTCTCTTCCAGTTGTCC  
CAGTCAAATTTGAAATTCAGCCTTGCCTTGCATATGCCGTGATTTCCCTGAGTACGCATTTGCATTCAATTTGCAACAGAATCAT  
CTTCATGCAAGAAAACCAATCATTTCTCAGAAAAGAACTTTCTACAAAGGTTTGTGCCATCTCATCGAGGCCACACTGATCTTTAA  
TGACTGAGGTGAAATACAAAGGTGACAGCTCTGTGGAACCTCAACAGCCTCACAGATAAATTTCAATGTCATCATTTGGTTAGACAT  
GATGGGTCAAAGTCTCTACTAAATGGAAGATATTTCTGACAAGATAACTTTTCTTAAGTGAGCCATCTCCCTGTTAGAATAAG  
CTGTAATGATGTAGTCTTTTGTATTTGTAAGTTTCTTCCATCTCCTTGTGATGAGGCTCTCTACCTCTTCTGTACCGTGCTA  
TTGTGGTGTGACCTTTTCTCGAGACTTTTGAAGAAGCTGTCTCTTCTTCCATCAAACATATTTTGCAGGTTGTCTTCC  
GATCTTCTCTCTCTCTCTCTTCCCTTGAACCGATGACCAATCTAGAGCTAACTTGAACCTTTATATTCATAGTCTGAGTGGCTCAA  
CTTATACTTTTGTCTTCTACGAACTCTCCGTAATTTGACTCAGACACTAACAAGCAATTTGTAAAGTCATATTCCAGAAGTC  
GTTCTCCATTTAGATGCTTATTAACCAACACACTTTTGTACTAGCAAGATCTAATGCTGTGCGACATCCAGAGTTAGTCATGGGA  
TCTAGGCTGTTTAGCTTCTCTCTCTCTTTGAAATTAAGGCTGTTGTTAAATGAAGACACCATTAGGCTAAAGGCTCCAGATT  
AACACCTGGAGTTGATGCTGACAGTCAATTTCTTACTAGTGAATCTCTTCATTTGCTCATAGAACACACATTTCTCTCCAGGAG

TGATTGCTTCCTTGGGGTTGACAAAAAACCAATTGACTTTTGGGCTCAAAGAACCTTTTCAAACATTTTATCTGATCTGTTAGC  
CTGTCAGGGGTCTCCTTTGTGATCAAAATGACACAGGTATGACACATTCAACATAAAATTTAAATTTTGCACTCAACACACCTTCTC  
ACCAGTACCAAAATAGTTTTTATTAGGAATCTAAGCAGCTTATACACCACCTTCTCAGCAGGTGTGATCAGATCCTCCCTCAACT  
TATCCATTAATGATGTAGATGAAAAATCTGACACTATTGCCATCACCATAATCTGACACTCTGTACCTGCTTTTGATTCTCTTT  
GTTGGGTTGGTGAGCATTAGCAACAATAGGGTCCCTCAGTGCAACCTCAATGTGCGTGAGACAGTCTTTCAAATCAGGACATGATCT  
AATCCATGAAATCATGATGTCTATCATATTGTATAAGACCTCATCTGAAAAAATGGTAAAAAGAACCTTTTAGGATCTGCATAGA  
AGGAAATTAATGACCATCCGGGCTTGTATGGAGTAGCACCTTGAAGATTCTCCAGTCTTCTGGTATAATAGGTGGTATTTCTCA  
GAGTCCAGTTTTATTACTTGGCAAAACACTTCTTGCATTCTACCACTTGATATCTCACAGACCTTATTGATTTTGCCTTAGTCT  
AGCAACTGAGCTAGTTTTCTACTGTTTGTAAAGGCCAGACAAACAGATGATAATCTTCTCAGGCTCTGTATGTTCTTCACTGCT  
CTGTGCTGGGTTGGAATTTGAATCTTCAAACCTCGTATAATACATTATCGGGTGAGCTCCAATTTTCATAAAGTTCTCAAATTC  
GTGAATGGTATGTGCATTCTTGTCTCAAGGTGTTGAGACAGTCCGTAATGCTCGAACTCAGTCCACCACCTAACAGGCATTTTGT  
AATTTTGGCAATGAACCTACTAATAGATGCCCTAAACAATCTCTCAAAGACACCTTTCTAAACACCTTTGACTTTTCTTATTC  
TCAAAGTCTAATGAACCTCTCTTGTAGTGTGTGAAGCTTACCAGCTTATCATTACACTACTATAGCAACACCCACCCAGTGT  
TTATCATTTTTTAACCTTTGAATTTGACTGTTTTATCAATGAGGAAAGACACAAAACATCCAGATTTAACAAGTGTCTCCTTCT  
AGTATTCACAGTTTTCAAACCTTGTACTTTGTTTTAACAATAGAGAGGAGCTCTCATATTCAGTGTAGTCTCACTTCCCCTTTCTG  
GCCCATGGGTCTCTGAGTTTATGAATCTCATCAAGGACAGGATTGACTGCTCCCTGCTTAAAGTTAAGTATACATCATCATCA  
GCAAGGTTTTCTATAGAGCTCAGAGAATTCCTTGATCAAGCTTCAAGGTTTACTTTCTGAAAGTTTCTCTTAAATTTCCCACTTTC  
TAAATCTCTTCTAAACCTGTGAAAGAGAGTTTATTCAAAAACCATCATCATCAGCTCATGTGGGGTTGATGCCTTCGTGGC  
ACATCCTCATAAATTTTCATCATTTGTGAGTTGACCTCGCATCTTTCAGAAATTTTCATAGAGTCCATACCGGAGCGCTTGTGATAGTA  
GTCTTTCAGGACTCAGAGTCTAAAATATTCAGACTCTTCAAAGACTTTCTCATTTTGGTTAGAATACCAAAAGTTTGAATTA  
AAGGTCTCTAAATTTGAAGTTTGCCCACTCTGGCATAAACTATTATCATAATCACAACGACCATCTACTATTGGAACATAATGTGA  
CACCCGCAACAGCAAGGTCTTCCCTGATGCATGCCAATTTGTTAGTGTCTCTATAAATTTCTTCTCAAACTGGCTGGAGTGTCT  
CTAACAAAACACTCAAGAAGATGAGAGAATTGTCTATCAGCTTGTAAACCATCAGGAATGATAAGTGGTAGTCTGGGCATACAT  
TCCAGACTCCACAAAATTTGTTCCACAGACTTATCGTGGTGTGTGTCAGCCACTTGTCTGCACTGTATTTCAATTCATATGC  
AGCGTGACAGCAACTTGAGTCCCTCAATCAGAACCATTCTGGGTTCCCTTGTCCAGAAAGTTGAGTTTCTGCCTTGACAACCTC  
TCATCTGTTCTATATAGTTTAAACATAACTCTCTCAATTTCTGAGATGATTTTATCCATTGCGCATCAAAAGCCTAGGATCCTCG  
GTGCG

SEQ ID NO: 16: LCMV Clone13 GPC.

ATGGGTCAGATTGTGACAATGTTTTGAGGCTCTGCCTCACATCATCGATGAGGTGATCAACATTGTCATTATTGTGCTTATCGTGAT  
CACGGGTATCAAGGCTGTCTACAATTTTGGCCACCTGTGGGATATTGCGATTGATCAGTTTCTACTTCTGGCTGGCAGGCTCTGTG  
GCATGTACGGTCTTAAAGGACCCGACATTTACAAAGGAGTTTACCAATTTAAGTCAGTGAGTTTGATATGTACATCTGAACCTG  
ACCATGCCCAACGCATGTTGAGCCAACTCCACCATTTACATCAGTATGGGGACTTCTGGACTAGAATTGACCTTCACCAATGA  
TTCCATCATCAGTCAACATTTTGAATCTGACCTCTGCCTTCAACAAAAAGACCTTTGACCACACACTCATGATATAGTTTTCGA  
GCCTACACCTCAGTATCAGAGGGAATCCAACTATAAGGCAGTATCCTGCGACTTCAACAATGGCATAACCATCCAATACAACCTG  
ACATTTCTCAGATGCACAAAGTGTCTCAGAGCCAGTGTAGAACCCTTCAAGAGTAGAGTCTTAGATATGTTTAGAACTGCCTTCGGGG  
GAAATACATGAGGAGTGGCTGGGGCTGGACAGGCTCAGATGGCAAGACCACCTGGTGTAGCCAGACGAGTTACCAATACCTGATTA  
TACAAATAGAACCTTGGGAAACCACTGCACATATGCAGGTCTTTTGGGATGTCCAGGATTCTCTTCCCAAGAGAAGACTAAG  
TTCCTCACTAGGAGACTAGCGGCACATTCACCTGGACTTTGTGACAGCTTTCAGGGGTGGAGAATCCAGGTGGTTATTGCTCTGAC  
CAATGGATGATTTCTGCTCAGAGCTTAAAGTGTTCGGGAACACAGCAGTTCGCAAAATGCAATGTAATCATGATGAAGAATTTCT  
GTGACATGCTGCGACTAATTGACTACAACAAGGCTGCTTTGAGTAAGTTCAAAGAGGACGTAGAATCTGCCTTGCACTTATTCAA  
ACAACAGTGAATTTCTTGAATTCAGATCACTACTGATGAGGAACCACTTGAAGATCTGATGGGGTGGCATATGCAATTACTC  
AAAGTTTGTGACCTAGAACATGCAAGACCGGCGAACTAGTGTCCCAAGTGTGGCTTGTCAACATGGTTCTTACTTAAATG  
AGACCCACTTCAGTGACCAATCGAACAGGAAGCCGATAACATGATTACAGAGATGTTGAGGAAGGATTACATAAAGAGGACGGG  
AGTACCCCCCTAGCATTGATGGACCTTCTGATGTTTTCCACATCTGCATATCTAGTCAGCATCTTCTGCACCTTGTCAAATACC  
AACACACAGGCACATAAAGGTGGCTCATGTCCAAAGCCACACCGATTAAACCAACAAAGGAATTTGATGTTGTGGTGATTTAAGG  
TGCCTGGTGTAAAAACCGCTCTGAAAGACGCTGA

SEQ ID NO: 17: LCMV Clone13 GPC.

