Background

[0004] Various strategies are available for stimulating T cell populations in vitro, including for expanding antigen-specific T cells in vitro for use in adoptive cellular immunotherapy or cancer therapy in which infusions of such T cells have been shown to have anti-tumor reactivity in a tumor-bearing host or for use to treat viral infections. Improved strategies are needed for expanding cell populations in vitro, including for research, diagnostic and therapeutic purposes.

Summary

[0005] Provided herein are an oligomeric particle reagents comprising a plurality of streptavidin or streptavidin mutein molecules, wherein the size of the oligomeric particle reagent comprises i) a radius, e.g., a hydrodynamic radius, of greater than 25 nm, ii) a molecular weight of at least 5 x 10^6 g/mol; and/or (iii) at least 100 streptavidin or streptavidin mutein tetramers per oligomeric particle reagent.

[0005a] In one aspect, the present disclosure refers to an oligomeric particle reagent comprising a plurality of streptavidin or streptavidin mutein molecules, wherein the oligomeric particle reagent is soluble and comprises between 1,500 and 7,500 tetramers or streptavidin or a streptavidin mutein.

[0006] In particular examples of any of the oligomeric particle reagents provided herein, the streptavidin or streptavidin mutein molecules bind to or are capable of binding to biotin, a biotin analog (e.g. desthiobiotin, iminobiotin) or to a streptavidin binding peptide (e.g. Strep-tagII (WSHPQFEK, SEQ ID NO:8)). In certain examples of any of the oligomeric particle reagents provided herein, the streptavidin or streptavidin mutein molecules reversibly bind to or are capable of reversibly binding to biotin, a biotin analog or to a streptavidin binding peptide (e.g. Strep-tagII (WSHPQFEK, SEQ ID NO:8)). In some examples of any of the oligomeric particle reagents provided herein, the oligomeric particle reagent comprises a plurality of streptavidin mutein molecules, wherein the streptavidin mutein molecules comprise the amino acid sequence Va1^{44}-Thr^{45}-Ala^{46}-Arg^{47} or lle^{44}-Gly^{45}-Ala^{46}-Arg^{47} at sequence positions corresponding to positions 44 to 47 with reference to positions in streptavidin in the sequence of amino acids set forth in SEQ ID NO: 1.

[0007] In particular examples of any of the oligomeric particle reagents provided herein, the streptavidin or streptavidin mutein molecules bind to or are capable of binding to biotin, avidin, a biotin analog or mutein, an avidin analog or mutein, and/or a biologically active fragment thereof. In certain examples of any of the oligomeric particle reagents provided herein, the streptavidin or streptavidin mutein molecules reversibly bind to or are capable of reversibly binding to biotin, avidin, a biotin analog or mutein, an avidin analog or mutein,

of the plurality the oligomer particles does not increase by more than 10% when stored at about or below 4°C for at least one week. In some examples of any of the compositions provided herein, the average radius of the plurality of the oligomer particles does not increase by more than 10% when stored at about or below 4°C for at least 3 weeks. In particular examples of any of the compositions provided herein, the average radius of the plurality of the oligomer particles does not increase by more than 10% when stored at about or below 4°C for at least 9 weeks, at least 27 weeks, or at least 46 weeks. In particular examples, the average radius of the plurality of the oligomer particles does not increase by more than 10% when stored at, at about, or below -20°C, -30°C, -40°C, -50°C, -60°C, -70°C,or -80°C, for at least 1 week, 3 weeks, 9 weeks, 27 weeks, or 46 weeks.

[0027] Provided herein are methods for producing an oligomeric particle reagent comprising streptavidin or a streptavidin mutein, the method comprising: incubating a plurality of activated streptavidin or streptavidin mutein molecules comprising a thiol-reactive functional group capable of reacting with a thiol functional group and a plurality of thiolated streptavidin or streptavidin mutein molecules comprising one or more thiol functional group, thereby generating oligomeric streptavidin or streptavidin mutein particles; separating the oligomeric particles from monomer and/or smaller oligomeric molecules; and contacting the oligomeric particle with a stabilizing agent, thereby producing the oligomeric particle reagent.

[0028] In some examples of any of the methods provided herein, the plurality of activated streptavidin or streptavidin mutein molecules is generated by incubating a first plurality of streptavidin or streptavidin mutein molecules with an activation agent that is capable of converting one or more amines to a thiol-reactive functional group. In particular examples of any of the methods provided herein, the plurality of thiolated streptavidin or streptavidin mutein molecules is generated by incubation of a second plurality of streptavidin or streptavidin mutein molecules with a thiolating agent that adds or is capable of adding a thiol functional group to one or more lysine residue.

