Summary

In one aspect, the disclosure relates to a use of one or more cells in the manufacture of a first medicament, wherein the one or more cells were transfected with RNA encoding a peptide or polypeptide comprising a first binding moiety, in which the peptide or polypeptide is expressed by the one or more cells such that the peptide or polypeptide becomes associated with target cells and the first binding moiety is displayed on the surface of the target cells; and use of a payload which comprises or is linked to a second binding moiety, wherein the first binding moiety and the second binding moiety bind to each other, in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy involving the targeted delivery of the payload to target cells.

In another aspect, the disclosure relates to a use of (i) RNA encoding a peptide or polypeptide comprising a first binding moiety in the manufacture of a first medicament; and use of (ii)a payload which comprises or is linked to a second binding moiety or RNA coding therefor in the manufacture of a second medicament; wherein the first and second medicaments are to be used in combination therapy involving the targeted delivery of the payload to target cells, wherein the first binding moiety and the second binding moiety bind to each other and wherein the peptide or polypeptide comprising a first binding moiety further comprises a third binding moiety binding to a target on target cells, optionally wherein the RNA is present in particles.

In one ~~aspect~~example, the ~~invention~~disclosure relates to a method for targeted delivery of a payload to target cells, comprising:

(i) transfecting one or more cells with RNA encoding a peptide or polypeptide comprising a first binding moiety;

(ii) allowing the one or more cells to express the peptide or polypeptide such that it becomes associated with target cells and the first binding moiety is displayed on the surface of the target cells; and

(iii) adding a payload which comprises or is linked to a second binding moiety;

wherein the first binding moiety and the second binding moiety bind to each other.

In one ~~embodiment~~example, the one or more cells are transfected with the RNA by contacting the one or more cells with particles comprising the RNA.

In one ~~embodiment~~example, the particles comprise a targeting molecule for targeting the one or more cells.

In one ~~embodiment~~example, the one or more cells comprise or consist of target cells.

In one ~~embodiment~~example, the one or more cells express the peptide or polypeptide comprising a first binding moiety such that it remains associated with the one or more cells.

In one ~~embodiment~~example, the one or more cells are different to the target cells.

In one ~~embodiment~~example, the one or more cells express the peptide or polypeptide comprising a first binding moiety such that it is secreted by the one or more cells.

In one ~~embodiment~~example, the one or more cells express the peptide or polypeptide comprising a first binding moiety such that it is released into the bloodstream.

In one ~~embodiment~~example, the peptide or polypeptide comprising a first binding moiety comprises a third binding moiety binding to a target on target cells.

In one ~~embodiment~~example, the target is a cell surface antigen.

In one ~~embodiment~~example, the first binding moiety and the third binding moiety are linked to each other. In one ~~embodiment~~example, the first binding moiety and the third binding moiety are covalently linked to each other.

In one ~~embodiment~~example, the first binding moiety is an antibody or an antibody derivative. In one ~~embodiment~~example, the second binding moiety is a peptide tag.

In one ~~embodiment~~example, the first binding moiety is a peptide tag. In one ~~embodiment~~example, the second binding moiety is an antibody or an antibody derivative.

In one ~~embodiment~~example, the third binding moiety is an antibody or an antibody derivative.

In one ~~embodiment~~example, the antibody derivative is an antibody fragment.

In one ~~embodiment~~example, the peptide or polypeptide is a bispecific antibody. In one ~~embodiment~~example, the bispecific antibody is a bispecific single chain antibody.

In one ~~embodiment~~example, the second binding moiety and the payload are covalently or non-covalently linked to each other. In one ~~embodiment~~example, the payload comprises a

pharmaceutically active agent. In one ~~embodiment~~example, the payload comprises a diagnostic compound. In one ~~embodiment~~example, the payload comprises a therapeutic compound. In one ~~embodiment~~example, the payload comprises a carrier. In one ~~embodiment~~example, the carrier is a particulate carrier. In one ~~embodiment~~example, the particulate carrier comprises lipid-based particles, polymer-based particles, or a mixture thereof. In one ~~embodiment~~example, the carrier incorporates a diagnostic compound. In one ~~embodiment~~example, the carrier incorporates a therapeutic compound. In one ~~embodiment~~example, the payload comprises a fourth binding moiety. In one ~~embodiment~~example, the fourth binding moiety binds to a cell surface antigen. In one ~~embodiment~~example, the cell surface antigen to which the fourth binding moiety binds is present on immune cells.

