CLAIMS

1. A particle having at least one surface and an agent immobilized on the surface, wherein:

the agent selectively binds to a target that is a first member of a specific binding pair;

binding of the target to the particle inhibits the interaction of the target with a second member of the specific binding pair;

the agent is oriented on the particle such that it has a reduced ability to bind to a molecule on the surface of a cell; and further wherein

(a) the particle comprises a coating;

(b) the particle is porous and comprises an outer surface and inner surfaces of the pores of the particle and the agent is immobilized on the inner surfaces; or

(c) the particle comprises at least one outward-facing protrusion from at least one of its vertices, and wherein one or more protrusions are sized and oriented to inhibit: (i) the agent immobilized on the surface of the particle from binding to, or activating, a cell surface receptor protein and/or (ii) when the target is bound to the agent, the interaction of the target and a second member of a specific binding pair of which the target is the first member.

2. A particle, comprising a surface and an agent immobilized on the surface, wherein:

the agent can selectively bind to a target;

binding of an agent to the target inhibits interactions between the target and a cell;

the agent is oriented on the particle such that it has a reduced ability to bind to a molecule on the surface of a cell; and further wherein

(a) the particle comprises a coating;

(b) the particle is porous and comprises an outer surface and inner surfaces of the pores of the particle and the agent is immobilized on the inner surfaces; or

(c) the particle comprises at least one outward-facing protrusion from at least one of its vertices, and wherein one or more protrusions are sized and oriented to inhibit: (i) the agent immobilized on the surface of the particle from binding to, or activating, a cell surface receptor protein and/or (ii) when the target is bound to the agent, the interaction of the target and a second member of a specific binding pair of which the target is the first member.

3. The particle of claim 1 or 2, wherein the agent is oriented on the particle such that it has a reduced ability to bind to a target expressed on the surface of a cell.

4. The particle of any one of the preceding claims, wherein the agent is oriented on the particle such that it is sterically inhibited from binding to a molecule on the surface of a cell.

5. The particle of any one of the preceding claims, wherein the agent is oriented on the particle such that it is sterically inhibited from binding to a target on the surface of a cell.

6. The particle of any one of the preceding claims, wherein the surface is oriented such that the agent has a reduced ability to bind to a molecule on the surface of a cell.

7. The particle of any one of the preceding claims, wherein the cell is a human cell.

8. The particle of any one of the preceding claims, wherein the target is

(i) a soluble biomolecule,
(ii) a small molecule, a protein, or a nucleic acid,
(iii) a viral protein,
(iv) a toxin,
(v) a drug,
(vi) a ligand for a cell surface receptor, or
(vii) a cytosolic receptor or a nuclear receptor.

9. The particle of claim 8, wherein

(i) the viral protein is a structural protein and is preferably a viral capsid protein or a viral envelope protein,
(ii) the toxin is a bacterial toxin, a plant toxin, or a zootoxin,
(iii) the small molecule, protein, or nucleic acid is a soluble form of a cell membrane-bound protein, and is preferably a cell surface receptor protein,
(iv) the ligand for a cell surface receptor is a cytokine, a chemokine, or a lymphokine and is preferably an interleukin protein or a chemokine,
(v) the ligand for a cell surface receptor is a tumor necrosis factor (TNF) family ligand or a variant thereof and is preferably TNFα or a variant thereof or is preferably Fas

ligand, lymphotoxin, lymphotoxin alpha, lymphotoxin beta, 4-lBB Ligand, CD30 Ligand, EDA-Al, LIGHT, TLA1, TWEAK, TNF, TRAIL, or a variant of any of the foregoing.

10. The particle of any one of the preceding claims, wherein the agent is a ligand of a cell surface receptor protein and is preferably a natural ligand of a cell surface receptor protein.

11. The particle of claim 10, wherein the agent is oriented on the particle such that it is sterically inhibited from binding to, or activating, the cell surface receptor protein on the surface of a cell.

12. A particle having at least one surface and an agent immobilized on the surface, wherein:

the agent selectively binds to a soluble biomolecule;

the soluble biomolecule is a form of a cell surface receptor protein;

the agent is oriented on the particle such that it is sterically inhibited from binding to, or activating, the cell surface receptor protein on the surface of a cell; and further wherein

(a) the particle comprises a coating;

(b) the particle is porous and comprises an outer surface and inner surfaces of the pores of the particle and the agent is immobilized on the inner surfaces; or

(c) the particle comprises at least one outward-facing protrusion from at least one of its vertices, and wherein one or more protrusions are sized and oriented to inhibit the agent immobilized on the surface of the particle from binding to, or activating, a cell surface receptor protein.

13. The particle of any one of claims 10 to 12, wherein the cell surface receptor protein is expressed by a cancer cell, and is preferably a protein shed by the cancer cell as a soluble form of the cell surface receptor protein.