MGQIVTMFEALPHIIDEVINIVIVLIVITGIKAVYNFATCGIFALISFLLLAGRSCGMYGLKGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSANNSSHYYISMGTSGLLELFTNDISIISHNFCNLTSAFNKTTFDHTLMSIVSSLHLSIRGNSNYKAVSCDFNNGITIQYNL  
TFSDAQSAQSQCRFTFRGRVLDMPRTAFGGKYMRSWGWTGSDGKTTWCSQTSYQYLI IQNRTWENHCTYAGPFGMSRILLSQEKTK  
FLTRRLAGTFTWTLSDSSGVENPGGYCLTKWMLAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKEDVESALHLFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMI TEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLVSIFLHLVKIPTHRIHKGSGCPKPHRLTNKGICSCGAFKVPKVKTWVKRR

SEQ ID NO: 18: LCMV Clone13 NP.

ATGTCCTTGTCTAAGGAAGTTAAGAGCTTCCAATGGACGCAAGCATTGAGAAGAGAATTGAGAGCTTCACATCAGATGTGAAGGC  
TGCTGTCTAATGAAGATGCAACCAACCTTCTGAATGGGTGGACTTCTCTGAGGTGAGCAATGTTGAGAGATCATGAGGAAGGAAA  
AGAGAGATGACAAAGACCTACAGAGACTCAGAAGTCTCAACAGACTGTACATTTCTTGTGGATTAAAGTCAACATCAAAGAAG  
AATGTTTTGAAAGTGGGAGGCTCAGTGCAGAAGAACTGATGTCTCTTGGCGCTGACCTTGAGAAGCTGAAGGCCAAGATCATGAG  
GTCTGAAAGGCCCGAGGCTTCAAGGGTATATATGGGGAATTAACAACACAGCACTAGACCAAGATCTCAGATCCTACAGATAT  
TTGGGATGAGAAAGCCTCAGCAGGTGCAAGTGGTGTGGAAGTGTGGGATGTGAAGACTCATCACTTTGAACAATCAATTT  
GGCACAATGCAAGCTTAACATATGCTTGTATGGCCAAACAGCTCACAGACTCCGCTCAATGACGTTGTACAAGCCCTCACAGACCT  
TGGCTTGCTTTACACAGTCAAGTATCCAAATCTTAATGATCTTGAAGGCTGAAAGACAAAGCACCAGTCTGGGGGTCTCACTG  
AACAGCAGTCCAGCATCAACATTTCTGGCTATAACTTTAGTCTTGGTGTGCGGTGAAGGCAGGGGCAGCCCTGTTGGATGGGGGT  
AACATGTTAGAGTCAATTTGATCAAGCCAGCAACAGCAGGAGACCTTGAAGGCAGTTCTCGGGCCAAAGAAACCTCAACAT  
GTTTGTGTTACAGCAAGTTGGGGACAGGAACCTTATGAAACATCTCTATAAAGTTTGCTTTTCAAGGTGAAGGATGGCCATACA

TAGCTTGTAGAACATCGATTGTGGGGAGAGCATGGGAAAACACAACAATTGATCTCACAAAGCGAGAAACCTCGAGTCAATTCACCC  
AGGCCAGCGCTGGAGCAGCAGGTCCACCTCAGGTGGGCTTAAGCTACAGCCAGACAATGCTTTTAAAGACCTCATGGGAGGAAT  
TGACCCCAACGCTCCTACATGGATTGACATTGAGGGTAGATTTAATGATCCAGTGGAATAGCAATTTTCCAACCACAGAACGGGC  
AGTTCATACACTTTTACAGGAACCCGTTGATCAAAAACAATTCAAGCAAGATTCCAAGTACTCACACGGCATGGATCTTGCCGAC  
CTCTTCAATGCGCAACCCGGTTGACCTCGTCAGTTATAGGTGCTCTTCCGCAAGGGATGGTTCTAAGCTGTCAAGGCTCCGATGA  
CATCAGAAAGCTTCTGGACTCACAGAATAGGAAGGACATTAAGCTTATCGATGTTGAAATGACCAGGGAAGCTTCGAGGGAGTATG  
AAGACAAAGTGTGGGACAAATATGGCTGGTGTGTAAGATGCATAGTGAATAGTAAGGGACAAAAGAGAAAGAGATCACCCCG  
CACTGTGCACTCATGGACTGCATCATTTTTGAAAGCGCTCCAAGCAAGGCTCCAGATCTGAAACTGTTTACAACATTCTGCC  
ACATGACCTAATTTTTAGAGGCCAAATGTTGTGACACTCTAA

SEQ ID NO: 19: LCMV Clone13 NP.

MSLSKEVKS FQWTQALRRELQSFTSDVKA AVIKDATNLLNGLDFSEVSNVQRIMRKEKRDDKDLQRLRLSNQTVHSLVDLKSTSKK  
NVLKVGRLSAEELMSLAADLEKLKAKIMRSERPQASGVYMGNLTTQQLDQRSQILQIVGMRKPQQGASGVVRVWDVKDSLNNQF  
GTMPSLTMAKMAQSQTPLNDVVQALTDLGLLYTVKYPNLNDLERLKDHPVLGVITEQQSSINISGYNFSLGA AVKAGAAALLDGG  
NMLESILIKPSNSEDLKAVLGAKRKLNMFVSDQVGDRNPYENILYKVLCSGEGWPYIACRTSIVGRAWENTTIDLITSEKPAVNSP  
RPAPGAAGPPQVGLSYSQTMLLKDLMMGIDPNAPTWIDI EGRFNDPVEIAIFQPQNGQFIHFYREPVQDKQFKQDSKYSHGMDLAD  
LFNAQPGLTSSVIGALPQGMVLSQCGSDDIRKLLDSQNRKDIKLIDVEMTREASREYEDKVVWDKYGWLCMKHTGIVRDKKKKEITP  
HCALMDCIIFESASKARLPDLKTVHNILPHDLIFRGPNNVTL

SEQ ID NO: 20: LCMV Clone13 ZP.

ATGGGTCAAGGCAAGTCCAGAGAGGAGAAAGGCACCAATAGTACAAACAGGGCCGAAATCCTACCAGATACCACCTATCTTGCCCC  
TTTAAAGCTGCAAATCTTGCTGGCAGAAATTTGACAGCTTGGTAAGATGCCATGACCCTACCTTTGCAGGCACTGTTTAAACCTTC  
TGCTGTCAGTATCCGACAGGTGCTCTCTTTGTAATATCCATTACCAACCAGATTGAAGATATCAACAGCCCCAAGCTCTCCACCT  
CCCTACGAAGAGTAA

SEQ ID NO: 21: LCMV Clone13 ZP.

MGQGSREEKGTNSTNRAEILPDTTYLGLPLSCKSCWQKFDSLVRCHDHYLCRHCLNLLLSVSDRCLCKYLPRLKISTAPSSPP  
PYEE

SEQ ID NO: 22: LCMV Clone13 LP.