[0029] In another example, the present disclosure refers to a method for producing oligomeric particle reagents, the method comprising: (a) incubating a first plurality of streptavidin or streptavidin mutein molecules with an activation agent under conditions to convert one or more amines to a thiol-reactive group capable of reacting with a thiol functional group, thereby generating a plurality of activated streptavidin or streptavidin mutein molecules; (b) incubating a second plurality of streptavidin or streptavidin mutein molecules with a thiolating agent that adds or is capable

molecules and the activated streptavidin or streptavidin mutein molecules, the method comprises (i) removing the activation agent from the composition comprising the activated streptavidin or streptavidin mutein molecules; and/or (ii) removing the thiolating agent from the composition comprising the thiolated streptavidin or streptavidin mutein molecules. .

[0040] In certain examples of any of the methods provided herein wherein the incubation of the plurality of activated streptavidin or streptavidin mutein molecules and the plurality of thiolated streptavidin or streptavidin mutein molecules is initiated within 15 minutes after the incubating of the second plurality of streptavidin molecules with the thiolating agent is ended and/or after the removing of the thiolating agent from composition comprising the thiolated streptavidin or streptavidin mutein molecules..

[0041] Provided herein are methods producing oligomeric particle reagents, comprising: incubating a first plurality of streptavidin or streptavidin mutein molecules with Succinimidyl-6-[(β-maleimidopropionamido)hexanoate (SMPH) for or for about 1 hour at a pH of or of about 7.2, thereby generating a plurality of activated streptavidin or streptavidin mutein molecules comprising a maleimide thiol-reacting functional group; incubating a second plurality of streptavidin or streptavidin mutein molecules with 2-iminothiolane for or for about 1 hour at a pH of between 7.5 and 8.5, inclusive, thereby generating a plurality of thiolated streptavidin molecules comprising one or more thiol functional groups; and incubating the plurality of activated streptavidin or streptavidin mutein molecules with the plurality of thiolated streptavidin molecules for or for about 1 hour at a pH of or of about 7.2, thereby generating a composition comprising the oligomeric particle reagents; wherein the incubating of the plurality of activated streptavidin molecules with the plurality of thiolated streptavidin molecules is initiated within 10 minutes after the incubation of the second plurality of streptavidin molecules with 2-iminothiolane ends.

[0042] In some examples of any of the methods provided herein the method further comprises contacting the oligomeric particle reagents with a stabilization agent. In particular examples of any of the methods provided herein the stabilization agent reduces an amount of N-substituted iminothiolane present on lysine residues of the oligomeric particle reagents. In certain examples of any of the methods provided herein the stabilization agent reduces an amount of N-substituted iminothiolane present on lysine residues of the oligomeric particle reagents by at least 25%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%,

or at least 95%. In some examples of any of the methods provided herein the stabilization agent comprises hydroxylamine.

[0043] In particular examples of any of the methods provided herein the oligomeric particle reagents have a radius of less than 150 nm. Certain examples of any of the methods provided herein further comprise filter sterilizing the oligomeric particle reagents. In some examples of any of the methods provided herein the oligomeric particle reagents are separated from the monomer or smaller oligomeric streptavidin or streptavidin mutein molecules by size exclusion chromatography. In particular examples of any of the methods provided herein, the size exclusion limit is greater than or greater than about 100 kDa, 500 kDa, 750 kDa, 1000 kDa or 2000 kDa. In certain examples of any of the methods provided herein, the size exclusion limit is from or from about 500 kDa to 1000 kDa. In some examples of any of the methods provided herein, the size exclusion limit is or is about 750 kDa.

[0044] Particular examples of any of the methods provided herein comprise collecting one or more fractions comprising the void volume, thereby separating oligomeric particle reagents from the monomer or smaller oligomeric streptavidin or streptavidin mutein molecules. In certain examples the methods further comprise storing the oligomeric particle reagents at a temperature at about or below 4°C, at about or below -20°C, or about or below -80°C. In some examples the methods further comprise mixing the oligomeric particle reagents with one or more agents under conditions to reversibly bind the one or more agents to the oligomeric particle reagents.