In one ~~embodiment~~example, the target cells are present in a subject.

In one ~~embodiment~~example, the method described herein is performed *in vivo*.

In one ~~embodiment~~example, the method described herein comprises administering to a subject:

(i) the RNA encoding a peptide or polypeptide comprising a first binding moiety or the particles comprising the RNA; and

(ii) the payload which comprises or is linked to a second binding moiety or RNA coding therefor.

In one ~~embodiment~~example, the method described herein is for diagnosing and/or treating a disease, wherein the target cells express or may express an antigen associated with the disease.

In one ~~embodiment~~example, the target cells are diseased cells.

In one ~~embodiment~~example, the target is a tumor antigen. In one ~~embodiment~~example, the target cells are tumor or cancer cells.

In one ~~embodiment~~example, the target cells are immune effector cells. In one ~~embodiment~~example, the target cells are T cells. In one ~~embodiment~~example, the target is an antigen characteristic for said immune effector cells.

In one ~~embodiment~~example, the method described herein is for delivering nucleic acid encoding an antigen receptor to the immune effector cells.

In one ~~aspect~~example, the ~~invention~~disclosure relates to a method for targeted delivery of a payload to target cells in a subject, comprising administering to the subject:

(i) RNA encoding a peptide or polypeptide comprising a first binding moiety; and

(ii) a payload which comprises or is linked to a second binding moiety or RNA coding therefor;

wherein the first binding moiety and the second binding moiety bind to each other and wherein the peptide or polypeptide comprising a first binding moiety further comprises a third binding moiety binding to a target on target cells.

In one ~~embodiment~~example, the RNA, when administered, is present in particles.

In one ~~embodiment~~example, following administration of the RNA, the peptide or polypeptide comprising a first binding moiety and a third binding moiety is expressed by one or more cells of the subject. In one ~~embodiment~~example, the one or more cells secrete the peptide or polypeptide comprising a first binding moiety and a third binding moiety. In one ~~embodiment~~example, the one or more cells express the peptide or polypeptide comprising a first binding moiety and a third binding moiety such that it is released into the bloodstream.

In ~~one~~ yet another aspect, the ~~invention~~disclosure relates to a kit for targeted delivery of a payload to target cells, comprising:

(i) RNA encoding a peptide or polypeptide comprising a first binding moiety; and

(ii) a payload which comprises or is linked to a second binding moiety or RNA coding therefor;

wherein the first binding moiety and the second binding moiety bind to each other.

In one ~~embodiment~~example, the peptide or polypeptide comprising a first binding moiety comprises a third binding moiety binding to a target on target cells.

In one ~~embodiment~~example, the target is a cell surface antigen.

In one ~~embodiment~~example, the first binding moiety and the third binding moiety are linked to each other. In one ~~embodiment~~example, the first binding moiety and the third binding moiety are covalently linked to each other.

In one ~~embodiment~~example, the first binding moiety is an antibody or an antibody derivative.

In one ~~embodiment~~example, the second binding moiety is a peptide tag.

In one ~~embodiment~~example, the first binding moiety is a peptide tag. In one ~~embodiment~~example, the second binding moiety is an antibody or an antibody derivative.

In one ~~embodiment~~example, the third binding moiety is an antibody or an antibody derivative.

In one ~~embodiment~~example, the antibody derivative is an antibody fragment.

In one ~~embodiment~~example, the peptide or polypeptide is a bispecific antibody. In one ~~embodiment~~example, the bispecific antibody is a bispecific single chain antibody.

