CLAIMS

1. An engineered lentivirus comprising:
   a heterologous ligand displayed on a surface of the lentivirus;
   a fusogen comprising a modified viral envelope protein, wherein the fusogen is capable of fusing the lentivirus to a host cell, wherein the host cell comprises an endogenous receptor for the ligand;
   a reporter protein operably linked to a lentiviral structural protein; and
   a barcoded RNA.

2. The engineered lentivirus of claim 1, wherein:
   (a) the fusogen is or comprises a modified VSV-G viral envelope protein;
   (b) the fusogen comprises a modified VSV-G viral envelope protein, wherein the modified VSV-G viral envelope protein comprises one or more amino acid substitutions at any one of the positions H8, K47, Y209, and R354 of the VSV-G polypeptide;
   (c) the fusogen comprises a modified VSV-G viral envelope protein , wherein the modified VSV-G viral envelope protein comprises a K47Q substitution and a R354A substitution;
   (d) the ligand is or comprises a protein or an epitope;
   (e) the ligand is or comprises a MHC peptide, an antibody, an antigen, a secreted protein, a cell-surface protein, or other form of antigen that is expressed by a cell;
   (f) the ligand is or comprises an antigen, wherein the antigen is an intracellular antigen;
   (g)the ligand is operably linked to an optimized transmembrane domain;
   (h) the ligand is operably linked to an optimized transmembrane domain, wherein the optimized transmembrane domain is transmembrane domain derived from HLA-DRA, HLA-DRB, HLA-A2, ICAM1, CD43, CD162, CD62L, CD49d, or LFA-1;
   (i) the ligand is operably linked to an optimized transmembrane domain and a signal peptide;
   (j) the engineered lentivirus comprises a defective integrase protein;
   (k) the reporter protein is GFP or mNeon;
   (l) the structural protein is a nucleocapsid protein;
   (m) the structural protein is a Gag protein; and/or

(n) the barcoded RNA:

(i) is encapsulated in viral particles;

(ii) encodes the ligand protein;

(iii) encodes a gene of interest to be delivered into host cells;

(iv) is read out by Next-generation sequencing technology; or

(v) comprises a capture sequence.

3. An *in vitro* or *ex vivo* method for identifying:

(a) a ligand-receptor pair, the method comprising:

providing at least one engineered lentivirus of claim 1 or 2;

combining the lentivirus with a population of cells; and

sorting the population of cells based on the presence of the reporter gene, thereby identifying a ligand-receptor pair;

(b) an immunogenic antigen, the method comprising:

providing an engineered lentivirus comprising a heterologous receptor protein displayed on the surface of the lentivirus, a fusogen comprising a modified VSV-G viral envelope protein wherein the fusogen is capable of fusing the lentivirus to a host cell, wherein the host cell comprises a native antigen for the receptor, a reporter transgene operably linked to a lentivirus structural protein, and a barcoded RNA, wherein the RNA encodes antigen information;

combining the lentivirus with the population of cells; and

sorting the population of cells based on the presence of the reporter;

(c) a T-cell receptor and paired pMHC, the method comprising:

providing an engineered lentivirus comprising a pMHC displayed on virus surface, a fusogen comprising a modified VSV-G viral envelope protein wherein the fusogen is capable of fusing the lentivirus to a host cell, wherein the host cell comprises a T-cell receptor for the PMHC, a reporter transgene operably linked to a lentivirus structural protein, and a barcoded RNA;

combining the lentivirus with the population of cells; and

sorting the population of cells based on the presence of the reporter thereby identifying the T-cell receptor;

(d) a B-cell receptor or antibody, the method comprising:

providing an engineered lentivirus comprising an epitope displayed on lentivirus surface wherein the epitope is operably linked with an ICAM1 transmembrane domain, a fusogen comprising a modified VSV-G viral envelope protein wherein the fusogen is capable of fusing the lentivirus to a host cell, wherein the host cell comprises a B-cell receptor for the intracellular epitope, a reporter transgene operably linked to a lentivirus structural protein, and a barcoded RNA;

combining the lentivirus with the population of B cells; and

sorting the population of cells based on the presence of the reporter thereby identifying the B-cell receptor or antibody; or

(e) an antigen for a B-cell receptor, the method comprising:

providing the engineered lentivirus of claim 1 or 2;

combining the lentivirus with the population of B cells; and

sorting the population of cells based on the presence of the reporter thereby identifying the B-cell antigen.

4. The method of claim 3(a), wherein the method comprises:

(a)

(i) providing a pool of engineered lentiviruses, the pool displaying different ligands;

(ii) combining the lentivirus with cells and incubating the virus/cell mixture at about 4°C;

(iii) combining the lentivirus with cells, and incubating the virus/cell mixture at room temperature; or

(iv) combining the lentivirus with cells and incubating the virus/cell mixture at about 37°C;

(b) incubating the virus/cell mixture for about 30 minutes, or about 1 hour or about 2 hours or any period from about 0.5 hours to about 2.5 hours;

(c) a step of single-cell sequencing of the viral RNA to identify the ligand sequence; and/or

(d) a step of single-cell sequencing of the cell's transcriptome to identify the receptor sequence.

