Claims

1. A multicomponent system wherein a first component is an engineered antigen-presenting cell (**eAPC**) designated **component A** and a second component is a pair of genetic donor vectors, **designated components C and E,** for delivery of one or more ORFs encoding an analyte antigen-presenting complex (aAPX) and/or an analyte antigenic molecule (aAM), wherein component A

    a. Is engineered and/or selected to lack endogenous surface expression of at least one family of aAPX and/or aAM and

    b. Contains at least two genomic receiver sites, **designated component B and component D**, each for integration of at least one ORF encoding at least one aAPX and/or aAM,

    and component **C** and E are matched to a component **B and D, respectively**, and wherein components **C** and E are designed to deliver

    c. A single ORF encoding at least one aAPX and/or aAM or

    d. Two or more ORF encoding at least one aAPX and/or aAM,

    wherein the genomic receiver sites B and D are synthetic constructs designed for recombinase mediated exchange (RMCE).

2. A multicomponent system according to claim 1, wherein c and/or d optionally encodes a selection marker of integration such that said ORF(s) can be stably integrated into the **B** genomic receiver site and the aAPX and/or aAM are expressed.

3. A multicomponent system according to **claim 1 or 2**, wherein a further component **designated E** is a genetic vector matched to **D**, wherein the component **E** is designed to deliver

    a. A single ORF encoding at least one aAPX and/or aAM or

    b. Two or more ORF encoding at least one aAPX and/or aAM

    and wherein a and/or b optionally encodes a selection marker of integration such that said ORF(s) can be stably integrated into the **D** genomic receiver site and the aAPX and/or aAM are expressed.

4. A multicomponent system according to **any of the preceding claims** wherein one or more additional genomic receiver site and matching genetic donor vector is added as additional components of the system.

5. A multicomponent system according to **any of the preceding claims** wherein the aAPX may be any of the following

    a. One or more members of HLA class I

    b. One or more members of HLA class II

    c. On or more non-HLA antigen-presenting complex, or

    d. Any combination of a, b and c.

6. A multicomponent system according to **any of the preceding claims** wherein the aAM is selected from

    a. a polypeptide or complex of polypeptides provided as analyte antigen

    b. a peptide derived from a polypeptide provided as analyte antigen

    c. a peptide provided as analyte antigen

    d. a metabolite provided as analyte antigen

    e. a polypeptide or complex of polypeptides translated from the analyte antigenic molecule ORF(s)

    f. a peptide derived from a polypeptide translated from the analyte antigenic molecule ORF(s)

    g. a peptide derived from altering the component A proteome

    h. a polypeptide derived from altering the component A proteome

    i. a metabolite derived from altering the component A metabolome

    and/or a combination thereof.

7. A multicomponent system according to **any of the preceding claims** wherein the **component B and/or D** comprises of at least one of the following genetic elements

    a. Heterospecific recombinase sites

b. Homologous arms
c. Eukaryotic promoter
d. Eukaryotic conditional regulatory element
e. Eukaryotic terminator
f. Selection marker
g. Splice acceptor site
h. Splice donor site
i. Non-protein coding gene
j. Insulator
k. Mobile genetic element
l. Meganuclease recognition site
m. Internal ribosome entry site (IRES)
n. viral self-cleaving peptide element
o. A kozak consensus sequence.

8. A multicomponent system according to **any of the preceding claims**, wherein the component **B** and/or **D** is for RMCE integration of a single ORF and comprises:
    a. A Eukaryotic promoter
    b. A pair of heterospecific recombinase sites
    c. A Kozak consensus sequence
    d. A selection marker
    e. A Eukaryotic terminator.

9. A multicomponent system according to **any of claims** 3-8, wherein component **E** is present and component C and/or E is for RMCE integration of a single ORF and comprises the following genetic elements:
    a. A pair of heterospecific recombinase sites
    b. A Kozak consensus sequence
    c. An antibiotic resistance cassette
    d. A bacterial origin of replication
    e. A cloning site for introduction of a single ORF encoding one or more aAPX and/or aAM and/or selection marker of integration.

10. A multicomponent system according to **any of** claims 3-9, wherein component C and/or E is combined with at least one ORF encoding at least one aAPX and/or aAM to obtain component

C’ and/or E’.