[0045] Also provided herein are methods of multimerizing one or more agents to an oligomeric particle reagent, the method comprising mixing an oligomeric particle reagent produced by the methods provided herein with one or more agents under conditions to reversibly bind the one or more agents to the oligomeric particle reagents. In particular examples of any of the methods provided herein, the one or more agents comprise a binding partner, wherein the binding partner is capable of binding to one or more binding site on the oligomeric particle reagent. In certain examples of any of the methods provided herein, the binding partner comprises a streptavidin-binding peptide.

[0046] In some examples of any of the methods provided herein, the binding partner comprises a streptavidin-binding peptide selected from the group consisting of Trp-Ser-His-Pro-Gln-Phe-Glu-Lys (SEQ ID NO: 8), Trp-Ser-His-Pro-Gln-Phe-Glu-Lys-$(GlyGlyGlySer)_3$-

[0053] In particular examples of any of the methods provided herein, the one or more agents comprises a selection agent, wherein the selection agent binds to or is capable of binding to a selection marker that is expressed on the surface of a target cell. In certain examples of any of the methods provided herein, the target cell is an immune cell. In some examples of any of the methods provided herein, the target cell is a lymphocyte or an antigen-presenting cell. In particular examples of any of the methods provided herein, the target cell is a T cell, B cell, NK cell, macrophage or dendritic cell. In certain examples of any of the methods provided herein, the target cell is a T cell. In some examples of any of the methods provided herein, the selection marker is CD25, CD28, CD62L, CCR7, CD27, CD127, CD3, CD4, CD8, CD45RA, and/or CD45RO.

[0054] Particular examples are directed to a composition comprising oligomeric particle reagents produced by the method of any of example provided herein. In another example, the present disclosure refers to a composition comprising a plurality of the oligomeric particle reagents produced by the method as disclosed herein. Certain examples are directed to an article of manufacture, comprising the oligomeric particle reagent of any of examples provided herein or the composition of any of examples provided herein.

[0054a] In another aspect, the present disclosure refers to an article of manufacture, comprising the oligomeric particle reagent as disclosed herein, or the composition comprising a plurality of oligomeric reagents as disclosed.

[0055] Provided herein are methods for modulating cells, the method comprising incubating a cell composition comprising target cells in the presence of the oligomeric particle reagent of any of examples provided herein or in the presence of the composition of any of examples provided herein, thereby modulating the target cells. In some examples of any of the methods provided herein, modulating the target cells comprises activating, enriching, and/or expanding the target cells.

[0055a] In another aspect, the present disclosure refers to a method for modulating cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising target cells in the presence of the oligomeric particle reagent as disclosed herein, or the composition comprising a plurality of oligomeric particle reagents as disclosed herein.

[0056] Provided herein are methods for culturing cells, the method comprising incubating a cell composition comprising target cells in the presence of the oligomeric particle reagent of any of examples provided herein or in the presence of the composition of any of examples provided herein. In certain examples of any of the methods provided herein, the oligomeric particle reagent comprises are reversibly bound to one or more agents. In particular examples of any of the methods provided herein, the one or more agents binds or is capable of binding to a molecule expressed on the surface of a target cell. In some examples of any of the methods provided herein, the one or more agents comprise an antibody, optionally a Fab.

[0056a] In another aspect, the present disclosure refers to a method for culturing cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising target cells in the presence of the oligomeric particle reagent as disclosed herein, or the composition comprising a plurality of oligomeric particle reagents as disclosed herein.

[0057] In certain examples of any of the methods provided herein, the one or more agents is a receptor binding-agent that binds to or is capable of binding to a receptor expressed on the surface of a target cell. In particular examples of any of the methods provided herein, the receptor binding agent is or comprises a stimulatory agent capable of binding to a molecule on the surface of a target cell, thereby inducing or modulating a signal in the target cell.

[0058] In some examples of any of the methods provided herein, the receptor-binding agent is capable of initiating a TCR/CD3 complex-associated signal in T cells, binds to a member of a TCR/CD3 complex; and/or specifically binds to CD3. In certain examples of any of the methods provided herein, the stimulatory agent is a first receptor-binding agent and the method further comprises reversibly binding to the oligomeric particle reagent a second receptor-binding agent, wherein the second receptor-binding agent is capable of specifically binding to a second molecule on the surface of the target cell, which binding to the second molecule is optionally capable of inducing or modulating a signal in the target cells.

