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 a~~n~~ multimerized oligomeric particle reagent that is soluble and ~~comprising~~ comprises (i) an oligomer of ~~a plurality of streptavidin or streptavidin mutein molecules, wherein the oligomeric particle reagent is soluble and comprises~~ between 2,000 and 4,000 ~~1,500 and 7,500~~ tetramers ~~or~~ of ~~streptavidin or~~ a streptavidin mutein molecule, (ii) a first receptor-binding agent comprising an anti-CD3 Fab and a first streptavidin-binding peptide, and (iii) a second receptor-binding agent comprising an anti-CD28 Fab and a second streptavidin-binding peptide, wherein the first and second streptavidin-binding peptides are each reversibly bound to one or more binding sites of the streptavidin mutein molecules.

[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,

[0020] In particular examples of any of the oligomeric particle reagents provided herein, the oligomeric particle reagent comprises a molecular weight of at least 1 x 10^7 g/mol, at least 5 x 10^7 g/mol, or at least 1 x 10^8 g/mol. In certain examples of any of the oligomeric particle reagents provided herein, the oligomeric particle reagent comprises a molecular weight of between 1 x 10^6 g/mol and 1 x 10^{10} g/mol, between 1 x 10^7 g/mol and 1 x 10^9 g/mol, between 5 x 10^7 g/mol and 5 x 10^8 g/mol, between 1 x 10^8 g/mol and 5 x 10^8 g/mol, or between 1 x 10^8 g/mol and 2 x 10^8 g/mol. In some examples of any of the oligomeric particle reagents provided herein, the oligomeric particle reagent comprises at least 100 streptavidin or streptavidin mutein tetramers, at least 500 streptavidin or streptavidin mutein tetramers, at least 1,000 streptavidin or streptavidin mutein tetramers, at least 1,500 streptavidin or streptavidin mutein tetramers, or at least 2,000 streptavidin or streptavidin mutein tetramers.

[0021] In particular examples of any of the oligomeric particle reagents provided herein, the oligomeric particle reagent comprises between 100 and 50,000 streptavidin or streptavidin mutein tetramers, between 1,000 and 20,000 streptavidin or streptavidin mutein tetramers, between 1,000 and 10,000 streptavidin or streptavidin mutein tetramers, or between 2,000 and 5,000 streptavidin or streptavidin mutein tetramers. In certain examples of any of the oligomeric particle reagents provided herein, the plurality of streptavidin or streptavidin muteins comprise lysine residues, wherein less than 20%, 10%, 5%, 1%, of the lysine residues comprise N-substituted iminothiolane.

[0022] Provided herein is a composition comprising one or more oligomeric particle reagents. In some examples of any of the compositions provided herein, the one or more oligomeric particle reagents is a plurality of oligomeric particle reagents. In particular examples of any of the compositions provided herein, the plurality of oligomeric particle reagents comprises i) an average radius of greater than 70 nm; ii) an average molecular weight of at least 1 x 10^8 g/mol; and/or iii) an average number of streptavidin or streptavidin tetramers per oligomeric particle reagent of at least 2,000 and/or iv) a radius size distribution wherein at least 95% of the plurality of oligomeric particle reagents comprise a radius of between 10 nm to 150 nm. In certain examples, the radius size distribution is a hydrodynamic radius size distribution.

[0022a] In another aspect, the present disclosure refers to a composition comprising a plurality of the multimerized oligomeric particle reagent as disclosed herein, wherein the plurality of multimerized oligomeric particle reagents comprises a plurality of the oligomer, a plurality of the first receptor-binding agent, and a plurality of the second receptor-binding agent.

[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 multimerized oligomeric particle reagent as disclosed herein, or the composition comprising a plurality of multimerized 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 T cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising ~~target~~ T cells in the presence of the multimerized oligomeric particle reagent as disclosed herein, or the composition comprising a plurality of multimerized oligomeric particle reagents as disclosed herein, thereby modulating the T cells.

[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 T cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising ~~target~~ T cells in the presence of the multimerized oligomeric particle reagent as disclosed herein, or the composition comprising a plurality of multimerized 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. A multimerized~~An~~ oligomeric particle reagent that ~~comprising a plurality of streptavidin or streptavidin mutein molecules, wherein the oligomeric particle reagent~~ is soluble and comprises (i) an oligomer of between 2,000 and 4,000 ~~1,500 and 7,500~~ tetramers of ~~streptavidin or~~ a streptavidin mutein molecule, (ii) a first receptor-binding agent comprising an anti-CD3 Fab and a first streptavidin-binding peptide, and (iii) a second receptor-binding agent comprising an anti-CD28 Fab and a second streptavidin-binding peptide, wherein the first and second streptavidin-binding peptides are each reversibly bound to one or more binding sites of the streptavidin mutein molecules.

~~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~~2. The multimerized 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~~3. The multimerized oligomeric particle reagent of claim 1 or claim 2~~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, and 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, and 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 the first and second streptavidin-binding peptides; orbiotin, a biotin analog or a streptavidin-binding peptide; or

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

54. The multimerized oligomeric particle reagent of any of claims 1-43, 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, and 60, or 61.

65. The multimerized oligomeric particle reagent of any of claims 1-54, 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.