ATGGATGAAATCATCTCAGAATTGAGAGAGTTATGTTTAACTATATAGAACAGGATGAGAGGTTGTCAAGGCAGAACTCAACTT  
TCTGGGACAAAGGGAACCCAGAATGTTCTGATTGAGGGACTCAAGTTGCTGTCACGCTGCATTGAAATAGACAGTGCAGACAAGA  
GTGGCTGCACACACAACCACGACGATAAGTCTGTGGAACAATTTTGGTGGAGTCTGGAATTGTATGCCAGGACTACCACCTTATC  
ATTCCTGATGGTTACAAGCTGATAGACAATCTCTCATTCTCTTGAGTGTGTTGTAGGAGCACTCCAGCCAGTTTGTAGAAGAA  
ATTTATAGAGGACACTAACAAATTTGGCATGCATCAGGGAAGACCTTGCTGTTGCGGGTGTACATTAGTTCGAATAGTAGATGGTC  
GTTGTGATTATAGTAATAGTTTATGCGCAGAGTGGCAGAACTTCAAAATTTAGAGACCTTTATTCAAACCTTTGGAGTATTTCAAC  
CAAAATGAGAAAGTCTTTGAAGAGTCTGAATATTTAGACTCTGTGAGTCCCTGAAGACTACTATCGACAAGCGCTCCGGTATGGA  
CTCTATGAAAATTTGAAAGATGCGAGGTCAACTCACAATGATGAAATTTAGAGGATGTGCCACGAAGGCATCAACCCCAACATGA  
GCTGTGATGATGTGGTTTGTGAATAAACCTCTCTTTTTCAGCAGTTTAGAAGAGATTTAGAAAGTGGGAAATTAAGAGAACTTT  
CAGAAAGTAAACCTTGAAGCTTGATCAAGGAATTTCTCTGAGCTCATGAAAACCTTGCTGATAGTATGATATCTTCAATATTAAG  
CAGGGAGGCAGTCAATCTGTCTTTGATGAGATTCACTAAGTGCAGAGACCCATGGGCACGAAGGGGAAGTGAGACTAGCACTG  
AATATGAGAGGCTCTCTCTATGTTAAACAAAGTCAAGAGTTTGAACCTGTTGAATAC TAGAAGGAGACAGTTGTTAAATCTGGAT  
GTTTTGTGCTTTCTCTCATTGATAAAACAGTCAAAATTTCAAAGGTTTAAAAATGATAAACACTGGGTGGGTTGTTGCTATAGTAG  
TGTAATGATAGCTGTTTGTCTGGCTTAACAAACAGTATGAAAACAGTCTTAGACTTTTGAAGAAAGTAAAGGAAATTAAGGTTT  
GAAAGGTGCTTTTGAAGAAATGTTTAGGGCATCTATTAGTGAGTTCATTGCAAAAATTTCAAAAATGCCGTGTTAGTGTTGGGACTG  
AGTTTCGAGCATTACGGACTGTCTGAACACCTTGAGCAAGAATGCCACATACATTCACTGAATTTGAGAACTTTATGAAATTTGG  
AGCTCACCCGATAATGTATTATACGAAGTTTGAAGATTACAATTTCAACCCAGCACAGAGCAGTGAAGAACATACAGAGCCTGA  
GAAGATTATCATCTGTTTGTCTGGCTTAACAAACAGTATGAAAACAGTCTTAGACTTTTGAAGAAAGTAAAGGAAATTAAGGTTT  
GTGAGATATCAAGTGGTAGAATGCAAGAAGTGTGTTGCCAAGTAATAAACTGGACTCTGAAGAATACCACCTATTATACCAGAA  
GACTGGAGAACTTCAAGGTGCTACTCCATACAAGGCCCGGATGGTCATTTAATTTCTCTATGCAGATCCTAAAAGGTTCTTTT  
TACCAATTTTTTCAGATGAGGTCTTATACAATATGATAGACATCATGATTTTCATGGATTAGATCATGTCTGATTTGAAAGACTGT  
CTCACCGACATTGAGGTTGCACTGAGGACCTATTGTTGCTAATGCTCACCAACCCAAGGAAGCAATCACTCCTGAGGAAGAATGTGTCTTATG  
TGTCAGATATTTGGTATGGCAATAGTGTGAGATTTTTCATCTACATCATTAATGGATAAGTTGAGGGAGGATCTGATCACACCTG  
CTGAGAAGGTGGTGTATAAGCTGCTTAGATTCCTAATAAAACTATTTTTGGTACTGGTGAGAAGGTGTTGTTGAGTGCAAAATTT  
AAATTTATGTTGAATGTGTACATCTGTGTCAATTTGATCACAAGGAGACCCCTGACAGGCTAACAGATCAGATAAAATGTTTGA  
AAAGTCTTTGAGCCCAAAAGTCAATTTGGTTTTTTTGTCAACCCCAAGGAAGCAATCACTCCTGAGGAAGAATGTGTCTTATG  
AGCAATGAAGAGATTCACTAGTAAAGAAATGACTGTGAGCATACAACTCCAGGTGTTAATCTGGAAGCCTTTAGCCTAATGGTG  
TCTTCATTTAACACGGCACTTTAATTTTCAAAGGAGAGAAGAAGCTAAACAGCCTAGATCCCATGACTAACTCTGGATGTGCGAC  
AGCATTAGATCTTGCTAGTAAACAAAGTGTGGTGGTTAATAAGCATCTAAATGGAGAAGCACTTCTGGAATATGACTTTAACAAT  
TGCTTGTGTTAGTGCTGAGTCAAAATACGGAGAGTTTCGTAAGAAAACAAAAGTATAAGTTGAGCCACTCAGACTATGAATATAAA  
GTTTCCAAGTTAGTCTCTAGATTGGTCATCGGTTCCAAGGAGAGAAGACAGGGAGATCGGAAGACAACCTGGCAGAAATATGTTTT  
TGATGGAGAAGAAGACAGCTTCTTCAAAGTCTCGAAGAAAAGGTCAACACCACAATAGCACGGTACAGAAGAGGTAGGAGGG  
CCAATGACAAAGGAGATGGAGAAAACCTTACAAATACAAAGGACTACATCATTTACAGCTTATTCTAACAGGGAAGATGGCTCAC  
TTAAGAAAAGTTATCTTGTGAGAAATATCTTTCCATTTAGTAGAAGACTTTGACCCATCATGTCTAACCAATGATGACATGAAAT  
TATCTGTGAGGCTGTTGAGGTTTCACAGAGCTGTACCTTTGTATTTACCTCAGTCATTAAAGATCAGTGTGGCTCGATGAGA  
TGGCAAAAACCTTTGTAGAAAGTCTTTTCTGAGAATGATGTTTTCTTGCAATGAAGATGATCTGTTGCAATGAATGCAAT  
CGCTACTCAGGGAATAACAGGCATATGCAAGGCAAGGCTGAATTTCAATTTGACTGGGACAACTGGAAGAGACGTGAGAAAT  
CAGTGAGAGGAAAAGTAATCTGAGTCCCTTAGTAAAGCTCTGTGCTTGACCAATGTATGAGTGTGCTTTGAAAACTGTGCT

