

CLAIMS

What is claimed:

1. An engineered viral particle comprising:
 - i. an engineered envelope comprising a recombinant Ebola virus glycoprotein, or a variant thereof, a gag-pol protein, and an engineered targeting moiety for binding to a target cell; and
 - ii. a nucleic acid molecule encoding a polypeptide of interest.
2. The engineered viral particle of claim 1, wherein the engineered targeting moiety is fused to the Ebola virus glycoprotein.
3. The engineered viral particle of claim 1 or 2, wherein the engineered viral particle is a pseudotyped lentivirus.
4. The engineered viral particle of any one of claims 1 to 3, wherein the Ebola virus glycoprotein comprises a sequence comprising a deletion, a substitution, an insertion, or any combination thereof, as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1.
5. The engineered viral particle of claim 4, wherein the deletion comprises an amino acid deletion of a glycan cap amino acid sequence, a mucin-like domain (MLD) amino acid sequence, or any combination thereof.
6. The engineered viral particle of claim 4 or 5, wherein the deletion comprises a deletion of a glycan cap sequence, a MLD amino acid sequence, or any combination thereof, from or

between positions 213-306, 232-306, 305-484, 213-484, 213-497, or 232-497, as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1.

7. The engineered viral particle of claim 4, wherein the substitution comprises an insertion of a targeting moiety amino acid sequence in place of the glycan cap amino acid sequence, a MLD amino acid sequence, or any combination thereof.

8. The engineered viral particle of claim 4 or 7, wherein the substitution comprises:

an insertion of a targeting moiety amino acid sequence in place of the amino acid sequence from or between positions 213-306 as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1;

an insertion of a targeting moiety amino acid sequence in place of the amino acid sequence from or between positions 305-484 as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1;

an insertion of a targeting moiety amino acid sequence in place of the amino acid sequence from or between positions 213-484 as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1;

an insertion of a targeting moiety amino acid sequence in place of the amino acid sequence from or between positions 232-306 as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1;

an insertion of a targeting moiety amino acid sequence in place of the amino acid sequence from or between positions 213-497 as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1; or

an insertion of a targeting moiety amino acid sequence in place of the amino acid sequence from or between positions 232-497 as compared to a polypeptide comprising an amino acid sequence of SEQ ID NO: 1.

9. The engineered viral particle of any one of claims 1 to 8, wherein the targeting moiety is an scFv, an antigen binding domain, a VHH, a DARPin, an adnectin, an affibody, an affilin, an affimer, an affitin, an alphabody, an anticalin, an aptamer, an armadillo repeat protein-based scaffold, an atrimer, an avimer, a fynomer, a knottin, a kunitz domain peptide, a monobody, a nanofitin, or any combination thereof.

10. The engineered viral particle of any one of claims 1 to 9, wherein the targeting moiety is fused to the Ebola virus glycoprotein via a peptide linker.

11. The engineered viral particle of any one of claims 1 to 10, wherein the targeting moiety binds to a target selected from the group consisting of Stem Cell Factor protein (SCF, KIT-ligand, KL, or steel factor) or a moiety that binds to cKit (CD117), CD4, CD8, CD3, CD5, CD6, CD7, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CXCR3, CD39, CD73, CTLA-4, GITR, LAG-3, LRRC32, Neuropilin-1, and CX3CR1.

12. The engineered viral particle of any one of claims 1 to 11, wherein the targeting moiety is a CD7 or CD8 binding moiety.

13. An engineered viral particle comprising:

i. an engineered envelope comprising an Ebola virus glycoprotein fused or linked to a targeting moiety, and a gag-pol protein, wherein the Ebola virus glycoprotein fused or linked to a targeting moiety comprises the amino acid sequence of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID NO: 9; and

ii. a nucleic acid molecule encoding a polypeptide of interest.

14. The engineered viral particle of claim 13, wherein the engineered viral particle is a pseudotyped lentivirus.

15. The engineered viral particle of claim 13 or 14, wherein the polypeptide of interest is a chimeric antigen receptor (CAR), an antigen, an enzyme, a protein.
16. An Ebola virus glycoprotein comprising a targeting moiety fused or linked to an Ebola virus glycoprotein, wherein the targeting moiety is an insertion in the glycan cap and/or the mucin-like domain (MLD) of the Ebola virus glycoprotein.17. The polypeptide of claim 16, wherein the targeting moiety is fused to the Ebola virus glycoprotein at a position from or between positions 213-306, 232-306, 305-484, 213-484, 213-497, and 232-497, as compared to the Ebola virus glycoprotein polypeptide comprising the amino acid sequence of SEQ ID NO: 1.
18. The engineered viral particle of any one of claims 1 to 17 for use in *in vivo* delivery of a polypeptide of interest to a target cell in a subject in need of delivery, wherein the engineered viral particle delivers the nucleic acid molecule encoding the polypeptide of interest to the cell.
19. A pharmaceutical composition comprising the engineered viral particle of any one of claims 1 to 17, and a pharmaceutically acceptable carrier.
20. The engineered viral particle of any one of claims 1 to 17 for use in treating a disease in a subject, wherein the engineered viral particle expresses the polypeptide of interest in a cell of the subject.