11. A multicomponent system according to **claim 10,** wherein the combination is performed multiple times to obtain a library of component C’ and/or E’.

12. A multicomponent system according to any of **claims 10 or 11,** wherein one or more component C’ and/or E’ is combined with component A, to integrate one or more aAPX ORF(s) encoded in component C’ and/or E’, into components **B** and/or **D**, to obtain a cell, **designated eAPC-p,** wherein components B and/or D become components B’ and/or D’ such that the eAPC-p expresses an **aAPX** on the cell surface.

13. A multicomponent system according to any of **claims 10 or 11,** wherein one or more component C’ and/or E’ is combined with component A, to integrate one or more **aAM** ORF(s) encoded in component C’ and/or E’, into components **B** and/or **D**, to obtain a cell, **designated eAPC-a,** wherein components B and/or D become components B’ and/or D’ such that the eAPC-a expresses an **aAM** on the cell surface or intracellularly.

14. A multicomponent system according to any of **claims 10 or 11** wherein one or more component C’ and/or E’ is combined with component **A**, to integrate one or more **aAPX** ORF(s) and/or one or more **aAM** encoded in component C’ and/or E’, into components **B** and/or **D**, to obtain a cell, **designated eAPC-pa,** wherein components B and/or D becomes components B’ and/or D’ such that the eAPC-pa expresses an **aAPX and aAM** and/or an **aAPX:aAM.**

15. A multicomponent system according to **claim 12** wherein one or more component C’ or E’ is combined with an **eAPC-p**, to integrate one or more **aAM** ORF(s) encoded in component C’ or E’, into components **B** or **D**, to obtain a cell, **designated an eAPC-pa,** wherein components B or D becomes components B’ or D’ such that it expresses an **aAPX and aAM** and/or an **aAPX:aAM.**

16. A multicomponent system according to **claims 13** wherein one or more component C’ or E’ is combined with an **eAPC-a**, to integrate one or more **aAPX** ORF(s) encoded in component C’ or E’, into components **B** or **D,** to obtain a cell, **designated an eAPC-pa,** wherein components B or D becomes components B’ or D’ such that it expresses an **aAPX and aAM** and/or an **aAPX:aAM.**

17. A method for preparing an eAPC-p as defined in **claim 12,** the method comprising
    a. Combining component A, with at least one of component C’ and/or E’, wherein the one or more component C’ and/or E’ encode one or more **aAPX**, and combining with

integration factors and at least one of

b. Selecting for loss of genomic receiver site selection marker(s)
c. Selecting for gain of a surface expression of one or more aAPX
d. Selecting for gain of one or more of a selection marker of integration.

18. A method according to **claim 17** wherein b, c and d are included.

19. A method according to **claim 17 or 18,** wherein the one or more component C' and/or E' encodes a single **aAPX.**

20. A method according to **claim 19** wherein the method is conducted multiple times wherein each time step a is performed using a distinct **aAPX**, such that a distinct eAPC-p is obtained, to obtain a library of discrete and defined **eAPC-p.**

21. A method according to **claim** 17 **or 18** wherein the one or more component C' and/or E' encodes a mixed pool of two or more distinct **aAPX** in step a, to obtain a library, wherein the library comprising a mixed population of eAPC-p, wherein each eAPC-p expresses a single **aAPX**.

22. A method for preparing an **eAPC-a** as defined in **claim 13,** the method comprising

a. Combining component A, with at least one of component C' and/or E', wherein the one or more component C' and/or E' encode one or more **aAM**, and combining with integration factors and at least one of
b. Selecting for loss of genomic receiver site selection marker(s)
c. Selecting for gain of expression of one or more **aAM**
d. Selecting for gain of one or more of a selection marker of integration.

23. A method according to **claim 22** wherein b and d are included.

24. A method according to **claim 22 or 23,** wherein the one or more component C' and/or E' encodes a single **aAM** in step a.

25. A method according to **claim 24,** wherein the method is conducted multiple times, wherein each time step a is performed using a distinct **aAM**, such that a distinct eAPC-a is obtained, to obtain a library of discrete and defined **eAPC-a.**

26. A method according to **claim** 22 **or 23** wherein the one or more component C’ and/or E’ encodes a mixed pool of two or more distinct **aAM** in step a, to obtain a library, wherein the library is comprised of a mixed population of eAPC-a wherein each eAPC-a expresses a single **aAM**.