In one ~~embodiment~~example, the second binding moiety and the payload are covalently or non-covalently linked to each other. In one ~~embodiment~~example, the payload comprises a pharmaceutically active agent. In one ~~embodiment~~example, the payload comprises a diagnostic compound. In one ~~embodiment~~example, the payload comprises a therapeutic compound. In one ~~embodiment~~example, the payload comprises a carrier. In one ~~embodiment~~example, the carrier is a particulate carrier. In one ~~embodiment~~example, the particulate carrier comprises lipid-based particles, polymer-based particles, or a mixture thereof. In one ~~embodiment~~example, the carrier incorporates a diagnostic compound. In one ~~embodiment~~example, the carrier incorporates a therapeutic compound. In one ~~embodiment~~example, the payload comprises a fourth binding moiety. In one ~~embodiment~~example, the fourth binding moiety binds to a cell surface antigen. In one ~~embodiment~~example, the cell surface antigen to which the fourth binding moiety binds is present on immune cells.

In one ~~embodiment~~example, the RNA is present in particles.

In one ~~aspect~~example, the ~~invention~~disclosure relates to an agent or composition described herein for use in a method described herein.

Claims

1. Use of one or more cells in the manufacture of a first medicament, wherein the one or more cells were transfected with RNA encoding a peptide or polypeptide comprising a first binding moiety, in which the peptide or polypeptide is expressed by the one or more cells such that the peptide or polypeptide becomes associated with target cells and the first binding moiety is displayed on the surface of the target cells; and

use of a payload which comprises or is linked to a second binding moiety, wherein the first binding moiety and the second binding moiety bind to each other, in the manufacture of a second medicament,

wherein the first and second medicaments are to be used in combination therapy involving the targeted delivery of the payload to target cells~~A method for targeted delivery of a payload to target cells, comprising:~~

~~(i) transfecting one or more cells with RNA encoding a peptide or polypeptide comprising a first binding moiety;~~

~~(ii) allowing the one or more cells to express the peptide or polypeptide such that it becomes associated with target cells and the first binding moiety is displayed on the surface of the target cells; and~~

~~(iii) adding a payload which comprises or is linked to a second binding moiety;~~

~~wherein the first binding moiety and the second binding moiety bind to each other~~.

2. The use~~method~~ of claim 1, wherein the one or more cells are transfected with the RNA by contacting the one or more cells with particles comprising the RNA, optionally~~.~~

~~3. The method of claim 1 or 2,~~ wherein the particles comprise a targeting molecule for targeting the one or more cells.

3~~4~~. The use~~method~~ of ~~any one of~~ claim~~s~~ 1 or 2~~to 3~~, wherein the one or more cells comprise or consist of target cells.

4~~5~~. The use~~method~~ of any one of claims 1 to 3~~4~~, wherein the one or more cells express the peptide or polypeptide comprising a first binding moiety such that it remains associated with the one or more cells.

5~~6~~. The use~~method~~ of any one of claims 1 to 3, wherein the one or more cells are different to the target cells.

67. The usemethod of any one of claims 1 to 56, wherein the one or more cells express the peptide or polypeptide comprising a first binding moiety such that it is secreted by the one or more cells.

78. The usemethod of any one of claims 1, 2, 5 and 6 to 3, 6, and 7, wherein the one or more cells express the peptide or polypeptide comprising a first binding moiety such that it is released into the bloodstream.

89. The usemethod of any one of claims 1 to 78, wherein the peptide or polypeptide comprising a first binding moiety comprises a third binding moiety binding to a target on target cells, optionally wherein the first binding moiety and the third binding moiety are linked to each other.

910. The usemethod of claim 89, wherein the target is a cell surface antigen.

11. The method of claim 9 or 10, wherein the first binding moiety and the third binding moiety are linked to each other.

1012. The usemethod of any one of claims 1 to 911, wherein the first binding moiety and the third binding moiety are covalently linked to each other.

1113. The usemethod of any one of claims 1 to 1012, wherein the first binding moiety is an antibody or an antibody derivative, or wherein the first binding moiety is a peptide tag.

1214. The usemethod of any one of claims 1 to 1113, wherein the second binding moiety is a peptide tag or wherein the second binding moiety is an antibody or an antibody derivative.