76. The multimerized oligomeric particle reagent of any of claims 1-65, wherein the oligomer is of oligomeric particle reagent comprises between between 2,000 and 5,000, between 2,000 and 4,000, between 2,000 and 3,500 tetramers of the, or between 2,000 and 3,000 streptavidin or streptavidin mutein moleculetetramers.

87. The multimerized oligomeric particle reagent of any of claims 1-76, wherein the oligomer is of oligomeric particle reagent comprises between 2,000 and 3,000 tetramers of the streptavidin or streptavidin mutein moleculetetramers.

98. The multimerized oligomeric particle reagent of any of claims 1-87, wherein the oligomeroligomeric 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.

109. The multimerized oligomeric particle reagent of any of claims 1-98, wherein the oligomeroligomeric particle reagent comprises a radius of between 90 nm and 110 nm, inclusive.

~~11~~10. The multimerized oligomeric particle reagent of any of claims 1-~~10~~9, wherein the ~~plurality of streptavidin or~~ streptavidin mutein molecules 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~~11. The multimerized oligomeric particle reagent of any of claims 1-10~~claim 12~~, wherein the first and second streptavidin-binding peptides are independently ~~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), SAWSHPQFEKGGGSGGGSGGSAWSHPQFEK (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~~12. The multimerized oligomeric particle reagent of any of claims 1-11~~claim 12 or claim 13~~, wherein the first and second streptavidin-binding peptides are each ~~peptide is~~ SAWSHPQFEKGGGSGGGSGGSAWSHPQFEK (SEQ ID NO: 16).

13. The multimerized oligomeric particle reagent of any of claims 1-12, wherein the streptavidin mutein molecules are crosslinked by a heterobifunctional crosslinker.

14. The multimerized oligomeric particle reagent of claim 13, wherein the heterobifunctional crosslinker is a amine-to-thiol crosslinker.

~~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~~15. A composition comprising a plurality of the multimerized oligomeric particle reagent of any of claims 1-14, wherein the plurality of multimerized oligomeric particle reagents comprises a plurality of the oligomer, a plurality of the first receptor-binding agent, and a plurality of the second receptor-binding agent~~claims 1-24~~.

~~26~~16. The composition of claim ~~25~~15, wherein~~:~~ the plurality of oligomers~~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~~

17. The composition of claim 15, wherein the plurality of oligomers comprises ~~oligomeric particle reagents comprise~~ an average radius of 90 nm ± 15 nm, 95 nm ± 20-25 nm, or 97 ± 10 nm.

~~27~~18. The composition of claim ~~25~~ 15 or claim ~~26~~16, wherein the plurality of oligomers ~~oligomeric particle reagents~~ comprises an average radius of between 90 nm and 110 nm, inclusive.

~~28~~19. The composition of any of claims 15-18~~25-27~~, wherein~~:~~ at least 95% of the plurality of oligomers~~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~~

20. The composition of any of claims 15-19, wherein at least 95% of the plurality of oligomers~~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 oligomers~~oligomeric particle reagents~~.

~~29~~21. The composition of any of claims 15-20~~25-28~~, wherein the plurality of oligomers comprises~~oligomeric particle reagents comprising~~ an average radius of between 80 nm and 115 nm, and ~~wherein~~ at least 95% of the oligomers~~oligomeric particle reagents~~ comprise a radius between ± 25% of the average radius.

~~30~~22. The composition of any of claims 15-21~~25-29~~, wherein the plurality of oligomers ~~oligomeric particle reagents~~ comprises an average number of ~~streptavidin or~~ streptavidin mutein tetramers of~~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~~23. The composition of any of claims 15-22~~25-30~~, wherein the plurality of oligomers ~~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~~24. The composition of any of claims 15-23~~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 oligomers~~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 oligomers~~oligomeric particle reagents~~.

~~33~~25. The composition of any of claims 15-24~~25-32~~, wherein the average radius of the plurality of oligomers~~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~~26. An article of manufacture, comprising the multimerized oligomeric particle reagent of any of claims 1-14~~24,~~ or the composition comprising a plurality of multimerized oligomeric particle reagents of any of claims 15-25~~25-33~~.

~~35~~27. A method for modulating T cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising ~~target~~ T cells in the presence of the multimerized oligomeric particle reagent of any of claims 1-14~~24,~~ or the composition comprising a plurality of multimerized oligomeric particle reagents of any of claims 15-25~~25-33~~, thereby modulating the ~~target~~ T cells.

~~36~~28. A method for culturing T cells, wherein the method is performed ex vivo and comprises incubating a cell composition comprising ~~target~~ T cells in the presence of the multimerized oligomeric particle reagent of any of claims 1-14~~24,~~ or the composition comprising a plurality of multimerized oligomeric particle reagents of any of claims 15-25~~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~~29. The method of claim 27 or claim 28~~any of claims 37-39~~, further comprising disrupting the reversible binding between the first and second streptavidin-binding peptides~~one or more agents~~ and the oligomer, the~~oligomeric particle reagent, said~~ disrupting comprising introducing to the T~~target~~ cells a substance that reverses or competes with the bond between the first and second streptavidin-binding peptides~~one or more agents~~ and the oligomer~~oligomeric particle reagent~~.

~~41~~30. The method of claim 29~~40~~, wherein the substance comprises biotin or a biotin analog.

~~42~~31. The method of claim 29~~40~~ or claim 30~~41~~, wherein the substance comprises D-biotin.

32. The method of claim 29 or claim 30, wherein the substance comprises desthiobiotin or iminobiotin.