14. The particle of any one of claims 10 to 13, wherein the cell surface receptor protein, when activated, induces apoptosis.

15. The particle of claim 14, wherein the cell surface receptor protein is a tumor necrosis factor receptor (TNFR) protein.

16. The particle of claim 14, wherein the cell surface receptor protein is a Fas receptor protein.

17. The particle of claim 14, wherein the cell surface receptor protein is a TNF-related apoptosis-inducing ligand receptor (TRAILR) protein, 4-IBB receptor protein, CD30 protein, EDA receptor protein, HVEM protein, lymphotoxin beta receptor protein, DR3 protein, TWEAK receptor protein, Soluble death receptor-3, Soluble death receptor-4, Soluble death receptor-5, Soluble Interleukin-1A receptor, Soluble Interleukin-5 receptor, Soluble Interleukin-6 receptor, Soluble Interleukin-8 receptor, or CXCR1.

18. The particle of any one of claims 10-14, wherein the cell surface receptor protein is an interleukin receptor protein, and is preferably an IL-2 receptor protein.

19. The particle of any one of the preceding claims, wherein the agent is a small molecule, a macrocycle compound, a polypeptide, a protein, a peptide, a peptidomimetic compound, a nucleic acid, or a nucleic acid analog.

20. The particle of claim 19, wherein the agent

(i) is an antibody or biomolecule-binding fragment of an antibody, and is preferably a biomolecule-binding fragment of an antibody, and the biomolecule-binding fragment is selected from a Fab fragment, a $F(ab)_2$ fragment, an scFv fragment, and a domain antibody, or

(ii) is a non-antibody scaffold protein.

21. The particle of claim 19, wherein the agent is an interleukin protein or variant thereof, and is preferably an IL-2 protein or variant thereof.

22. The particle of claim 19, wherein the agent comprises a tumor necrosis factor (TNF) family ligand or a variant thereof, wherein the TNF family ligand is preferably TNFα or a variant thereof or is preferably selected from Fas ligand, lymphotoxin, lymphotoxin alpha,

lymphotoxin beta, 4-IBB Ligand, CD30 Ligand, EDA-Al, LIGHT, TLA1, TWEAK, TNF, TRAIL, and a variant of any of the foregoing.

23. The particle of any one of claims 10-22, wherein the agent has a reduced ability to activate the cell surface receptor protein, relative to the ability of the natural ligand of the cell surface receptor protein.

24. The particle of any one of claims 10-22, wherein the agent does not activate the cell surface receptor protein.

25. The particle of any one of the preceding claims, wherein the particle is cubic or spherical.

26. The particle of any one of the preceding claims, wherein the particle is porous and comprises an outer surface and inner surfaces of the pores of the particle and the agent is immobilized on the inner surfaces, preferably wherein a plurality of pores has a cross-sectional dimension of at least 50 nm and preferably at least 100 nm.

27. The particle of any one of the preceding claims, wherein the diameter of the particle is no greater than 300 nm and is preferably no greater than 250 nm; or wherein the longest dimension of the particle is no greater than 1 μm, preferably no greater than 750 nm, and most preferably no greater than 500 nm.

28. The particle of any one of claims 25 to 27, wherein the particle comprises at least one outward-facing protrusion from at least one of its vertices, and wherein the particle comprises more than one outward-facing protrusion from its vertices.

29. The particle of claim 28, wherein one or more protrusions are sized and oriented to inhibit: (i) the agent immobilized on the surface of the particle from binding to, or activating, a cell surface receptor protein and/or (ii) when the target is bound to the agent, the interaction of the target and a second member of a specific binding pair of which the target is the first member.

30. The particle of any one of the preceding claims, wherein the particle is shaped and sized to circulate in the vasculature of a subject.

31. The particle of any one of the preceding claims, wherein the smallest dimension of the particle is at least 300 nm.

32. The particle of any one of the preceding claims, comprising a plurality of agents, wherein the plurality of agents consists of 10 to 10^9 agents, preferably of 10^3 to 10^7 agents, and most preferably of 10^4 to 10^6 agents.

33. The particle of any one of the preceding claims, wherein the particle comprises more than one different type of agent.

34. The particle of any one of the preceding claims, wherein the particle comprises at least two agents, each agent capable of selectively binding to a different target, wherein the surface of the particle preferably comprises a plurality of binding sites, each binding site comprising a different agent.

35. The particle of any one of the preceding claims, wherein the surface of the particle comprises an excretion inducer compound, and wherein the particle preferably has a toroidal shape and the excretion inducer is bound to an outer circumferential surface of the ring.

36. The particle of any one of the preceding claims, wherein the body of the particle comprises alumina, metal, glass, silica, latex, plastic, agarose, polyacrylamide, methacrylate, or a polymer.