5. An *in vitro* or *ex vivo* method of delivering a nucleic acid of interest or a protein of interest to a user-defined target cell, comprising:
providing the engineered lentivirus of claim 1 or 2;
contacting the lentivirus with a cell mixture comprising the target cell, and
delivering the nucleic acid or protein only to the target cell, wherein the target cell expresses a receptor specific to the ligand on the lentivirus surface.

6. The method of claim 5, wherein:
(a) the ligand is modified in order to deliver cargo to the user-defined target cell;
(b) the ligand is modified in order to deliver cargo to the user-defined target cell, wherein the nucleic acid of interest is packaged inside the engineered lentiviral particle;
(c) the ligand is modified in order to deliver cargo to the user-defined target cell, wherein the protein of interest is operably linked to a lentiviral structural protein of the lentivirus; or
(d) the ligand is modified in order to deliver cargo to the user-defined target cell, wherein the protein of interest operably linked to a gag protein.

7. The method of claim 5 or 6, wherein the target cell is:
(a) a mammalian cell;
(b) a human cell;
(c) an immune cell;
(d) a T cell or a B cell; and/or
(e) a primary human blood cell (PBMC).

8. The method of claim 3(b), wherein the method further comprises a step for sequencing of:
(a) the viral RNA to identify the antigen sequence; or
(b) the cell's receptor RNA.

9. The method of claim 3(c), wherein:
(a) the population of cells comprises human primary T-cells;

(b) the pMHC is encoded by a RNA comprising a signal peptide, the PMHC, a G4S linker, b2m gene, a G4S linker and a MH allele in tandem; or

(c) the method further comprises a step for single cell sequencing of the viral RNA to identify the MHC peptide sequence.

10. The method of claim 3(c) or 9, wherein the method further comprises a step for sequencing of the cell's receptor sequence to identify the MHC peptide and T-cell receptor sequence.

11. The method of claim 3(d), wherein:

(a) the antigen is a cell surface membrane protein, an intracellular protein, a secreted protein, or glycosylated protein; and/or

(b) the method further comprises the step of single cell sequencing of the viral RNA to identify the antigen and matching B-cell receptor sequences.

12. A method of single-cell multiomics, comprising:

providing an engineered lentivirus comprising a heterologous ligand displayed on the surface of the lentivirus, a fusogen comprising a modified VSV-G viral envelope protein wherein the fusogen is capable of fusing the lentivirus to a host cell, wherein the host cell comprises an endogenous receptor for the ligand, a reporter transgene operably linked to a lentivirus structural protein, and a RNA, wherein the RNA comprises an antigen sequence and a capture tag for single cell sequencing; and

retrieving transcriptome and phenotype information simultaneously at the single cell level.

13. The method of claim 12, wherein:

(a) the single cells sequencing is a droplet based platform;

(b) the cell's phenotype comprise surface markers by CITE-seq;

(c) the information comprises ligand and receptor sequences;

(d) the single cells multiomics use whole cell as input; or

(e) the single cells multiomics use whole cell as input and comprises a step of reverse transcription.

14. A method for selectively depleting or enriching a target cell population in a cell mixture, the method comprising:

providing (a) an engineered lentivirus according to claim 1 or 2, and (b) a cell mixture comprising

i. a target cell population expressing a receptor specific for the ligand displayed on the surface of the engineered lentivirus, and

ii. a non-target cell population that does not express the receptor;

contacting the engineered lentivirus with the cell population, and delivering the nucleic acid or protein only to the target cell;

adding a reagent that specifically inhibits growth of the target cell population or inhibits growth of the non-target cell population, thereby selectively depleting or enriching the target cell population.

15. The method of claim 14, wherein:

(a) the target cell expresses a herpes simplex virus thymidine kinase (HSV-TK) transgene, and the added reagent comprises or is ganciclovir (GCV);

(b) the target cell expresses shRNA to decrease expression of cell death receptor FAS to prevent cell death of the target population;

(c) the target cell population comprises immune cells;

(d) the target cell population comprises comprise a T cell or a B cell;

(e) the target cell population comprises immune cells, wherein the immune cells are autoreactive immune cells;

(f) the target cell population comprises immune cells, wherein the immune cells are specific for an antigen associated with a health condition;

(g) the target cell population comprises immune cells specific for an antigen associated with a health condition, wherein the health condition is a proliferative disorder, inflammatory disorder, autoimmune disorder, or a microbial infection; and/or

(h) the target cell population comprises immune cells specific for an antigen associated with a cancer, a bacterial infection, a viral infection, or a microfungal infection.