TCTACTCAGAAGAATCACCAACATCATACACCTCAGTAGGTCCTGACTCTGGAAGGCTGAAATTTGCACATATCTTATAAAGAGCAG  
GTTGGGGGAAATAGAGAACCTATATTGGAGATTTGAGGACAAAAATGTTACAAGGTTAATAGAAGATTATTTTGTGCTTTTTT  
AAGTTTCTTTTCAGGCTCCTGTTTTAAACAATGATAAGGAATTTGAAAATGCAATCTTGTCATGACTATCAATGTGCGGGAGGGT  
TCTTAAACTATAGTATGGATCACAGCAAAATGGGGACCAATGATGTGCCCATTTTGTCTTAATGTTTCTACAAAATCTCAAAC  
GGTGATGACCAGTATGTGCGTTCCGGGAAAGATCATGTTAGCACTTTGTTAACTTGGCACATGCATAAGCTTGTGCGAGGTCCCTT  
TCCTGTTGTGAATGCAATGATGAAATCATATGTCAAGTCGAAGCTAAACTTCTCAGGGGTTCAGAAACAACTGTTACTGAGAGAA  
TTTTCAGACAAATATTTTGAATGGGGATAGTGCCATCCCATATATCCAGCCTTATGATATGGGCGAGGGAATCTGCATAATGCT  
TCTGACTTCTATGGTTTGTCTAGCGAGAGGTTCACTACTGCATTGGTGTATCTTTGGCGAAAGACCAGAGGCTTACACATC  
AAGTGATGATCAGATCTTTATTTGATAGGAGGCTGAGTGACCTGGTTGTAAGTGATCCGGAGGAAGCTCTTGCTGTTGGAAAT  
TCCAATCTCATCTGAGCGGCTTGTAAACAATTTATCAGCCCAAAAGTGTTGGTGGGAGGTTGCTGCAGAATTTAAATCTAGA  
TTCTATGTATGGGGGAGGAAGTCCCTCTTCTCACAAGTTTGTATCTGCAGCGCTACACAATGTCAAGTGTAAGAGGCCACATCA  
ACTTTGTGAACAATAGATACAATTCAGATCAAGCCATCGCAAAATGGCGTCCAGTCTCCCTAGTTAATAGATCCAAAGGAGAA  
CACTGGACCTCCATAAGTATGCCAATTTCCCTTTGGATCCATTTCTACTGAATACCAACACTGATGTGAAGATTGGCTGGATGGT  
TCTAGAGGTTACAGAATACAAAGACTCATTGAGGAACCTGTGCTCAATGAACAAGGTTGTAAGAAAGCTTGTAAAGAACTGCA  
TCATAAGCTCAAAAATGGTGAATTTAATGAAGAATTTTCTTAGACCTATTTAACAAGAGATAAAAAGGAGGCCATTTCTCAATGG  
GAGACTTCCCTGGTCTTGAAGAAGATCTGAATCAGTTAGCAGATGTTAAGTGGTGAATTTGAATGAAATGAAATGAAATGAAATG  
GTTTTAAGACAAAAGGTGGTTTATCCATCAGTGATGACTTTCCAGAGGAAAGAAATCCCATTGATCAAGACACTCCAGAACAA  
ACTTTGTAGTAAATTCACAAGGGGTGCACAGAAGCTGCTGTCAGAAAGCAATCAACAAGTCAGCTTCCAGAGTTGATCTCATCTG  
GCTTTATAGGCTTTGCAAACTCTAGGAAGCAGGTGTGTGAGAAACAAAAATAGGGAAAATCTGTATATCAAAAAGCTGCTTGAG  
GATCTAACCCAGATGCCATGTGACAAGAGTTTGCAATCGGGATGGTATAACGCTGTACATTTGTGACAAACAGCTCTCATCCAGA  
AGCCCCACGTGATCATATATGCCTTTTAAAGGCTCTTCTTTGGGACTACATTTGTATTTTATTGAGCAACTCTTTGAGTTGGGTG  
TTTGGGTCTTAGCAGAACCGACCAAGGGGAGAAATAACAGTGAGAACCTAACTCTTAAGCACTTAAACCATGTGATTATGTAGCA  
AGAAAGCCTGAGAGCTCAAGGCTACTGGAGGACAAAGTGAATTTGAACCAAGTGATTCATCTGTGAGGCGGCTATATCCCAAGAT  
CTTTGAGGATCAGCTTCTTCCATTTATGCTGACATGAGCTCAAAAACATGAGGTGGAGTCCAGAAATTAATTCCTTGACCTCT  
GTGTTTTAATGATATTAACCTAGAATCCTTGTCACTCATTTCTCATGTTGTTAAGTGGAAAAGGGATGAACATTACACTGTTCTG  
TTTTCTGACCTTGCCAATTTCTCATCAGCGATCTGACTCCAGTCTGGTGTGTAATTTGTTGTTAGCACAGGGGATGTCTGCAAGAA  
CTTCTTAAACAGGTGATTTTGAATCATTTGTTTCGAGAATTTGTTGCAACAACCAGGACATTAGGCAATTTTTCATGGTTCCCTC  
ATAAAGAAATGATGCCATCTGAAGATGGTGTGAGGCACCTGGGCCCTTTCAATCATTTGTCTCAAAAGGTGGTGAACAAAAATGTG  
GAGAGGCCTATGTTTAGGAATGATTGTCAGTTTGGTTTGGGTGGTTCTCTTACCGAATGGGAGATGTTGTGTGAATGCTGCCAT  
GTTGATTAGGCAGGGCTGACAAACCCAAAGGCATTTAAATCCTTAAAGGATCTGTGGGACTACATGCTCAACTACACAAAAGGGG  
TATTGGAGTTTTCATTTTCAAGTGGACTTTACGCACAATCAGAATAATACTGACTGTTTAAAGGAAATTTTCAATTGATATCTTGGTT  
AGGTGCCAATTACAGAATCCAGGTGTGGCTGAACTTTATCATGCTCTCACCTCTTAAAGGGTGAGATAGATAGAAGAAATGTTGGA  
TGAATGCCTCCACTTACTGAGGACAGACTCTGTCTTCAAGGTGAACGATGGTGTCTTTGATATCAGATCTGAAGAGTTTGAAGATT  
ACATGGAAGATCCCTTGATACTTGGTGATTCTCTTGAGCTTGAGTTGTTGGGCTCCAAAAGAATACTGGATGGGATTAGATCTATT  
GACTTTGAGAGAGTTGGACCTGAGTGGGAGCCTGTGCCACTGACTGTAAGATGGGTGCCCTTTTGAAGGAAGAAACCTTGTCCA  
AAATATCATGTTGTAAGCTTGAGACCAAGGACATGAAAGCTTTCTAGCAGGACTTGAGGGCTATGAAAAGATTAGTGATGCTCTTG  
GGAACCTCTTCTGCATCGATTGAGAACTGGTGAACATTTGTTGGGTTTCAAGATAAGTGAATCCTCCAGGAACATGTATAGAC  
AGATCTATTCTGCTGATTCACCTGTCGCTTTTGCCAGACTGGTTGCCTTTAAGGATTGCAGACTTTGTTTGTAGCAAATCTAGGAG  
CACTTTGATGATGAACAGTGGGGGGCAGGTTTAGACTCAAGGGGAGGTCTGCGACGATTGGCTGGGCGGTCGGTGGCCGAGG  
ACATCGACTGA

SEQ ID NO: 23: LCMV Clone13 LP.

MDEIISSELRLCLNYIEQDERLSRQKLNFLGQREPRMVLIEGLKLLSRCIEIDSADKSGCTHNDKSVETILVESGIVCPGLPLI  
IPDGKYLIDNSLILLECFLVSTPASFEKKFIEDTNKLACIREDLAVAGVTLVPIVDGRCDYDNSFMPWANFKFRDLLFLLEYNS  
QNEKVFESEYFRLESKTTIDKRSMDSMKILKDARSTHNDIMRMCHEGINPNMSCDDVVFINSLSFRFRDLESGLKLRNF  
QKVNPEGLIKEFSELYENLADSDDLTSLREAVESCPLMRFTAEETHGERGSETSTEYERLLSMLNKVSKLKLNTRRQLNLND  
VLCLSSLIKQSKFKGLKNDKHVWGCCYSSVNDRLVSFHSTKEEFIRLLNRKKSQVFRKVSFEELFRASISEFIAKIQKCLLVGL  
SFEHYGLSEHLEQECHIPFTEFENFMKIGAHIMYTKFEDYFNPSTEQKLNQSLRRLSSVCLALTNMKTSSVARLRQNQIGS  
VRYQVVECKEVFCQVIKLDSEYHLLYQKTGESSRCYSIQGPDGHLISFYADPKRFFLPIFSDEVLYNMIDIMISWIRSCPDLDKC  
LTDIEVALRLLLLMLTNPTRNQKQVQSVRYLVMAIVSDFSSTSLMDKLREDLITPAEKVVYKLLRFLIKTIFGTGEKVLSSAKF  
KFMLNVSYLCHLITKETPDRLTDQIKCFEKFEPKSKQGFVFNPKAITEPEECVFYEQMKRFTSKEIDCQHTTPGVNLEAFSLMV  
SSFNNGTLIFKEGKLNLSLDPMTNSGCATALDLASNKSVVNKHLNGERLLEYDFNKLIVSAVSQITESFVRKQKYKLSHSDYKY  
VSKLVSRLVIGSKGEETGRSEDNLAEICFDGEEETSFFKSLEEKVNTTIARYRRGRANDKGDGEKLTNTKGLHHLQLILTGKMAH  
LRKVLSEISFHLVEDFDPCLTNDMDKFICEAVEGSTELSPLYFTSVIKDQCGLDEMAKNLCRKFFSENDWFSCKMMLLQMNAN  
AYSGKYRHMQRQGLNFKFDWDKLEEDVRI SERESNESLSKALSITQCMSAALKNLFCYSEESPTSYTSVGPDSGRKFALSYKEQ  
VGGNRELYIGDLRTKMFTRLI EDYFESFSSFFSGSCLNNDKEFENAILSMTINVREGFLNYSMDHSKWGPMMPCLFLMFLQNLKL  
GDDQYVRSKGDHVSLLTWHMHKLVEVPFPVNVAMMKS YVKS KLKLLRGSETTVTERIFRQYFEMGIVP SHISSLIDMGQGI L HNA  
SDFYGLLSERFINYIGVIFGERPEAYTSDDQITLFDRLSLDLVSDPEEVLVLEFQSHLSGLLNKFS PKSVAGRF AAEFKSR  
FYVWGEVPLLTKFVSAALHNKCKEPHQLCETIDTADQAIANGVPVSLVNSIQRTLDLLKYANFPLDFLLNTNTDVKDWLDG  
SRGYRIQRLIEELCPNETKVVRKLVRLKHLKNGEFNEEFFLDLFNRDKKEATLQLGDLGLLEDLNLQADVNWNLNLMFPPLRM  
VLRQKVVPVSMVFQBERIPSLIKTLQNKLC SKFTRGAQKLLSEAINKSAFQSCISSGFIGLCKTLGSRVNRKNRENLYIKKLE  
DLTDDHVTVCNRDGTLYICDKQSHPEAHRDHICLLRPLLDWYICISLSNSFELGVVWLAEPKTKGKNSENLT LKHLNPNCDYVA  
RKPESSRLLEDKVNQVIQSVRRLYPKIFEDQLPFMSDMS SKNMRWSPRIKFLDLCLVIDINSESLISHVVKWKRDEHYTNL  
FSDLANSHQRS DSSLVDEFVSTRDVCNFKLQVYFESFVRE FVATRTLGNSFWFPHKEMMPSEDEGAEALGPQSFSVSVNVNKNV  
ERPMPFRNDLQFGFGWFSYRMGDVVCNAAMLIRQGLTNP KAFKSLKDLWDYMLNLTGKVLBFSISVDFTHNQNNTDCLRKFS LI FLV  
RCQLQNPGEVALLSCSHLFKEIDRRMLDECLHLLRTDSVFKVNDGVFDIRSEEFEDYMEDPLILGDSLELELLGSKRILDGIRSI  
DFERVGPEWEPVPLTVKMGALFEGRNLVQNIIVKLETGMKVLFLAGLEGYEKISDVLGNLFLHRFRTGEHLLGSEISVILQELCID  
RSILLIPLSLPDWFAFKDCRLCFSKSRSTIMYETVGGFRFLKGRSCDDWLGGVVAEDID

