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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

In one 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 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 example, the target cells are diseased cells.

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

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

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

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

In one 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 example, the one or more cells secrete the peptide or polypeptide comprising a first binding moiety and a third binding moiety. In one 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 yet another aspect, the 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 example, the peptide or polypeptide comprising a first binding moiety comprises a third binding moiety binding to a target on target cells.

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

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

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

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

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

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

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

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

In one example, the RNA is present in particles.

In one example, the 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.

2. The use 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 wherein the particles comprise a targeting molecule for targeting the one or more cells.

3. The use of claim 1 or 2, wherein the one or more cells comprise or consist of target cells.

4. The use of any one of claims 1 to 3, 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. The use of any one of claims 1 to 3, wherein the one or more cells are different to the target cells.

6. The use of any one of claims 1 to 5, 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.

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

8. The use of any one of claims 1 to 7, 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.

9. The use of claim 8, wherein the target is a cell surface antigen.

10. The use of any one of claims 1 to 9, wherein the first binding moiety and the third binding moiety are covalently linked to each other.

11. The use of any one of claims 1 to 10, wherein the first binding moiety is an antibody or an antibody derivative, or wherein the first binding moiety is a peptide tag.

12. The use of any one of claims 1 to 11, wherein the second binding moiety is a peptide tag or wherein the second binding moiety is an antibody or an antibody derivative.

13. The use of any one of claims 8 to 12, wherein the third binding moiety is an antibody or an antibody derivative.

14. The use of any one of claims 11, 12, and 13, wherein the antibody derivative is an antibody fragment.

15. The use of any one of claims 1 to 14, wherein the peptide or polypeptide is a bispecific antibody, optionally wherein the bispecific antibody is a bispecific single chain antibody.

16. The use of any one of claims 1 to 15, wherein the second binding moiety and the payload are covalently or non-covalently linked to each other.

17. The use of any one of claims 1 to 16, wherein the payload comprises a pharmaceutically active agent, or wherein the payload comprises a diagnostic compound, or wherein the payload comprises a therapeutic compound, or wherein the payload comprises a carrier, optionally wherein the carrier is a particulate carrier, optionally wherein the particulate carrier comprises lipid-based particles, polymer-based particles, or a mixture thereof.

18. The use of claim 17, wherein the carrier incorporates a diagnostic compound or wherein the carrier incorporates a therapeutic compound.

19. The use of any one of claims 1 to 18, wherein the payload comprises a fourth binding moiety, optionally wherein the fourth binding moiety binds to a cell surface antigen, optionally wherein the cell surface antigen to which the fourth binding moiety binds is present on immune cells.

20. The use of any one of claims 1 to 19, wherein the target cells are present in a subject.

21. The use of any one of claims 1 to 20, which is for diagnosing and/or treating a disease, wherein the target cells express or may express an antigen associated with the disease.

22. The use of any one of claims 1 to 21, wherein the target cells are diseased cells, optionally wherein the target cells are tumor or cancer cells.

23. The use of any one of claims 8 to 22, wherein the target is a tumor antigen.

24. The use of any one of claims 1 to 23, wherein the target cells are immune effector cells.

25. The use of any one of claims 1 to 20, and 24, wherein the target cells are T cells.

26. The use of claim 24 or 25, wherein the target is an antigen characteristic for said immune effector cells.

27. The use of any one of claims 1 to 20, and 24 to 26, which is for delivering nucleic acid encoding an antigen receptor to the immune effector cells.

28. 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.

29. The use of claim 28, 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.

30. The use of claim 29, wherein the one or more cells secrete the peptide or polypeptide comprising a first binding moiety and a third binding moiety, or 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.

31. 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.

32. The kit of claim 31, 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 target is a cell surface antigen.

33. The kit of claim 32, wherein the first binding moiety and the third binding moiety are linked to each other or wherein the first binding moiety and the third binding moiety are covalently linked to each other.

34. The kit of any one of claims 31 to 33, wherein the first binding moiety is an antibody or an antibody derivative or wherein the first binding moiety is a peptide tag.

35. The kit of any one of claims 31 to 34, wherein the second binding moiety is a peptide tag or wherein the second binding moiety is an antibody or an antibody derivative.

36. The kit of any one of claims 32 to 35, wherein the third binding moiety is an antibody or an antibody derivative.

37. The kit of any one of claims 34, 35, and 36, wherein the antibody derivative is an antibody fragment.

38. The kit of any one of claims 31 to 37, wherein the peptide or polypeptide is a bispecific antibody, optionally wherein the bispecific antibody is a bispecific single chain antibody.

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

40. The kit of any one of claims 31 to 39, wherein the payload comprises a pharmaceutically active agent, or wherein the payload comprises a diagnostic compound, or wherein the payload comprises a therapeutic compound, or wherein the payload comprises a carrier, optionally wherein the carrier is a particulate carrier, optionally wherein the particulate carrier comprises lipid-based particles, polymer-based particles, or a mixture thereof.

41. The kit of any one of claims 40, wherein the carrier incorporates a diagnostic compound, or wherein the carrier incorporates a therapeutic compound.

42. The kit of any one of claims 31 to 41, wherein the payload comprises a fourth binding moiety, optionally wherein the fourth binding moiety binds to a cell surface antigen, optionally wherein the cell surface antigen to which the fourth binding moiety binds is present on immune cells.

43. The kit of any one of claims 31 to 42, wherein the RNA is present in particles.