27. A method for preparing an **eAPC-pa** as defined in **claim 16,** the method comprising
    a. Combining **eAPC-a**, with at least one of component C’ or E’, wherein one or more component C’ or E’ encode one or more **aAPX** ORF, and combining with integration factors and at least one of
    b. Selecting for loss of genomic receiver site selection marker(s)
    c. Selecting for gain of a surface expression of one or more **aAPX**
    d. Selecting for gain of one or more of a selection marker of integration.

28. A method according to **claim 27,** wherein b, c and d are included.

29. A method according to **claim 27 or 28** wherein the one or more component C’ or E’ encodes a single **aAPX** in step a.

30. A method according to **claim 29** wherein the method is conducted multiple times wherein each time step a is performed using a distinct **aAPX**, such that a distinct **eAPC-pa** is obtained, to obtain a library of discrete and defined **eAPC-pa.**

31. A method according to **claim 39 or 40** wherein the one or more component C’ or E’ encodes a mixed pool of two or more distinct **aAPX** in step a of claim 39, to obtain a library, wherein the library is comprised of a mixed population of **eAPC-pa**, wherein each **eAPC-pa** expresses a single **aAPX** from the pool used in step a of claim 39.

32. A method for preparing an **eAPC-pa** as defined in **claim 15** the method comprising
    a. Combining **eAPC-p**, with at least one of component C’ or E’, wherein the one or more component C’ or E’ encode one or more **aAM** ORF, and combining with integration factors and at least one of
    b. Selecting for loss of genomic receiver site selection marker(s)
    c. Selecting for gain of expression of one or more **aAM**
    d. Selecting for gain of one or more of a selection marker of integration.

33. A method according to **claim 32** wherein b and d are included.

34. A method according to **claim 32 or 33** wherein the one or more component C’ or E’ encodes a single **aAM** in step a.

35. A method according to **claim 34,** wherein the method is conducted multiple times wherein each time step a is performed using a distinct **aAM**, such that a distinct **eAPC-pa** is obtained, to obtain a library of discrete and defined **eAPC-pa.**

36. A method according to **claim** 32 **or 33,** wherein the one or more component C’ or E’ encodes a mixed pool of two or more distinct **aAM** in step a, to obtain a library, wherein the library is comprised of a mixed population of **eAPC-pa**, wherein each **eAPC-pa** expresses a single **aAM** from the pool used in step a.

37. A method for preparing an **eAPC-pa** as defined in **claim 14,** the method comprising
    a. Combining **eAPC**, with at least one of component C’ or E’, wherein the one or more component C’ and/or E’ encode one or more **aAM** ORF and one or more **aAPX** ORF, and combining with integration factors and at least one of
    b. Selecting for loss of genomic receiver site selection marker(s)
    c. Selecting for gain of expression of one or more **aAM** and/or surface expression one or more **aAPX**
    d. Selecting for gain of one or more of a selection marker of integration.

38. A method according to **claim 37** wherein b, c and d are included.

39. A method according to **claim 37 or 38** wherein the one or more component C’ and/or E’ encodes a single **aAM** and a single **aAPX** in step a.

40. A method according to **claim 39** wherein the method is conducted multiple times, wherein each time step a is performed using at least one of a distinct **aAM** and/or a distinct **aAPX**, such that a distinct **eAPC-pa** is obtained, to obtain a library of discrete and defined **eAPC-pa.**

41. A method according to **claim** 37 **or 38** wherein the one or more component C’ and/or E’ encodes a mixed pool of two or more distinct **aAM** and/or two or more distinct **aAPX** in step a, to obtain a library, wherein the library is comprised of a mixed population of **eAPC-pa**, wherein

each **eAPC-pa** expresses a single **aAM** and a single **aAPX** from the pool used in step a.

42. Use of a multicomponent system as defined in any of claims 1-16 to generate one or more of analyte eAPCs selected from eAPC-p and/or eAPCa and/or eAPC-pa.

43. Use of one or more analyte eAPCs as defined in claim 12 to16 for manufacturing antigen-specific T cells.