SEQ ID NO: 24: LCMV WE S-Segment 5' UTR.  
GCGCACCGGGGATCCTAGGCTTTTGGATTGCGCTTTCCTTTAGGACAATTGGGTGCTGGATTCTATCCAATAAAAGG

SEQ ID NO: 25: LCMV WE S-Segment 3' UTR.  
TTTGTACACAATGAATTTCCAATAAAAGCGCAATTAATGCCTAGGATCCACTGTGCG

SEQ ID NO: 26: LCMV WE L-Segment 5' UTR.  
GCGCACCGGGGATCCTAGGCGTTTAGTTGCGCTGCTTTATTGCACAGCTTCACTCTGCTAAACCATCAGGAAGTGACCGATCATCA  
GTC

SEQ ID NO: 27: LCMV WE L-Segment 3' UTR.  
TGCGCATCAAAAAGCCTAGGATCCTCGGTGCG

SEQ ID NO: 28: LCMV Clone 13 L-Segment 5' UTR.  
GCGCACCGGGGATCCTAGGCGTTTAGTTGCGCTGTTTGGTTGCACAACTTCTTCGTGAGGCTGTCAGAAGTGACCTGGCTGATA  
GCG

SEQ ID NO: 29: LCMV Clone 13 L-Segment 3' UTR.  
TGCGCATCAAAAAGCCTAGGATCCTCGGTGCG

SEQ ID NO: 30: GP of strain 181h2.  
MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSGLLELTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLD MFRTAFGGKYMRS GWGAGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFC DMLRLIDYNKAALSKFKQDVESALHVFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFS DQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 31: GP of strain 181h5.  
MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSGLLELTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLD MFRTAFGGKYMRS GWGAGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFC DMLRLIDYNKAALSKFKQDVESALHVFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFS DQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 32: GP of strain 181h7.  
MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSGLLELTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLD MFRTAFGGKYMRS GWGAGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQEKTK  
FFTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFC DMLRLIDYNKAALSKFKQDVESALHVFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFS DQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 33: GP of strain 153h7.  
MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSGLLELTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLD MFRTAFGGKYMRS GWGAGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFC DMLRLIDYNKAALSKFKQDVESALHVFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFS DQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 34: GP of strain 122h5.  
MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSGLLELTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLD MFRTAFGGKYMRS GWGAGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFC DMLRLIDYNKAALSKFKQDVESALHVFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFS DQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 35: GP of strain 122h2.  
MGQIVTMFEALPHIIDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSGLLELTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLD MFRTAFGGKYMRS GWGAGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFC DMLRLIDYNKAALSKFKQDVESALHVFK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFS DQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKI PTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 36: GP of strain 122h3.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 37: GP of strain 181h8.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 38: GP of strain 153h3.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMKNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 39: GP of strain 153h8.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQERTK  
FFTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 40: GP of strain 153h6.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQGKTK  
FFTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 41: GP of strain 153h5.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQGKTK  
FFTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 42: GP of strain 156h3.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 43: GP of strain 153h9.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGAGSDGKTTWCSTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQERTK  
FFTRRLAGTFTWTLSDSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTSAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 44: GP of strain 122h4.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANNSHHYISMGSSGLELFTFTNDSILNHNLCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNPNHKAVSCDFNNGITIQYNL

SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 45: GP of strain 181h9.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAMSQCWTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVITIWKR

SEQ ID NO: 46: GP of strain 102h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR

SEQ ID NO: 47: GP of strain 122h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR

SEQ ID NO: 48: GP of strain 129h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR

SEQ ID NO: 49: GP of strain 136h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR

SEQ ID NO: 50: GP of strain 153h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR

SEQ ID NO: 51: GP of strain 154h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR

SEQ ID NO: 52: GP of strain 155h1.

MGQIVTMFEALPHIIDEVINIVIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKTTWCSTSYQYLIIQNRTWENHCRYAGPFGMSRILFAQERTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCMDLRLIDYNKAALSKFKQDVESALHVPK  
TTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKITIWKR



SEQ ID NO: 53: GP of strain 217h1.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIYQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKITWCSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSDQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKTIWKRR

SEQ ID NO: 54: GP of strain 218h1.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIYQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKITWCSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSDQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKTIWKRR

SEQ ID NO: 55: GP of strain 260h1.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIYQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKITWCSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FFTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSDQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKTIWKRR

SEQ ID NO: 56: GP of strain 328h1.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIYQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKITWCSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSDQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKTIWKRR

SEQ ID NO: 57: GP of strain 332h1.

MGQIVTMFEALPHIIDDEVINIVIIIVLIIITSIKAVYNFATCGILALVSFLFLAGRSCGMYGLNGPDIYKGVYQFKSVEFDMSHLNL  
TMPNACSAANSHHYISMGSSGLELFTFTNDSILNHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNHKAVSCDFNNGITIYQYNL  
SFSDPQSAISQCRTFRGRVLDMFRTAFGGKYMRSWGWSGSDGKITWCSQTSYQYLI IQNRTWENHCRYAGPFGMSRILFAQEKTK  
FLTRRLAGTFTWTLSDSGSGVENPGGYCLTKWMILAAELKCFGNTAVAKCNVNHDEEFCDMLRLIDYNKAALSKFKQDVESALHVF  
KTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCWLVTNGSYLNETHFSDQIEQEADNMITEMLRKDYIKRQG  
STPLALMDLLMFSTAYLISIFLHLVKIPTHRHIKGGSCPKPHRLTNKGICSCGAFKVPGVKTIWKRR

SEQ ID NO: 58: GP of strain 181h2.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaatgtgtgacaatttcgccacctgtgggatattagcactggcagcttccttttttgctggttaggtcctgtg  
gcatgtacggccttaaatggtcccgacatctataaagggtttaccagttcaaatacagtgaggatttgatatgtctcacttaaatctg  
acgatgccaatgcgtgctcagccaacaactctcatcactacatcagatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagattagaggaattccaaccacaaagcagtgctctgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggaaccacagagcgctatgagccagtggtggactttcagaggttagagtccttgacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctgggctgggctggcaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtaaccta  
tacaacacaggacttggaacaaactgtagatatgcaggcccttttggtgatgtcagaatcctctttgtctcaggaaaagacaaag  
tttctcactaggagacttgaggcacattcacctggaccctgtcagactcctcaggagtagaaaatccaggtggtttattgctgac  
caaatggatgatccttgctgcagagctcaaatgttttggaatacagctgttgcaaaatgtaattgtaacatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgcccgtgagtaagttcaagcaagatgtagagtcctgcttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatctggaacatgctaagactggtgagactagtgaccgaagtgctggcttgctactaatggctcctacttgatg  
agaccacttttagtgatcaaatcgaacaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaagacaagg  
agtactccttagccttaattggatcctttgatgtttcaacatcagcatatctaatacagcatccttctgcatcttggaagatacc  
aacacatagacacataaaggggggttatgtccaaagccacaccgcttgaccaacaaggggactctgtagttgtggtgcattcaagg  
tgccctggtgtaataactatctggaagacgctga

SEQ ID NO: 59: GP of strain 181h5.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaatgtgtgacaatttcgccacctgtgggatattagcactggcagcttccttttttgctggttaggtcctgtg  
gcatgtacggccttaaatggtcccgacatctataaagggtttaccagttcaaatacagtgaggatttgatatgtctcacttaaatctg  
acgatgccaatgcgtgctcagccaacaactctcatcactacatcagatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagattagaggaattccaaccacaaagcagtgctctgtgattttaacaatggcatcaccattcaatacaacttg

tcattttcggacccacagagcgctatgagccagtggtggactttcagaggtagagtcctggacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctggggctggacaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtaacctaataca  
tacaacacaggactttgggaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
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caaatggatgatccttgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaagggccgctgagtaagttcaagcaagatgtagagtccttgcatgtattcaaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatctggaacatgctaagactggtgagactagtgtacccaagtgtggttgcactaatggctcctacttgatg  
agaccactttagtgtcaaatcgaaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggg  
agtactcctttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatctttctgcatcttgtgaagatacc  
aacacatagacacataaaggggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgctggtgttaaaaactatctggaaaagacgctga

