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kind of national protection available): AE, AG, AL, AM,
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CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO,
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(54) Title: CELL SURFACE CONJUGATES AND RELATED CELL COMPOSITIONS AND METHODS

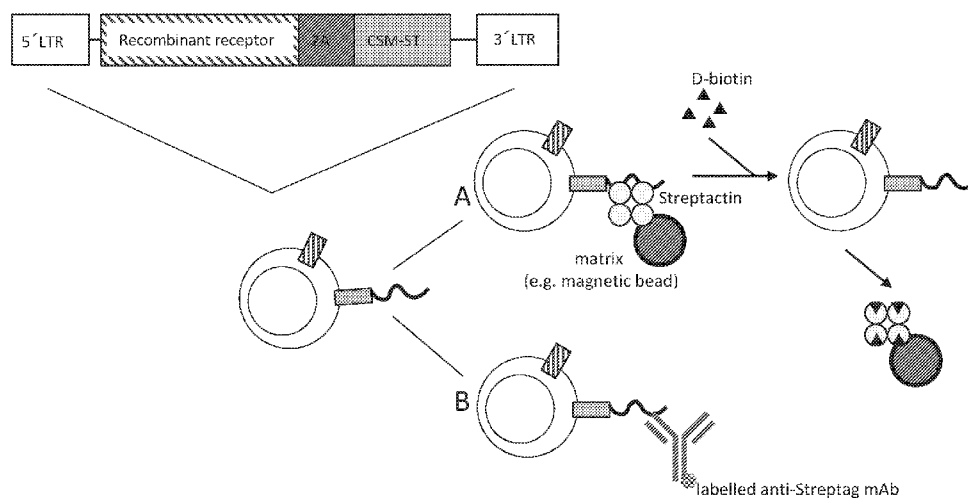


FIG. 1

(57) Abstract: Provided herein are cell surface conjugates containing a cell surface molecule and at least one agent, such as at least one affinity tag, and engineered cells expressing such cell surface conjugates. In some embodiments, the cell surface molecule does not contain an intracellular signaling domain or is not capable of mediating intracellular signaling. In some embodiments, the cells engineered to contain the cell surface conjugate, such as T cells, further contain a genetically engineered recombinant receptor that specifically binds to antigens, such as a chimeric antigen receptor (CAR). Also provided are methods of detecting, identifying, selecting or targeting cells expressing the cell surface conjugates, such as in connection with methods of manufacturing engineered cells or in connection with administration of such cells to subjects, including methods of adoptive cell therapy.



UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
- *with sequence listing part of description (Rule 5.2(a))*

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2018/000380

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K14/705 A61K39/00 C07K14/47 C12N5/0783
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07K A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 3 115 066 A1 (TECHNISCHE UNIVERSITÄT MÜNCHEN [DE]; CZECH ACADEMY OF SCIENCES [CZ]) 11 January 2017 (2017-01-11) figure 1A paragraphs [0156], [0161] ----- -/--	1-61, 64-72, 86-190

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

5 July 2018

Date of mailing of the international search report

09/10/2018

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2018/000380

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

13(completely); 1-12, 14-61, 64-72, 86-190(partially)