[0059] In particular examples of any of the methods provided herein, the second receptor-binding agent specifically binds to a costimulatory molecule, accessory molecule, immune checkpoint molecule, is a member of the TNF family or the TNF family receptor, cytokine receptor, chemokine receptor, or is or comprises an adhesion molecule or a factor that induces cytokine production, chemokine production and/or expression of an adhesion molecule. In some examples of any of the methods provided herein, the receptor-binding agent specifically binds to a costimulatory molecule, accessory molecule, immune checkpoint molecule, is a member of the TNF family or the TNF family receptor, cytokine receptor, chemokine receptor, or is or comprises an adhesion molecule or a factor that induces cytokine production, chemokine production and/or expression of an adhesion molecule.

[0060] In certain examples of any of the methods provided herein, the receptor-binding agent (second receptor-binding agent) binds to a costimulatory or accessory molecule and the costimulatory or accessory molecule is selected from CD28, CD90 (Thy-1), CD95 (Apo-/Fas), CD137 (4-1BB), CD154 (CD40L), ICOS, LAT, CD27, OX40 or HVEM. In particular examples of any of the methods provided herein, the receptor-binding agent (second receptor-binding agent) specifically binds to a cytokine receptor and the cytokine receptor is selected from among IL-2R, IL-1R, IL-15R, IFN-gammaR, TNF-alphaR, IL-4R, IL-10R,

CLAIMS

WHAT IS CLAIMED:

1. An oligomeric particle reagent comprising a plurality of streptavidin or streptavidin mutein molecules, wherein the oligomeric particle reagent is soluble and comprises between 1,500 and 7,500 tetramers of streptavidin or a streptavidin mutein.

2. The oligomeric particle reagent of claim 1, wherein the plurality of streptavidin or streptavidin mutein molecules reversibly bind to biotin, a biotin analog or a streptavidin-binding peptide.

3. The oligomeric particle reagent of claim 1 or claim 2, wherein the oligomeric particle reagent comprises streptavidin mutein molecules and each of the streptavidin mutein molecules comprises the amino acid sequence $Va1^{44}$-Thr^{45}-Ala^{46}-Arg^{47} or Ile^{44}-Gly^{45}-Ala^{46}-Arg^{47} at sequence positions corresponding to positions 44 to 47 with reference to positions in streptavidin in the sequence of amino acids set forth in SEQ ID NO: 1.

4. The oligomeric particle reagent of any of claims 1-3, wherein the oligomeric particle reagent comprises streptavidin mutein molecules and each of the plurality of streptavidin mutein molecules comprises:

a) the sequence of amino acids set forth in any of SEQ ID NOS: 3-6, 27, 28, 60, or 61;

b) a sequence of amino acids that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to any of SEQ ID NOS: 3-6, 27, 28, 60, or 61 and contains the amino acid sequence corresponding to $Va1^{44}$-Thr^{45}-Ala^{46}-Arg^{47} or Ile^{44}-Gly^{45}-Ala^{46}-Arg^{47} at sequence positions corresponding to positions 44 to 47 with reference to positions in streptavidin in the sequence of amino acids set forth in SEQ ID NO: 1 and/or reversibly binds to biotin, a biotin analog or a streptavidin-binding peptide; or

c) a functional fragment of a) or b) that reversibly binds to biotin, a biotin analog or a streptavidin-binding peptide.

5. The oligomeric particle reagent of any of claims 1-4, wherein the oligomeric particle reagent comprises streptavidin mutein molecules and each of the plurality of

streptavidin mutein molecules comprises the sequence of amino acids set forth in any of SEQ ID NOS: 3-6, 27, 28, 60, or 61.

6. The oligomeric particle reagent of any of claims 1-5, wherein the oligomeric particle reagent comprises streptavidin mutein molecules and each of the plurality of streptavidin mutein molecules comprises the sequence of amino acids set forth in SEQ ID NO: 6.

7. The oligomeric particle reagent of any of claims 1-6, wherein the oligomeric particle reagent comprises between between 2,000 and 5,000, between 2,000 and 4,000, between 2,000 and 3,500, or between 2,000 and 3,000 streptavidin or streptavidin mutein tetramers.

8. The oligomeric particle reagent of any of claims 1-7, wherein the oligomeric particle reagent comprises between 2,000 and 3,000 streptavidin or streptavidin mutein tetramers.

9. The oligomeric particle reagent of any of claims 1-8, wherein the oligomeric particle reagent comprises a radius of between 50 nm and 150 nm, between 75 nm and 125 nm, between 80 nm and 140 nm, between 85 nm and 135 nm, between 80 nm and 120 nm, between 80 nm and 115 nm, or between 90 nm and 110 nm, each inclusive.