SEQ ID NO: 60: GP of strain 181h7.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaagggtttaccagttcaaatcagtgaggttgatagtgtcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaattttgcaacttaacctccgctttcaacaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagattagaggggaattccaaccacaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggacccacagagcgctatgagccagtggtggactttcagaggtagagtcctggacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtaacctaataca  
tacaacacaggactttgggaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
ttttcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgcttgac  
caaatggatgatccttgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaagggccgctgagtaagttcaagcaagatgtagagtccttgcatgtattcaaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatctggaacatgctaagactggtgagactagtgtacccaagtgtggttgcactaatggctcctacttgatg  
agaccacttttagtgatcaaatcgaaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggg  
agtactcctttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatctttctgcatcttgtgaagatacc  
aacacatagacacataaaggggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgctggtgttaataactatctggaaaagacgctga

SEQ ID NO: 61: GP of strain 153h7.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaagggtttaccagttcaaatcagtgaggttgatagtgtcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaattttgcaacttaacctccgctttcaacaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagattagaggggaatccaaccacaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggacccacagagcgctatgagccagtggtggactttcagaggtagagtcctggacatgtttagaactgcctttggagg  
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acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatctggaacatgctaagactggtgagactagtgtacccaagtgtggttgcactaatggctcctacttgatg  
agaccacttttagtgatcaaatcgaaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggg  
agtactcctttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatctttctgcatcttgtgaagatacc  
aacacatagacacataaaggggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgctggtgttaataactatctggaaaagacgctga

SEQ ID NO: 62: GP of strain 122h5.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaagggtttaccagttcaaatcagtgaggttgatagtgtcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaattttgcaacttaacctccgctttcaacaaaagacttttgaccaaacactcatgagtatagtctcga  
gtctgcacctcagattagaggggaatccaaccacaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggacccacagagcgctatgagccagtggtggactttcagaggtagagtcctggacatgtttagaactgcctttggagg  
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tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgcttgac  
caaatggatgatccttgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaagggccgctgagtaagttcaagcaagatgtagagtccttgcatgtattcaaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatctggaacatgctaagactggtgagactagtgtacccaagtgtggttgcactaatggctcctacttgatg

agaccactttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagatacc  
aacacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagtttggtgcatccaagg  
tgctgtgtgtaaaaactatctggaaaagacgctga

SEQ ID NO: 63: GP of strain 122h2.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatcagtgagggttgatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatctttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagtagaggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcgacccacagagcgctatgagccagtggtggactttcagaggttagagcttgagacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaataca  
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tttctcactaggagacttgaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgacctgagtaggttcaagcaagatgtagagctctgccttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagttctggttagtggacaatgctaagactggtgagactgtgacccaagtgtggcttgctactaatggctcctacttgaatg  
agaccacttttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagatacc  
aacacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagtttggtgcatccaagg  
tgctgtgtgtaataactatctggaaaagacgctga

SEQ ID NO: 64: GP of strain 122h3.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatcagtgagggttgatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatctttgcaacttaacctccgctttcaacaaaaagacttttgaccaaacactcatgagtatagtctcga  
gtctgcacctcagtagtagaggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcgacccacagagcgctatgagccagtggtggactttcagaggttagagcttgagacatgtttagaactgcctttggagg  
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tacaacacaggacttgggaaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaagacaaaag  
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caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgacctgagtaggttcaagcaagatgtagagctctgccttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtctgttagtctggaacatgctaagactggtgagactgtgacccaagtgtggcttgctactaatggctcctacttgaatg  
agaccacttttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagatacc  
aacacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagtttggtgcatccaagg  
tgctgtgtgtaataactatctggaaaagacgctga

SEQ ID NO: 65: GP of strain 181h8.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatcagtgagggttgatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatctttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagtagaggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
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caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgacctgagtaggttcaagcaagatgtagagctctgccttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtctgttagtctggaacatgctaagactggtgagactgtgacccaagtgtggcttgctactaatggctcctacttgaatg  
agaccacttttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagatacc  
aacacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagtttggtgcatccaagg  
tgctgtgtgtaataactatctggaaaagacgctga

SEQ ID NO: 66: GP of strain 153h3.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg

gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgaggtttgatattgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagtagagggaaatCccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
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aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaataca  
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tttctcactaggagacttgaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgacctgac  
caaatggatgaccttgcgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaattgtaattcatgatgaagagttct  
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acaacagtaaatctctgattttccgatcagctgttgatgaAgaatcatctaagagatctaattgggggtaccatactgtaattactc  
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agaccacttttagtgatcaaatcgaaacaagacagataacatgacacagagatgttgaggaaggactacataaaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatctttctgcatcttgtgaagatacc  
aacacatagacacataaaggggcgttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgacctggtgtaaaaaactatctggaaaagacgctga

SEQ ID NO: 67: GP of strain 153h8.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaattttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgaggtttgatattgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
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tttctcactaggagacttgaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgacctgac  
caaatggatgaccttgcgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaattgtaattcatgatgaagagttct  
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acaacagtaaatctctgattttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
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agaccacttttagtgatcaaatcgaaacaagacagataacatgacacagagatgttgaggaaggactacataaaaaagacaagg  
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aacacatagacacataaaggggcgttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgacctggtgtaataaactatctggaaaagacgctga

SEQ ID NO: 68: GP of strain 153h6.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaattttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgaggtttgatattgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
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aaagtcttggtatctggaacatgctaagactggtgagactagtgtacccaagtgtggttgctactaatggctcctacttgtaatg  
agaccacttttagtgatcaaatcgaaacaagacagataacatgacacagagatgttgaggaaggactacataaaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatctttctgcatcttgtgaagatacc  
aacacatagacacataaaggggcgttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgacctggtgtaaaaaactatctggaaaagacgctga

SEQ ID NO: 69: GP of strain 153h5.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaattttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgaggtttgatattgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtatgggaagctctggactggagctaactttcactaacga  
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SEQ ID NO: 70: GP of strain 156h3.

atgggtcagattgtgacaatgtttgaggctttgctccacatcattgatgaggtcatcaacattgtcattattgtgctcattataatcacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtggcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatcagtgagggttgatgtgctcacttaaatctgacgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaaactttcactaacgactccatccttaatacacaattttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcgaagtctgcacctcagattagagggaattccaaccacgaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttgcattttcgacccacagagcgctatgagccagttgtggactttcagaggtagagtttgagacatgtttagaactgcctttggaggaaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaatacacaacacagagacttggaaccactgtagatatgcaggcccttttgggatgtctagaatcctcttctgctcaggaaaagacaaaagtcttcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgaccaaattgatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttctgtgacatgctacgactaattgattacaacaaggccgcctgagtaagttcaagcaagatgtagagttgccttgcatgtattcaaaacaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactcaagttctgtgtattctggaacatgctaagactggtagactagtgtacccaagtgtcgttgctactaatggctcctacttgaatgagaccacttttagtgatcaaatcgacaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggagtagtactccttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagataccaacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagggtgctggtgtataaactatctggaaaagacgctga

SEQ ID NO: 71: GP of strain 153h9.

atgggtcagattgtgacaatgtttgaggctttgctccacatcattgatgaggtcatcaacattgtcattattgtgctcattataatcacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtggcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatcagtgagggttgatgtgctcacttaaatctgacgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaaactttcactaacgactccatccttaatacacaattttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcgaagtctgcacctcagatttagagggaatcccaaccacaaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttgcattttcgacccacagagcgctatgagccagttgtggactttcagaggtagagtttgagacatgtttagaactgcctttggaggaaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaatacacaacacagagacttggaaccactgtagatatgcaggcccttttgggatgtctagaatcctcttctgctcaggaaaggacaaaagtcttcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgaccaaattgatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttctgtgacatgctacgactaattgattacaacaaggccgcctgagtaagttcaagcaagatgtagagttgccttgcatgtattcaaaacaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactcaagttctgtgatctgggaacatgctaagactggtagactagtgtacccaagtgtcgttgctactaatggctcctacttgaatgagaccacttttagtgatcaaatcgacaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggagtagtactccttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagataccaacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagggtgctggtgtataaactatctggaaaagacgctga

SEQ ID NO: 72: GP of strain 122h4.

atgggtcagattgtgacaatgtttgaggctttgctccacatcattgatgaggtcatcaacattgtcattattgtgctcattataatcacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtggcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatcagtgagggttgatgtgctcacttaaatctgacgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaaactttcactaacgactccatccttaatacacaattttgcaacttaacctccgctttcaacaaaaagacttttgaccaaacactcatgagtatagtctcgaagtctgcacctcagatttagagggaatcccaaccacaaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttgcattttcgacccacagagcgctatgagccagttgtggactttcagaggtagagtttgagacatgtttagaactgcctttggaggaaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaatacacaacacagagacttggaaccactgtagatatgcaggcccttttgggatgtctagaatcctcttctgctcaggaaaggacaaaagtcttcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgaccaaattgatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttctgtgacatgctacgactaattgattacaacaaggccgcctgagtaagttcaagcaagatgtagagttgccttgcatgtattcaaaacaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactcaagttctgtgtattctgggaacatgctaagactggtagactagtgtacccaagtgtcgttgctactaatggctcctacttgaatgagaccacttttagtgatcaaatcgacaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggagtagtactccttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatcttctgcatcttgtgaagataccaacatagacacataaaggcggttcattgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagggtgctggtgtataaactatctggaaaagacgctga

