Claims

1. A fusosome comprising:

(a) a lipid bilayer comprising a plurality of lipids derived from a source cell;

(b) a lumen surrounded by the lipid bilayer;

(c) a fusogen that is disposed in the lipid bilayer, wherein the fusogen is a Class 1 viral fusogen or a Class II viral fusogen; and

(d) a membrane protein payload agent that comprises or encodes a chimeric antigen receptor;

wherein the fusosome comprises a targeting domain which localizes the fusosome to a target cell.

2. The fusosome of claim 1, wherein the membrane protein payload is encoded by a nucleic acid that comprises a signal sequence that is heterologous relative to the naturally occurring membrane protein.

3. The fusosome of claim 1 or claim 2, wherein the membrane protein payload is exogenous or overexpressed relative to the source cell.

4. The fusosome of any of claims 1-3, wherein the source cell is a primary cell, a cultured cell, an immortalized cell, or a cell line.

5. The fusosome of any of claims 1-4, wherein the source cell is an endothelial cell, a fibroblast, a blood cell, a stem cell, an embryonic stem cell, a myoblast, a parenchymal cell, an alveolar cell, a neuron, a precursor cell, a progenitor cell, or an immortalized cell.

6. The fusosome of any of claims 1-5, wherein the source cell is an allogeneic source cell which is HLA matched with an HLA of a recipient who will receive administration of the fusosome.

7. The fusosome of any of claims 1-6, wherein the source cell is an autologous source cell that is obtained from a recipient who will receive administration of the fusosome.

8. The fusosome of any of claims 1-7, wherein the source cell is selected from a white blood cell or a stem cell.

9. The fusosome of any of claims 1-8, wherein the source cell is selected from a neutrophil, a lymphocyte, a macrophage, a granulocyte, a mesenchymal stem cell, a bone marrow stem cell, an induced pluripotent stem cell, an embryonic stem cell, or a myeloblast.

10. The fusosome of any of claims 1-9, wherein the fusosome is from a source cell having a modified genome to reduce immunogenicity.

11. The fusosome of claim 10, wherein the modified genome is by genome editing to remove an MHC protein.

12. The fusosome of any of claims 1-11, wherein the fusosome has a diameter that is less than about 0.01% or 1%, of that of the source cell.

13. The fusosome of any of claims 1-12, wherein the Class I viral fusogen or Class II viral fusogen comprises a paramyxovirus fusogen.

14. The fusosome of claim 13, wherein the paramyxovirus fusogen comprises a Nipah virus protein F, a measles virus F protein, a tupaia paramyxovirus F protein, a paramyxovirus F protein, a Hendra virus F protein, a Henipavirus F protein, a Morbilivirus F protein, a respirovirus F protein, a Sendai virus F protein, a rubulavirus F protein, or an avulavirus F protein.

15. The fusosome of any of claims 1-14, wherein the fusogen is active at a pH of 6-8.

16. The fusosome of any of claims 1-15, wherein the fusosome comprises a membrane protein payload agent at a copy number of at least 1,000 copies.

17. The fusosome of any of claims 1-16, wherein the membrane protein payload agent is a membrane protein that is disposed in the fusosome lipid bilayer.

18. The fusosome of any of claims 1-17, wherein the membrane protein payload agent is a nucleic acid, disposed in the fusosome lumen, that encodes a membrane protein.

19. The fusosome of any of claims 1-18, wherein the CAR comprises an antigen binding domain, a transmembrane domain and one, two or three signaling domains.

20. The fusosome of any of claims 1-19, wherein the antigen binding domain is an antibody or antigen-binding portion thereof.

21. The fusosome of claim 20, wherein the antigen binding domain is or comprises an scFv or a Fab.

22. The fusosome of any of claims 19-21, wherein the one, two, or three signaling domains are selected from:

(i) a CD3 zeta domain, or an immunoreceptor tyrosine-based activation motif (ITAM), or functional variant thereof;

(ii) a CD28 domain or functional variant thereof; and

(iii) a 4-1BB domain, or a CD134 domain, or functional variant thereof.

23. The fusosome of any of claims 19-22, wherein the one, two, or three signaling domains comprise a CD3 zeta domain and a 4-1BB domain.

24. The fusosome of any of claims 1-23, wherein the targeting domain binds to a target cell moiety on the target cell.

25. The fusosome of claim 24, wherein the targeting domain is linked to the fusogen.

26. The fusosome of any of claims 1-25, wherein the target cell is in an organism.

27. The fusosome of any of claims 1-26, wherein the target cell is a primary cell isolated from an organism.

28. The fusosome of any of claims 1-27, wherein the target cell is selected from a neutrophil, a lymphocyte, a macrophage, a granulocyte, a mesenchymal stem cell, a bone marrow stem cell, an induced pluripotent stem cell, an embryonic stem cell, or a myeloblast.

29. The fusosome of any of claims 1-28, wherein the target cell is an immune effector cell.

30. The fusosome of claim 29, wherein the target cell is selected from a monocyte, macrophage, neutrophil, dendritic cell, eosinophil, mast cell, platelet, large granular lymphocyte, Langerhans' cell, natural killer (NK) cell, T-lymphocyte, a Gamma delta T cell, or a B- lymphocyte.

31. The fusosome of any of claims 28-30, wherein the target cells is a T lymphocyte, or a natural killer cell.

32. A method of manufacturing a fusosome composition, comprising:

i) providing a plurality of fusosomes according to any of claims 1-31; and ii) formulating the plurality of fusosomes as a pharmaceutical composition suitable for administration to a subject.

33. A fusosome composition comprising a plurality of fusosomes according to any of claims 1-31 for use in treating a disease, disorder, or condition in a subject by delivery of the chimeric antigen receptor payload to a target cell of a subject.

34. The fusosome composition of claim 33, wherein the disease, disorder, or condition is a neoplastic disease, a cancer, an infectious disease or an autoimmune or inflammatory disease, and wherein the CAR comprises an antigen binding domain that targets an antigen characteristic of the disease.

35. Use of a fusosome composition comprising a plurality of fusosomes according to any of claims 1-31 in the manufacture of a pharmaceutical composition for delivery of the chimeric antigen receptor payload to a target cell of a subject having a disease, disorder, or condition, wherein the disease, disorder, or condition is a neoplastic disease, a cancer, an infectious disease or an autoimmune or inflammatory disease, and wherein the CAR comprises an antigen binding domain that targets an antigen characteristic of the disease, disorder, or condition.