10. The oligomeric particle reagent of any of claims 1-9, wherein the oligomeric particle reagent comprises a radius of between 90 nm and 110 nm, inclusive.

11. The oligomeric particle reagent of any of claims 1-10, wherein the plurality of streptavidin or streptavidin mutein comprise lysine residues, wherein less than 20%, 10%, 5%, 1%, of the lysine residues comprise N-substituted iminothiolane.

12. The oligomeric particle reagent of any of claims 1-11, wherein the oligomeric particle reagent comprises one or more agents, wherein each of the one or more agents comprises a streptavidin-binding peptide and the streptavidin-binding peptide is reversibly bound to a binding site of the streptavidin or streptavidin mutein.

13. The oligomeric particle reagent of claim 12, wherein the streptavidin-binding peptide is selected from the group consisting of Trp-Arg-His-Pro-Gln-Phe- Gly-Gly (SEQ ID NO: 7), Trp-Ser-His-Pro-Gln-Phe-Glu-Lys (SEQ ID NO: 8), SAWSHPQFEKGGGSGGGSGGGSWSHPQFEK (SEQ ID NO: 15), SAWSHPQFEKGGGSGGGSGGGSAWSHPQFEK (SEQ ID NO: 16), Trp-Ser-His-Pro-Gln-Phe-Glu-Lys-$(GlyGlyGlySer)_3$-Trp-Ser-His-Pro-Gln-Phe-Glu-Lys (SEQ ID NO: 17), Trp-Ser-His-Pro-Gln-Phe-Glu-Lys-$(GlyGlyGlySer)_2$-Trp-Ser-His-Pro-Gln-Phe-Glu-Lys (SEQ ID NO:18) and Trp-Ser-His-Pro-Gln-Phe-Glu-Lys-$(GlyGlyGlySer)_2$Gly-Gly-Ser-Ala-Trp-Ser-His-Pro-Gln-Phe-Glu-Lys (SEQ ID NO: 19).

14. The oligomeric particle reagent of claim 12 or claim 13, wherein the streptavidin-binding peptide is SAWSHPQFEKGGGSGGGSGGGSAWSHPQFEK (SEQ ID NO: 16).

15. The oligomeric particle reagent of any of claims 12-14, wherein the one or more agents is or comprises an antibody or an antigen-binding fragment thereof.

16. The oligomeric particle reagent of claim 15, wherein the one or more agents is or comprises a monovalent antibody fragment.

17. The oligomeric particle reagent of claim 15 or claim 16, wherein the one or more agents is or comprises a Fab.

18. The oligomeric particle reagent of any of claims 12-17, wherein the one or more agents is a receptor-binding agent comprising an antibody or antigen-binding fragment thereof or a proteinaceous binding molecule with antibody-like functions that binds to a receptor expressed on the surface of a target cell.

19. The oligomeric particle reagent of claim 18, wherein the receptor-binding agent is a stimulatory agent that binds to a molecule on the surface of the target cell, wherein binding induces a signal in the target cell.

20. The oligomeric particle reagent of claim 18 or claim 19, wherein the receptor-binding agent initiates a TCR/CD3 complex-associated signal in T cells, binds to a member of a TCR/CD3 complex, and/or specifically binds to CD3.

21. The oligomeric particle reagent of claim 19 or claim 20, wherein the stimulatory agent is a first receptor-binding agent and the oligomeric particle reagent comprises a second receptor-binding agent comprising an antibody or antigen-binding fragment thereof or a proteinaceous binding molecule with antibody-like functions that binds to a costimulatory molecule on the surface of the target cell, wherein binding to the costimulatory molecule induces or modulates a signal in the target cells.

22. The oligomeric particle reagent of claim 21, wherein the costimulatory molecule is CD28.

23. The oligomeric particle reagent of any of claims 12-22, wherein the one or more agents comprises an anti-CD3 antibody or antigen-binding fragment thereof and an anti-CD28 antibody or antigen-binding fragment thereof.

24. The oligomeric particle reagent of any of claims 12-23, wherein the one or more agents is or comprises an anti-CD3 Fab and an anti-CD28 Fab.

25. A composition comprising a plurality of the oligomeric particle reagent of any of claims 1-24.

26. The composition of claim 25, wherein:
the plurality of oligomeric particle reagents comprises an average radius of between 50 nm and 150 nm, between 75 nm and 125 nm, between 80 nm and 140 nm, between 85 nm and 135 nm, between 80 nm and 120 nm, between 80 nm and 110 nm, or between 90 nm and 110 nm, inclusive; or the plurality of oligomeric particle reagents comprise an average radius of 90 nm ±15 nm, 95 nm ± 20-25 nm, or 97 ± 10 nm.