SEQ ID NO: 73: GP of strain 181h9.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactgggtcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgagggttgatatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtaggggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagattagagggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggacccacagagcgctatgagccagtggttgactttcagaggtagagtcctggacatggttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaataca  
tacaacacaggacttgggaaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgacctgagtaggttcaagcaagatgtagagtccttgcatgtattcaaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagttctggtatctgaaccatgctaagactggtagactgtgtacccaagtgctggcttgctactaatggctcctactgtaattg  
agaccacttttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatctttctgcatctttgtgaagatacc  
aacacatagacacataaaggggcgttcatgtccaaggccacaccgcttgaccaacaagggtatctgtagttgtggtgcattcaagg  
tgctggtgtataaactatctgaaaagacgctga

SEQ ID NO: 74: GP of strain 102h1.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactgggtcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgagggttgatatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcaaatatgggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagattagagggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggacccacagagcgctataagccagtgtaggactttcagaggtagagtcctggacatggttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaataca  
tacaacacaggacttgggaaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgacctgagtaggttcaagcaagatgtagagtccttgcatgtattcaaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagttctggtatctggaacatgctaagactggtagactgtgtacccaagtgctggcttgctactaatggctcctactgtaattg  
agaccacttttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatctttctgcatctttgtgaagatacc  
aacacatagacacataaaggggcgttcatgtccaaggccacaccgcttgaccaacaagggtatctgtagttgtggtgcattcaagg  
tgctggtgtataaaaactatctgaaaagacgctga

SEQ ID NO: 75: GP of strain 122h1 .

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactgggtcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgagggttgatatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtaggggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagattagagggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg  
tcattttcggacccacagagcgctataagccagtgtaggactttcagaggtagagtcctggacatggttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagcctaataca  
tacaacacaggacttgggaaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgctgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgacctgagtaggttcaagcaagatgtagagtccttgcatgtattcaaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagttctggtatctggaacatgctaagactggtagactagtgacccaagtgctggcttgctactaatggctcctactgtaattg  
agaccacttttagtgatcaaatcgaaagaagcagataacatgatcacagagatgttgaggaaggactacataaaaaagacaagg  
agtactcctttagccttaattggatcttttgatgttttcaacatcagcatatctaatacagcatctttctgcatctttgtgaagatacc  
aacacatagacacataaaggggcgttcatgtccaaggccacaccgcttgaccaacaagggtatctgtagttgtggtgcattcaagg  
tgctggtgtataaaaactatctgaaaagacgctga

SEQ ID NO: 76: GP of strain 129h1.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgagggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactgggtcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaaaggggtttaccagttcaaatacagtgagggttgatatgtctcacttaaatctg  
acgatgcccaatgctgtgctcagccaacaactctcatcactacatcagtaggggaagctctggactggagctaactttcactaacga  
ctccatccttaatacacaatttttgcaacttaacctccgctttcaacaaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagtagattagagggaattccaaccacaaagcagtgctttgtgattttaacaatggcatcaccattcaatacaacttg

tcatttttcggacccacagagcgctataagccagtgtaggactttcagaggtagagtccttgacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagctaatca  
tacaacacaggactttgggaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgcttgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgcctgagtaagttcaagcaagatgtagagtccttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatctggaacatgctaagactggtgagactagtgtacccaagtgtggttgctactaatggctcctacttgatg  
agaccacttttagtgatcaaatcgaaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggg  
agtactcctttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatctttctgcatcttctggaagatacc  
aacacatagacacataaaggggcggttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgctggtgttaaaaactatctggaaaagacgctga

SEQ ID NO: 77: GP of strain 136h1.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaagggtttaccagttcaaatcagtgaggttgatagtctcacttaaatctg  
acgatgcccaatgcgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaaactttcactaacga  
ctccatccttaatacacaatttttgaacttaacctccgctttcaacaaaagacttttgaccaaacactcatgagtatagtctcga  
gtctgcacctcagattagaggggaattccaaccacaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttg  
tcatttttcggacccacagagcgctataagccagtgtaggactttcagaggttagagtccttgacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagctaatca  
tacaacacaggactttgggaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgcttgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgcctgagtaagttcaagcaagatgtagagtccttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatcttggaacatgctaagactggtgagactagtgtacccaagtgtggttgctactaatggctcctacttgatg  
agaccacttttagtgatcaaatcgaaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggg  
agtactcctttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatctttctgcatcttctggaagatacc  
aacacatagacacataaaggggcggttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgctggtgttaaaaactatctggaaaagacgctga

SEQ ID NO: 78: GP of strain 153h1.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaagggtttaccagttcaaatcagtgaggttgatagtctcacttaaatctg  
acgatgcccaatgcgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaaactttcactaacga  
ctccatccttaatacacaatttttgaacttaacctccgctttcaacaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagattagaggggaattccaaccacaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttg  
tcatttttcggacccacagagcgctataagccagtgtaggactttcagaggttagagtccttgacatgtttagaactgcctttggagg  
aaaatacatgagaagtggctggggctgggaggttcagatggcaagaccacttggtgcagccaaacaagctatcagtagctaatca  
tacaacacaggactttgggaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgcttgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
gtgacatgctacgactaattgattacaacaaggccgcctgagtaagttcaagcaagatgtagagtccttgcatgtattcaaa  
acaacagtaaatctctgatttccgatcagctgttgatgaggaatcatctaagagatctaattgggggtaccatactgtaattactc  
aaagtcttggtatcttggaacatgctaagactggtgagactagtgtacccaagtgtggttgctactaatggctcctacttgatg  
agaccacttttagtgatcaaatcgaaagaagcagataaacatgatcacagagatgttgaggaaggactacataaaaagacaaggg  
agtactcctttagccttaattggatcttttgatgtttcaacatcagcatatctaatacagcatctttctgcatcttctggaagatacc  
aacacatagacacataaaggggcggttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
tgctggtgttaaaaactatctggaaaagacgctga

SEQ ID NO: 79: GP of strain 154h1.

atgggtcagattgtgacaatgtttgaggctttgcctcacatcattgatgaggtcatcaacattgtcattattgtgctcattataat  
cacgagcatcaaagctgtgtacaatttcgccacctgtgggatattagcactggcagcttccttttttggctggtaggtcctgtg  
gcatgtacggccttaattggtcccgacatctataaagggtttaccagttcaaatcagtgaggttgatagtctcacttaaatctg  
acgatgcccaatgcgtgctcagccaacaactctcatcactacatcagtagtggaagctctggactggagctaaactttcactaacga  
ctccatccttaatacacaatttttgaacttaacctccgctttcaacaaaagacttttgaccatacactcatgagtatagtctcga  
gtctgcacctcagattagaggggaattccgaccacaagcagtgcttctgtgattttaacaatggcatcaccattcaatacaacttg  
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tacaacacaggactttgggaaaccactgtagatatgcaggcccttttgggatgtctagaatcctctttgctcaggaaaagacaaaag  
tttctcactaggagacttgcaggcacattcacctggaccctgtcagactcctcaggagtagaaaaatccagggtggttattgcttgac  
caaatggatgatccttgctgcagagctcaaatgttttgggaatacagctgttgcaaaatgtaatgtcaatcatgatgaagagttct  
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aacacatagacacataaaggggcggttcatgtccaaagccacaccgcttgaccaacaaggggatctgtagttgtggtgcattcaagg  
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SEQ ID NO: 80: GP of strain 155h1.

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SEQ ID NO: 81: GP of strain 217h1.

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SEQ ID NO: 82: GP of strain 218h1.

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SEQ ID NO: 83: GP of strain 260h1.

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SEQ ID NO: 84: GP of strain 328h1.

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SEQ ID NO: 85: GP of strain 332h1.