15. The method of any one of claims 1 to 12, wherein the first binding moiety is a peptide tag.

16. The method of any one of claims 1 to 12, and 15, wherein the second binding moiety is an antibody or an antibody derivative.

1317. The usemethod of any one of claims 89 to 1216, wherein the third binding moiety is an antibody or an antibody derivative.

1418. The usemethod of any one of claims 11, 12, and 13~~, 14, 16, and 17~~, wherein the antibody derivative is an antibody fragment.

1519. The usemethod of any one of claims 1 to 14~~, 17, and 18~~, wherein the peptide or polypeptide is a bispecific antibody, optionally~~.~~

~~20. The method of claim 19,~~ wherein the bispecific antibody is a bispecific single chain antibody.

1621. The usemethod of any one of claims 1 to 1520, wherein the second binding moiety and the payload are covalently or non-covalently linked to each other.

1722. The usemethod of any one of claims 1 to 1621, wherein the payload comprises a pharmaceutically active agent, or~~.~~

~~23. The method of any one of claims 1 to 22,~~ wherein the payload comprises a diagnostic compound, or~~.~~

~~24. The method of any one of claims 1 to 23,~~ wherein the payload comprises a therapeutic compound, or~~.~~

~~25. The method of any one of claims 1 to 24,~~ wherein the payload comprises a carrier, optionally~~.~~

~~26. The method of claim 25,~~ wherein the carrier is a particulate carrier, optionally~~.~~

~~27. The method of claim 26,~~ wherein the particulate carrier comprises lipid-based particles, polymer-based particles, or a mixture thereof.

1828. The usemethod of ~~any one of~~ claim~~s~~ 1725 to 27, wherein the carrier incorporates a diagnostic compound or~~.~~

~~29. The method of any one of claims 25 to 28,~~ wherein the carrier incorporates a therapeutic compound.

1930. The usemethod of any one of claims 1 to 1829, wherein the payload comprises a fourth binding moiety, optionally.

~~31. The method of claim 30,~~ wherein the fourth binding moiety binds to a cell surface antigen, optionally.

~~32. The method of claim 31,~~ wherein the cell surface antigen to which the fourth binding moiety binds is present on immune cells.

2033. The usemethod of any one of claims 1 to 1932, wherein the target cells are present in a subject.

~~34. The method of any one of claims 1 to 33, which is performed in vivo.~~

~~35. The method of any one of claims 1 to 34, comprising administering to a subject:~~

~~(i) the RNA encoding a peptide or polypeptide comprising a first binding moiety or the particles comprising the RNA; and~~

~~(ii) the payload which comprises or is linked to a second binding moiety or RNA coding therefor.~~

2136. The usemethod of any one of claims 1 to 2035, which is for diagnosing and/or treating a disease, wherein the target cells express or may express an antigen associated with the disease.

2237. The usemethod of any one of claims 1 to 2136, wherein the target cells are diseased cells, optionally wherein the target cells are tumor or cancer cells.

2338. The usemethod of any one of claims 89 to 2237, wherein the target is a tumor antigen.

~~39. The method of any one of claims 1 to 38, wherein the target cells are tumor or cancer cells~~

2440. The usemethod of any one of claims 1 to 2339, wherein the target cells are immune effector cells.

2541. The usemethod of any one of claims 1 to 2035, and 2440, wherein the target cells are T cells.

2642. The usemethod of claim 2440 or 2541, wherein the target is an antigen characteristic for said immune effector cells.

2743. The usemethod of any one of claims 1 to 2035, and 2440 to 2642, which is for delivering nucleic acid encoding an antigen receptor to the immune effector cells.

2844. Use ofA method for targeted delivery of a payload to target cells in a subject, comprising administering to the subject:

(i) RNA encoding a peptide or polypeptide comprising a first binding moiety in the manufacture of a first medicament; and

use of

(ii) a payload which comprises or is linked to a second binding moiety or RNA coding therefor in the manufacture of a second medicament;

wherein the first and second medicaments are to be used in combination therapy involving the targeted delivery of the payload to target cells, wherein the first binding moiety and the second binding moiety bind to each other and wherein the peptide or polypeptide comprising a first binding moiety further comprises a third binding moiety binding to a target on target cells, optionally.