27. The composition of claim 25 or claim 26, wherein the plurality of oligomeric particle reagents comprises an average radius of between 90 nm and 110 nm, inclusive.

28. The composition of any of claims 25-27, wherein:

at least 95% of the plurality of oligomeric particle reagents comprise a radius of between 50 and 150 nm, between 70 nm and 140 nm, between 70 and 130 nm, between 70 and 100 nm, between 80 nm and 140 nm, between 85 nm and 135 nm, between 80 nm and 120 nm, between 80 nm and 115 nm, between 80 nm and 110 nm, between 80 nm and 100 nm, between 85 nm and 115 nm, between 90 and 120 nm, or between 90 nm and 110 nm; and/or

at least 95% of the plurality of oligomeric particle reagents comprise a radius between ± 50%, ± 25%, ± 20%, ± 15%, ± 10%, and/or ± 5% of the average and/or the median radius of the plurality of oligomeric particle reagents.

29. The composition of any of claims 25-28, wherein the plurality of oligomeric particle reagents comprising an average radius of between 80 nm and 115 nm and wherein at least 95% of the oligomeric particle reagents comprise a radius between ± 25% of the average radius.

30. The composition of any of claims 25-29, wherein the plurality of oligomeric particle reagents comprises an average number of streptavidin or streptavidin mutein tetramers per oligomeric particle reagent of between 1,500 and 7,500, between 2,000 and 5,000, between 2,000 and 4,000, between 2,000 and 3,500 or between 2,000 and 3,000, each inclusive.

31. The composition of any of claims 25-30, wherein the plurality of oligomeric particle reagents comprises an average number of streptavidin or streptavidin mutein tetramers per oligomeric particle reagent of between 2,000 and 3,000, inclusive.

32. The composition of any of claims 25-31, wherein:

at least 95% of the plurality of oligomeric particle reagents comprise between 1,500 and 4,000, between 1,500 and 3,500, or between 2,000 and 4,500 streptavidin or streptavidin mutein tetramers; and/or

at least 95% of the plurality of oligomeric particle reagents comprise a number of streptavidin or streptavidin mutein tetramers that is between ± 50%, ± 25%, ± 20%, ± 15%, ± 10%, and/or ± 5% of the average and/or the median number of streptavidin or streptavidin mutein tetramers of the plurality of oligomeric particle reagents.

33. The composition of any of claims 25-32, wherein the average radius of the plurality of oligomer particles does not increase by more than 25% or 10% when stored at about or below -80°C, at about or below -20°C, and/or at about or below 4°C for at least 1 week.

34. An article of manufacture, comprising the oligomeric particle reagent of any of claims 1-24, or the composition comprising a plurality of oligomeric particle reagents of any of claims 25-33.

35. A method for modulating cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising target cells in the presence of the oligomeric particle reagent of any of claims 1-24, or the composition comprising a plurality of oligomeric particle reagents of any of claims 25-33, thereby modulating the target cells.

36. A method for culturing cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising target cells in the presence of the oligomeric particle reagent of any of claims 1-24, or the composition comprising a plurality of oligomeric particle reagents of any of claims 25-33.

37. The method of claim 35 or claim 36, wherein the oligomeric particle reagent comprises one or more receptor-binding agents reversibly bound to the streptavidin or streptavidin mutein of the oligomeric particle reagent, wherein the one or more receptor-binding agents comprise an antibody or antigen-binding fragment thereof or a proteinaceous binding molecule with antibody-like functions that binds to a receptor expressed on the surface of a target cell.

38. The method of any of claims 35-37, wherein the receptor-binding agent is a stimulatory agent that binds to a molecule on the surface of the target cell, wherein binding induces a signal in the target cell.

39. The method of any of claims 35-38, wherein the target cell is a T cell.

40. The method of any of claims 37-39, further comprising disrupting the reversible binding between the one or more agents and the oligomeric particle reagent, said disrupting comprising introducing to the target cells a substance that reverses or competes with the bond between the one or more agents and the oligomeric particle reagent.

41. The method of claim 40, wherein the substance comprises biotin or a biotin analog.

42. The method of claim 40 or claim 41, wherein the substance comprises D-biotin.