

Claims

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

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wherein said eAPCS comprises

a first component which is an **engineered antigen-presenting cell (eAPC)**,
designated component 1A, wherein component 1A lacks endogenous surface
 10 expression of at least one family of analyte antigen presenting complexes
 (aAPX) and/or analyte antigenic molecules (aAM) and contains a second com-
 ponent **designated component 1B**, a **synthetic** genomic receiver site, for re-
 combinase mediated cassette exchange (RMCE) integration of one or two
 ORFs encoding an aAPX and/or an aAM, and
 15 a third component which is a genetic donor vector **designated component 1C**,
 for delivery and integration into 1B of ORF encoding aAPX and/or aAM, wherein
 component 1C is matched to component 1B, and wherein component 1C is de-
 signed to deliver one or two ORFs encoding an aAPX and/or an aAM
 and wherein said one or two ORFs optionally also encodes a selection marker
 20 of integration, such that the aAPX and/or aAM can be expressed by component
 1A.

2. A two-part device according to **claim 1** wherein said eTPCS comprises

a first component, which is an engineered TCR-presenting cell (eTPC), **desig-**
 25 **nated component 2A**, wherein component **2A** lacks endogenous surface
 expression of at least one family of analyte antigen-presenting complexes
 (**aAPX**) and/or analyte antigenic molecule (**aAM**), lacks endogenous expres-
 sion of TCR chains alpha, beta, delta and gamma, and expresses CD3 pro-
 teins which are conditionally presented on the surface of the cell only when
 30 the cell expresses a complementary pair of TCR chains and contains a sec-
 ond component **designated 2B**, a genomic receiver site for recombinase
 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

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

5 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.

and wherein a and/or b optionally encodes a selection marker of integration, such that the analyte TCR chains can be expressed as TCR surface protein
10 in complex with the CD3 (**TCRsp**) on component **A**.

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

a. eAPC-p,

b. eAPC-a,

15 c. eAPC-pa, and

d. a library of a, b or c.

4. A two-part device according to **claim 3**, wherein an eAPC-p, eAPC-a or eAPC-pa expresses an **analyte antigen** selected from

e. an aAPX or

20 f. an aAM or

g. an aAPX:aAM or

h. an aAPX:CM or

i. a combination thereof.

5. A two-part device according to any of the previous claims wherein **eTPCS** provides
25 one or more analyte eTPC selected from

a. eTPC-t and

b. a library thereof.

6. A two-part device according to claim 5, wherein an analyte pair of TCR chains are expressed as TCR surface proteins in complex with CD3 (analyte **TCRsp**) by an analyte eTPC.
- 5 7. A two-part device according to claim 6, wherein the eTPC contains a component 2F, representing a synthetic TCR signal response element engineered to the genome of the eTPC, and which is used to report the formation of complex between analyte TCRsp and a analyte antigen presented by eAPC –p, -a or –pa, and which results in a signal response in the eTPC.
- 10 8. A two-part device according to any of the preceding claims, wherein one or more analyte eAPC, is combined with one or more analyte eTPC.
9. A two-part device according to **claim 8**, wherein the combination results in a contact between an analyte TCRsp and an analyte antigen as defined in claim 4, wherein the contact may or may not result in a signal response.
- 15 10. A two-part device according to **claim 9**, wherein the contact may result in the formation of a complex between the analyte TCRsp and the analyte antigen.
11. A two-part device according to **claim 10** wherein a formation of a complex, if any, can induce a signal response in the analyte eTPC and/or the analyte eAPC.
12. A two-part device according to any of claims 8-10, wherein the signal response is
20 used to select an analyte eTPC or a pool of analyte eTPC with or without a signal response and/or analyte eAPC or a pool of analyte eAPC with or without a signal response.