37. The particle of any one of claims 1 to 35, wherein the body of the particle comprises silicon, wherein the silicon is porous silicon.

38. The particle of any one of the preceding claims, wherein the coating comprises a plurality of coating moieties or coating molecules.

39. The particle of claim 38, wherein the plurality of coating moieties or coating molecules inhibits interactions between the agent and molecules on a cell surface.

40. The particle of claim 38 or 39, wherein the plurality of coating moieties or coating molecules inhibits interactions between the agent and a target on the surface of a cell.

41. The particle of any one of claims 38-40, wherein the plurality of coating moieties or coating molecules comprises a polymer.

42. The particle of any one of claims 38-41, wherein the plurality of coating moieties or coating molecules comprises polyethylene glycol (PEG), polylactate, polylactic acid, sugar, lipid, polyglutamic acid, polyglycolic acid (PGA), polylactic acid (PLA), poly(lactic-co-glycolic acid) (PLGA), or polyvinyl acetate (PVA).

43. The particle of claim 38, further comprising a second surface, wherein at least one molecule of the plurality of coating moieties or coating molecules is bound to the second surface.

44. The particle of claim 43, wherein the surface is an interior surface of the particle and the second surface is an exterior surface of the particle.

45. The particle of any one of claims 43 or 44, further comprising a second plurality of coating molecules, wherein:

at least one molecule of the second plurality of coating molecules is bound to the second surface; and

the second plurality of coating molecules decreases the clearance of the particle in vivo.

46. The particle of claim 45, wherein the second plurality of coating molecules comprises a polymer.

47. The particle of claim 46, wherein the second plurality of coating molecules comprises polyethylene glycol (PEG), polylactate, polylactic acid, sugar, lipid, polyglutamic acid,

polyglycolic acid (PGA), polylactic acid (PLA), poly(lactic-co-glycolic acid) (PLGA), or polyvinyl acetate (PVA).

48. The particle of claim 45, wherein the second plurality of coating molecules inhibits interactions between the plurality of coating moieties or coating molecules and cells and/or extracellular proteins, thereby decreasing the clearance of the particle in vivo, wherein the second plurality of coating molecules are preferably biodegradable and most preferably comprise a biodegradable polymer.

49. The particle of claim 48, wherein the second plurality of coating molecules is configured to biodegrade after exposure to a biological fluid for 1 day to four years, and preferably after exposure to a biological fluid for 1 day to 1 year.

50. The particle of any one of claims 45 to 49, wherein the second plurality of coating molecules comprise CD47.

51. The particle of any one of claims 38 to 50, wherein the plurality of coating moieties or coating molecules increases the clearance of the particle in vivo, preferably by phagocytosis, and preferably wherein the plurality of coating molecules comprises calreticulin.

52. The particle of any one of claims 38 to 51, wherein the plurality of coating moieties or coating molecules comprises a pathogen-associated molecular pattern, wherein the pathogen-associated molecular pattern is preferably unmethylated CpG DNA, double-stranded RNA, a lipopolysaccharide, a peptidoglycan, lipoarabinomannan, zymosan, a mycoplasmal lipoprotein, flagellin, poly(inosinic-cytidylic) acid, lipoteichoic acid, or an imidazoquinoline.

53. The particle of claim 38, wherein the plurality of coating moieties or coating molecules increases

(i) the renal clearance of the particle, or

(ii) the hepatobiliary clearance of the particle, wherein the plurality of coating molecules preferably comprises a hydrophobic molecule.

54. The particle of claim 38, wherein the plurality of coating moieties or coating molecules decreases the clearance of the particle in vivo, wherein the plurality of coating moieties or coating molecules is preferably biodegradable and most preferably comprises a biodegradable polymer.

55. A composition comprising a plurality of particles according to any one of the preceding claims.

56. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and the particle of any one of claims 1 to 54 or the composition of claim 55.

57. The composition according to claim 55 or the pharmaceutical composition according to claim 56 for use in inhibiting the biological activity of a soluble biomolecule in a subject.

58. Use of particles according to any one of claims 1 to 54 in the manufacture of a medicament for treating a subject afflicted with a cancer comprising cancer cells that shed a soluble form of at least one cytokine receptor.

59. The use according to claim 58, wherein the cancer cells shed a soluble form of TNF receptor, and wherein the plurality of particles comprises an agent comprising a TNFα polypeptide or a variant thereof.

60. The use according to claim 58, wherein the cancer cells shed a soluble form of IL-2 receptor, and wherein the plurality of particles comprises an agent comprising a IL-2 polypeptide or a variant thereof.

61. The composition according to claim 55 or the pharmaceutical composition according to claim 56, for use in treating a subject afflicted with cancer or an autoimmune disease.

62. The particle of any one of claims 38-54, wherein at least one molecule of the plurality of coating moieties or coating molecules is bound to the surface of the particle.