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2018/000380

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CYRIL BARINKA ET AL: "Selection and characterization of Anticalins targeting human prostate-specific membrane antigen (PSMA)", PROTEIN ENGINEERING, DESIGN AND SELECTION, vol. 29, no. 3, 21 January 2016 (2016-01-21), pages 105-115, XP055490037, GB ISSN: 1741-0126, DOI: 10.1093/protein/gzv065 figure 1a section "SF-PSMA"; page 112</p>	1-61, 64-72, 86-190
X	<p>PETRA MLCOCHOVÁ ET AL: "Prostate-specific membrane antigen and its truncated form PSM'", PROSTATE., vol. 69, no. 5, 1 April 2009 (2009-04-01), pages 471-479, XP055490378, US ISSN: 0270-4137, DOI: 10.1002/pros.20894 page 473, last paragraph - page 474, paragraph 1 figures 1, 2</p>	1-61, 64-72, 86-190
X	<p>WO 2016/176651 A2 (HUTCHINSON FRED CANCER RES [US]) 3 November 2016 (2016-11-03)</p> <p>figures 25-28 claims 1, 3, 4, 12 example 1 paragraph [0286]; example 2</p>	1-61, 64-72, 86-190
X	<p>X. WANG ET AL: "A transgene-encoded cell surface polypeptide for selection, in vivo tracking, and ablation of engineered cells", BLOOD, vol. 118, no. 5, 4 August 2011 (2011-08-04), pages 1255-1263, XP055062819, ISSN: 0006-4971, DOI: 10.1182/blood-2011-02-337360 the whole document</p>	1-61, 64-72, 86-190
A	<p>CHRISTIAN STEMBERGER ET AL: "Novel Serial Positive Enrichment Technology Enables Clinical Multiparameter Cell Sorting", PLOS ONE, vol. 7, no. 4, 24 April 2012 (2012-04-24), page e35798, XP055043969, DOI: 10.1371/journal.pone.0035798 the whole document</p>	1-61, 64-72, 86-190

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2018/000380

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SKERRA A ET AL: "Use of the Strep-Tag and streptavidin for detection and purification of recombinant proteins", METHODS IN ENZYMO, ACADEMIC PRESS, US, vol. 326, 1 January 2000 (2000-01-01), pages 271-304, XP009176755, ISSN: 0076-6879 the whole document	1-61, 64-72, 86-190
A	----- LINGFENG LIU ET AL: "Inclusion of Strep-tag II in design of antigen receptors for T-cell immunotherapy", NATURE BIOTECHNOLOGY, vol. 34, no. 4, 22 February 2016 (2016-02-22), pages 430-434, XP055290073, US ISSN: 1087-0156, DOI: 10.1038/nbt.3461 the whole document	1-61, 64-72, 86-190
A	----- SCHMIDT THOMAS G M ET AL: "The Strep-tag system for one-step purification and high-affinity detection or capturing of proteins", NATURE PROTOCOLS, NATURE PUBLISHING GROUP, GB, vol. 2, no. 6, 1 January 2007 (2007-01-01), pages 1528-1535, XP001536704, ISSN: 1750-2799, DOI: 10.1038/NPROT.2007.209 the whole document -----	1-61, 64-72, 86-190

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2018/000380

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
EP 3115066	A1	11-01-2017	EP 3115066 A1	11-01-2017
			EP 3319641 A1	16-05-2018
			WO 2017005799 A1	12-01-2017

WO 2016176651	A2	03-11-2016	EP 3288569 A2	07-03-2018
			JP 2018521628 A	09-08-2018
			WO 2016176651 A2	03-11-2016

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 13(completely); 1-12, 14-61, 64-72, 86-190(partially)

Cell surface conjugate comprising PSMA lacking a functional intracellular domain and an agent capable of binding streptavidin.

- 2-65. claims: 1-12, 14-190(all partially)

As invention 1, but relating to a cell surface molecule selected from EpCAM, VEGFR, integrins alphavbeta3, alpha4, alphaIibbeta3, alpha4beta7, alpha5beta1, alphavbeta3 or alphav, TRAIL-R1 or TRAIL-R2, PDGF Receptor, interferon receptor, folate receptor, GPNMB, ICAM-1, HLA-DR, CEA, CA-125, MUC1, TAG-72, IL-6 receptor, 5T4, GD2, GD3, or CD2, CD3, CD4, CD5, CD11, CD11a/LFA-1, CD15, CD18/ITGB2, CD19, CD20, CD22, CD23/IgE Receptor, CD25, CD28, CD30, CD33, CD38, CD40, CD41, CD44, CD51, CD52, CD62L, CD74, CD80, CD125, CD147/basigin, CD152/CTLA-4, CD154/CD40L, CD195/CCR5 and CD319/SLAMF7, epidermal growth factor receptor (EGFR), an erbB-2 receptor tyrosine-protein kinase (errb2, HER2), an erbB-3 receptor tyrosine-protein kinase, an erbB-4 receptor tyrosine-protein kinase, a hepatocyte growth factor receptor (HGFR/c-MET) or an insulin-like growth factor receptor-1 (IGF-1 R) respectively.
