

Claims

1. A two-part system forming a combined eAPC:eTPC analytical system, wherein a first part is an **engineered antigen-presenting cell system (eAPCS)**, and a second part is
 5 an **engineered TCR-presenting cell system (eTPCS)**,

wherein said eAPCS comprises

10 a first component which is an **engineered antigen-presenting cell (eAPC)**,
designated component 1A, wherein component 1A lacks endogenous surface expression of at least one family of analyte antigen presenting complexes (aAPX) and/or analyte antigenic molecules (aAM) and contains a second component **designated component 1B**, a **synthetic** genomic receiver site, for recombina-
 15 ORFs encoding an aAPX and/or an aAM, and

a third component which is a genetic donor vector **designated component 1C**, for delivery and integration into 1B of ORF encoding said aAPX and/or said aAM, wherein said aAPX and/or said aAM belong to the at least one family of
 20 aAPX and/or aAM for which component 1A lacks endogeneous surface expression, wherein component 1C is matched to component 1B, and wherein component 1C is designed to deliver one or two ORFs encoding an aAPX and/or an aAM such that the aAPX and/or aAM can be expressed by
 component 1A,

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and wherein said eTPCS comprises

a first component, which is an engineered TCR-presenting cell (eTPC),
designated component 2A, wherein component **2A** lacks endogenous surface
 30 expression of at least one family of analyte antigen-presenting complexes (**aAPX**) and/or analyte antigenic molecule (**aAM**) from which said aAPX and/or said aAM encoded by the ORF in component 1C belong to, lacks endogenous expression of TCR chains alpha, beta, delta and gamma, and expresses CD3 proteins which are conditionally presented on the surface of the cell only when
 35 the cell expresses a complementary pair of TCR chains and contains a second component **designated 2B**, a genomic receiver site for recombina-
 mediated

cassette exchange (RMCE) integration of a single ORF encoding at least one analyte TCR chain of alpha, beta, delta or gamma, and/or two ORFs encoding a pair of analyte TCR chains, and

5 a third component is a genetic donor vector, **designated component 2C**, for delivery of ORF encoding analyte TCR chains, wherein **component 2C**, is matched to component **2B**, and wherein the component **2C** is designed to deliver

10 a. A single ORF encoding at least one analyte TCR chain of alpha, beta, delta and/or gamma and/or

b. Two ORFs encoding a pair of analyte TCR chains

such that the analyte TCR chains can be expressed as TCR surface protein in complex with the CD3 (**TCRsp**) on component **2A**.

15 2. A two-part system according to **claim 1** wherein **eAPCS** comprises the one or more of analyte eAPC selected from at least one of:

a. eAPC-p,

b. eAPC-a,

c. eAPC-pa, and

d. a library of a, b or c.

20 3. A two-part system according to **claim 2**, wherein an eAPC-p, eAPC-a or eAPC-pa can express an **analyte antigen** selected from

a. an aAPX or

b. an aAM or

c. an aAPX:aAM or

25 d. an aAPX:CM or

e. a combination thereof.

4. A two-part system according to any of the previous claims wherein **eTPCS** comprises one or more analyte eTPC selected from
 - a. eTPC-t and
 - b. a library thereof.
- 5 5. A two-part system according to claim 4, comprising an analyte eTPC, which can express an analyte pair of TCR chains as TCR surface proteins in complex with CD3 (analyte **TCRsp**).
6. A two-part system according to claim 5, wherein the eTPC contains a component 2F, representing a synthetic TCR signal response element engineered to the genome of
 - 10 the eTPC, and which is used to report the formation of complex between analyte TCRsp and an analyte antigen presented by eAPC -p, -a or -pa, and which results in a signal response in the eTPC.
7. Use of a two-part system as defined in any of the preceding claims, wherein said use comprises combining one or more analyte eAPC with one or more analyte eTPC.
- 15 8. Use according to claim 7, wherein the combination results in a contact between an analyte TCRsp and an analyte antigen as defined in claim 3, wherein the contact results in a signal response.
9. Use according to claim 8, wherein the contact results in the formation of a complex between the analyte TCRsp and the analyte antigen.
- 20 10. Use according to claim 9 wherein the formation of a complex induces a signal response in the analyte eTPC or the analyte eAPC.
11. Use according to any of claims 7-9 for selecting an analyte eTPC or a pool of analyte eTPC, or a pool of analyte eAPC using the signal response.