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tgctgtgtgtaaaaaactatctggaagacgctga

## CLAIMS

1. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said GP, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue selected from the group consisting of Lys 492→ Ile, Ser 102 → Asn, Phe 122 → Leu, Phe 129 → Ser, Lys 132 → Arg, His 136 → Gln, Asn 152 → Tyr, Ser 153 → Pro, Phe or Tyr, Asn 154 → Asp, His 155 → Leu or Tyr, Lys 156 → Glu, Thr 217 → Ile, Thr 218 → Ile, Lys 256 → Arg, Leu 260 → Ile, Tyr 284 → His, Ala 328 → Ser, Phe 332 → Leu, Val 342 → Ala, and Arg 358→ Lys, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.
2. The virus particle of claim 1, wherein the glycoprotein has at least 95% sequence identity to SEQ ID NO: 4.
3. The virus particle of claim 1 or 2, wherein the GP comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4:
  - (a) Lys 492→ Ile;
  - (b) Ala 211→ Thr;
  - (c) Lys 260→ Phe and Lys 492→ Ile;
  - (d) Ser 153 → Pro and Lys 492→ Ile,;
  - (e) Phe 122 → Leu, His 136 → Gln, and Ser 153 → Pro;
  - (f) Phe 122 → Leu, and Lys 492→ Ile,;
  - (g) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, and Lys 492→ Ile,;
  - (h) Glu 255 →Gly and Lys 492→ Ile,;
  - (i) Ser 153 → Pro and Arg 358→ Lys;
  - (j) Ser 153 → Pro, Lys 256 →Arg, Leu 260 → Phe and Lys 492→ Ile,;
  - (k) Ser 153 → Phe, Glu 255 →Gly, and Leu 260 → Phe;
  - (l) Lys 156 → Glu and Lys 492→ Ile,;
  - (m) Ser 153 → Pro, Lys 256 →Arg, and Leu 260 → Phe;

- (n) Phe 122 → Leu, His 136 → Gln, Ser 153 → Pro, Lys 256 → Arg and Lys 492 → Ile;  
or
  - (o) Glu 379 → Asn and Lys 492 → Ile.
4. The virus particle any one of the preceding claims, wherein said GP has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in any one of SEQ ID NOs: 30-57.
  5. The virus particle of any one of the preceding claims, wherein the virus particle has an increased capacity to enter a human tumor cell as compared to said reference virus particle, or wherein the virus particle has an increased tropism for a human tumor cell as compared to said reference virus particle.
  6. An LCMV GP, wherein the glycoprotein comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue as defined in any one of claims 1-5.
  7. A nucleic acid molecule encoding a LCMV GP of claim 6, wherein the nucleic acid molecule preferably comprises a sequence that has at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NOs: 58-85, or a respective complementary sequence.
  8. A virus particle comprising a glycoprotein (GP) of an arenavirus and/or a nucleic acid encoding said GP, wherein the glycoprotein comprises at least one of the following amino acid residues:

- (a) at the position corresponding to Lys 492 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ile residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (b) at the position corresponding to Ser 102 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Asn residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
- (c) at the position corresponding to Phe 122 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Leu residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (d) at the position corresponding to Phe 129 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Ser residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (e) at the position corresponding to His 136 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Gln residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a His residue at said position;
- (f) at the position corresponding to Asn 152 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Tyr residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (g) at the position corresponding to Ser 153 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Pro, Phe, or Tyr residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ser residue at said position;
- (h) at the position corresponding to Asn 154 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Asp residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (i) at the position corresponding to His 155 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Leu or Tyr residue, wherein the virus particle has an

increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;

- (j) at the position corresponding to Lys 156 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Glu residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (l) at the position corresponding to Thr 217 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ile residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (m) at the position corresponding to Thr 218 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ile residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;
- (n) at the position corresponding to Lys 256 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Arg residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Lys residue at said position;
- (o) at the position corresponding to Leu 260 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Phe residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Leu residue at said position;
- (p) at the position corresponding to Tyr 284 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a His residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Tyr residue at said position;
- (q) at the position corresponding to Ala 328 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Ser residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Ala residue at said position;
- (r) at the position corresponding to Phe 332 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Leu residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Phe residue at said position;

- (s) at the position corresponding to Val 342 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 an Ala residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Val residue at said position; and
  - (t) at the position corresponding to Arg 358 of the GP of LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 a Lys residue, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises a Arg residue at said position.
- 9. A host cell comprising the nucleic acid molecule of claim 7 or a cDNA of the genome of a virus particle of any one of claims 1-5 and 8.
  - 10. A method of producing a virus particle of any one of claims 1-5 and 8 comprising cultivating the host cell of claim 9 under conditions suitable for virus particle formation.
  - 11. A pharmaceutical composition comprising a virus particle of any one of claims 1-5, a GP of claim 6, a nucleic acid molecule of claim 7, or an arenavirus particle of claim 8.
  - 12. A virus particle of any one of claims 1-5, a GP of claim 6, a nucleic acid molecule of claim 7, or an arenavirus particle of claim 8, for use in therapy.
  - 13. The virus particle for the use of claim 12, for use in the treatment of cancer.
  - 14. A use of a virus particle of any one of claims 1-5, a GP of claim 6, a nucleic acid molecule of claim 7, or an arenavirus particle of claim 8, for the manufacture of a medicament, wherein the medicament is preferably for the treatment of cancer.
  - 15. A method of treating a disease comprising administering to a subject in need thereof an effective amount of a virus particle of any one of claims 1-5, a GP of claim 6, a nucleic acid molecule of claim 7, or an arenavirus particle of claim 8, wherein the disease is preferably cancer.

16. A method of producing a virus particle having an increased capacity to enter a tumor cell, comprising:
- (i) Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
    - (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
    - (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
    - (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
    - (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
    - (e) Helix  $\alpha$ 3 as defined by positions 187-199;
    - (f) Loop 3 as defined by positions 200-226;
    - (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
    - (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
    - (i) the H1,H2 domain as defined by positions 1-58; and/or
    - (j) the TM cytoplasmic domain as defined by positions 439-498; and
  - (ii) Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
  - (iii) Assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell, preferably comprising comparing the

virus particle comprising said mutated LCMV strain WE glycoprotein to a value, wherein the reference value is preferably at least as high or higher than the value that is obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

17. A method of producing a virus particle having an increased tropism for a tumor cell, comprising:
- (i) Providing a nucleic acid encoding a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
    - (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
    - (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;
    - (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
    - (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
    - (e) Helix  $\alpha$ 3 as defined by positions 187-199;
    - (f) Loop 3 as defined by positions 200-226;
    - (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
    - (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
    - (i) the H1,H2 domain as defined by positions 1-58; and/or
    - (j) the TM cytoplasmic domain as defined by positions 439-498; and



- (ii) Expressing the mutated LCMV strain WE glycoprotein and further viral proteins to produce a virus particle comprising said mutated LCMV strain WE glycoprotein; and
  - (iii) Assessing the capacity of a virus particle comprising said mutated LCMV strain WE glycoprotein to enter and/or infect a tumor cell and/or a non-tumor cell, preferably comprising comparing the virus particle comprising said mutated LCMV strain WE glycoprotein to a reference value, wherein the reference value is preferably at least as high or higher than the value that is obtained for a virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.
18. The method of claim 16 or 17, wherein the virus particle has increased capacity to enter or an increased tropism for at least one of the following tumor cells: lung tumor cells, such as H1975 or A549, LLC, TC-1, gastrointestinal tumor cells, such as Gist-T1, melanoma cells, such as MaMel86a, MaMel51, A375, B16F10, or RPMI-7951, pancreatic tumor cells, such as 511950, 60590, 511950R, or 60590R, thyroid tumor cells, such as 8305C or C643, sarcoma cells, such as Gist-T1, breast tumor cells, such as HCC1954, cervical tumor cells, such as HeLa, liver tumor cells, such as HepG2, colon tumor cells, such as MC38, Sw620, or Sw480, neuroblastoma cells, such as SK-N-BE(2), and/or prostate tumor cells, such as TrampC2.
19. A virus particle having an increased capacity to enter a tumor cell or having an increased tropism for a tumor cell obtainable by the method of claim 15 or 16.
20. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said GP, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions comprised in
- (a) Strand  $\beta$ 1 N terminal defined by positions 59-89, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 59-78 and 81-87;
  - (b) Strands  $\beta$ 3,  $\beta$ 4, and/or  $\beta$ 5 as defined by positions 90-113, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 90-93, 98-103, and 106-113;

- (c) Helix  $\alpha$  1 and/or  $\alpha$  2 as defined by positions 114-147, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 126-130 and 136-147;
- (d) Loop 1 as defined by positions 148-157, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 148-157;
- (e) Helix  $\alpha$ 3 as defined by positions 187-199;
- (f) Loop 3 as defined by positions 200-226;
- (g) the  $\alpha$ 4,  $\alpha$ 5 domain as defined by positions 245-265, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 245-251 and 253-258;
- (h) the N-Helix as defined by positions 313-373, wherein the at least one mutated amino acid residue is preferably at one or more positions selected from the group consisting of 313-349 and 353-365;
- (i) the H1,H2 domain as defined by positions 1-58; and/or
- (j) the TM cytoplasmic domain as defined by positions 439-498;

wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.

21. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) glycoprotein (GP) and/or a nucleic acid encoding said glycoprotein, wherein the glycoprotein is a mutated LCMV strain WE glycoprotein which comprises in comparison with the wild type LCMV strain WE glycoprotein set forth in SEQ ID NO: 4 at least one mutated amino acid residue at one or more positions selected from the group consisting of 18, 28, 36, 39, 48, 51, 60, 61, 62, 63, 66, 71, 74, 88, 94, 102, 103, 105, 106, 112, 119, 120, 121, 122, 128, 129, 132, 133, 136, 141, 144, 149, 151, 152, 153, 154, 155, 156, 163, 188, 198, 203, 207, 211, 217, 218, 222, 236, 252, 255, 256, 260, 280, 284, 308, 327, 328, 332, 335, 339, 342, 343, 344, 357, 358, 369, 374, 382, 388, 406, 426, 451, 456, 471, 477, 491, and 492, wherein the virus particle has an increased capacity to enter a tumor cell as compared to a reference virus particle that comprises the wild type glycoprotein set forth in SEQ ID NO: 4.