45. The method of claim 44, wherein the RNA, when administered, is present in particles.

2946. The usemethod of claim 2844 or 45, wherein, following administration of the RNA to the subject, the peptide or polypeptide comprising a first binding moiety and a third binding moiety is expressed by one or more cells of the subject.

3047. The usemethod of claim 2946, wherein the one or more cells secrete the peptide or polypeptide comprising a first binding moiety and a third binding moiety, or.

48. The method of claim 46 or 47, wherein the one or more cells express the peptide or polypeptide comprising a first binding moiety and a third binding moiety such that it is released into the bloodstream.

3149. A kit for targeted delivery of a payload to target cells, comprising:

(i) RNA encoding a peptide or polypeptide comprising a first binding moiety; and

(ii) a payload which comprises or is linked to a second binding moiety or RNA coding therefor;

wherein the first binding moiety and the second binding moiety bind to each other.

3250. The kit of claim 3149, wherein the peptide or polypeptide comprising a first binding moiety comprises a third binding moiety binding to a target on target cells, optionally.

~~51. The kit of claim 50,~~ wherein the target is a cell surface antigen.

3352. The kit of claim 3250 ~~or 51~~, wherein the first binding moiety and the third binding moiety are linked to each other or.

~~53. The kit of any one of claims 50 to 52,~~ wherein the first binding moiety and the third binding moiety are covalently linked to each other.

3454. The kit of any one of claims 3149 to 3353, wherein the first binding moiety is an antibody or an antibody derivative or wherein the first binding moiety is a peptide tag.

3555. The kit of any one of claims 3149 to 3454, wherein the second binding moiety is a peptide tag or wherein the second binding moiety is an antibody or an antibody derivative.

~~56. The kit of any one of claims 49 to 53, wherein the first binding moiety is a peptide tag.~~

~~57. The kit of any one of claims 49 to 53, and 56, wherein the second binding moiety is an antibody or an antibody derivative.~~

3658. The kit of any one of claims 3250 to 3557, wherein the third binding moiety is an antibody or an antibody derivative.

3759. The kit of any one of claims 34, 3554, 55, 57, and 3658, wherein the antibody derivative is an antibody fragment.

3860. The kit of any one of claims 3149 to 3755, 58, and 59, wherein the peptide or polypeptide is a bispecific antibody, optionally.

~~61. The kit of claim 60,~~ wherein the bispecific antibody is a bispecific single chain antibody.

39~~62~~. The kit of any one of claims 31~~49~~ to 38~~61~~, wherein the second binding moiety and the payload are covalently or non-covalently linked to each other.

40~~63~~. The kit of any one of claims 31~~49~~ to 39~~62~~, wherein the payload comprises a pharmaceutically active agent, or~~.~~

~~64. The kit of any one of claims 49 to 63,~~ wherein the payload comprises a diagnostic compound, or~~.~~

~~65. The kit of any one of claims 49 to 64,~~ wherein the payload comprises a therapeutic compound, or~~.~~

~~66. The kit of any one of claims 49 to 65,~~ wherein the payload comprises a carrier, optionally~~.~~

~~67. The kit of claim 66,~~ wherein the carrier is a particulate carrier, optionally~~.~~

~~68. The kit of claim 67,~~ wherein the particulate carrier comprises lipid-based particles, polymer-based particles, or a mixture thereof.

41~~69~~. The kit of any one of claims 40~~66 to 68~~, wherein the carrier incorporates a diagnostic compound, or~~.~~

~~70. The kit of any one of claims 66 to 69,~~ wherein the carrier incorporates a therapeutic compound.

42~~71~~. The kit of any one of claims 31~~49~~ to 41~~70~~, wherein the payload comprises a fourth binding moiety, optionally~~.~~

~~72. The kit of claim 71,~~ wherein the fourth binding moiety binds to a cell surface antigen, optionally~~.~~

~~73. The kit of claim 72,~~ wherein the cell surface antigen to which the fourth binding moiety binds is present on immune cells.

4374. The kit of any one of claims 3149 to 4273, wherein the RNA is present in particles.