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(54) Title: CHIMERIC POLYPEPTIDES AND METHODS OF USING THE SAME

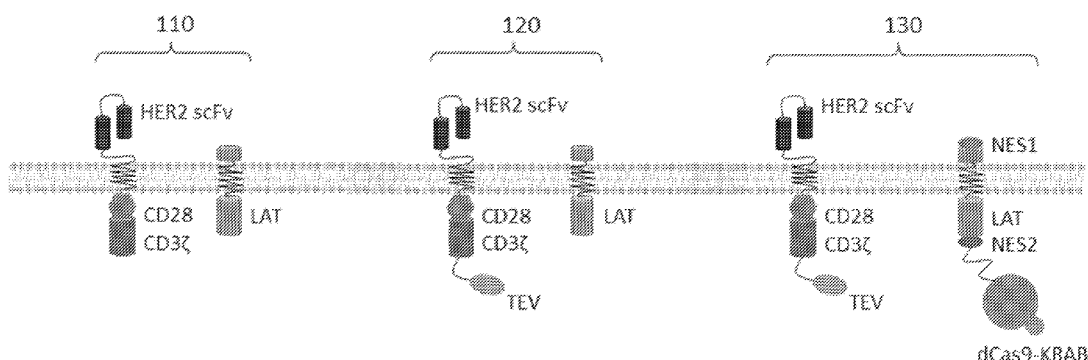


FIG. 1A

(57) Abstract: The present disclosure provides a chimeric polypeptide comprising at least one heterologous nuclear export signal linked to an adaptor protein of a receptor. The adaptor protein may be a Linker for Activation of T cell (LAT). The receptor may comprise a chimeric receptor.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/19358

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C12N 15/79; C07K 14/705; C07K 19/00 (2020.01)

CPC - C07K 19/00; C07K 14/705; C07K 2319/00; C07K 2319/095; C12N 15/79

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)

See Search History document

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

See Search History document

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2018/0273980 A1 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 27 September 2018 (27.09.2018). Especially para [0067], [0080], [0104], [0127], [0210], [0392], sheet 21 fig 21B, claim 1.	1-7, 10-13, 17-18, 23, 30-33, (34-37,39,40)/(1-7,10-13,17-18,23,30-33) ----- 8, 9, 14-16, 19-22, 24-29, (34-37,39,40)/(8,9,14-16,19-22,24-29)
Y	KUNII et al. Enhanced function of redirected human T cells expressing linker for activation of T cells that is resistant to ubiquitylation. Hum Gene Ther, January 2013, Vol 24, No 1, Pages 27-37. Especially abstract, pg 28 col 2 para 1, pg 29 col 2 para 5.	8-9, (34-37,39,40)/(8-9)
Y	US 2013/0115700 A1 (FUJII) 9 May 2013 (09.05.2013). Especially para [0063]; SEQ ID NO: 10.	14-16, (34-37,39,40)/(14-16)
Y	VISHNIVETSKIY et al. Functional role of the three conserved cysteines in the N domain of visual arrestin-1. J Biol Chem. 28 June 2017, Vol 292, No 30, Pages 12496-12502. Especially abstract.	19-20, (34-37,39,40)/(19-20)

☒ 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

"D" document cited by the applicant in the international application

"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

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Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/19358

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SHUKLA et al. Structure of active beta-arrestin-1 bound to a G-protein-coupled receptor phosphopeptide. Nature. 2 May 2013, Vol 497, No. 7447, Pages 137-141 [HHS Public Access Copy provided]. Especially pg 4 col 2 para 1.	21-22, (34-37,39,40)/(21-22)
Y	US 2006/0263828 A1 (SHENOY et al.) 23 November 2006 (23.11.2006). Especially para [0036], claims 1, 5.	24-29, (34-37,39,40)/(24-29)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/19358

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.: 38
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:

-----Go to Extra Sheet for continuation-----

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 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.:
Claim 1-37, 39, 40

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
Information on patent family members

International application No.

PCT/US 20/19358

continuation of Box III: Observations where Unity of Invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I: Claims 1-37, 39, 40, drawn to a chimeric polypeptide comprising at least one heterologous nuclear export signal (NES) linked to an adaptor protein of a receptor.

Group II: Claims 41-165, drawn to a system or method for regulating or enhancing signaling of a receptor in a cell. The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I has the special technical feature of a composition comprising a heterologous NES linked to an adaptor protein of a receptor, not required by Group II.

Group II has the special technical feature of "upon introducing the system into the cell, the chimeric polypeptide prolongs or enhances the signaling of the receptor", not required by Group I.

Group II has the special technical feature of the method step of "expressing a system in the cell", not required by Group I.

Common Technical Feature:

Groups I and II share the common technical feature of: a chimeric polypeptide comprising at least one heterologous nuclear export signal (NES) linked to an adaptor protein of a receptor.

However, said common technical feature of does not represent a contribution over the prior art, and is disclosed by US 2018/0273980 A1 in The Board of Trustees of the Leland Stanford Junior University (hereinafter "Stanford").

As to the common technical feature, Stanford discloses a chimeric polypeptide comprising at least one heterologous nuclear export signal (NES) linked to an adaptor protein of a receptor (para [0210]; "In some embodiments, a targeting sequence comprises a nuclear export signal (NES) and directs the chimeric adaptor polypeptide outside of a cell nucleus"; para [0104]; "To de-activate this signaling, a GPCR [i.e. G Protein Coupled Receptor] can first be chemically modified by phosphorylation. Phosphorylation can then recruit co-adaptor proteins (e.g., arrestin proteins) for additional signaling") para [0127]; "receptor polypeptide comprises a cell surface antigen receptor such as a T cell receptor (TCR), a B cell receptor (BCR)";

As the common technical feature was known in the art at the time of the invention, this cannot be considered a common special technical feature that would otherwise unify the groups. The inventions lack unity with one another.

Therefore, Groups I and II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note concerning item 4: Claims 38 is a multiple dependent claim and is not drafted according to the second and third sentences of PCT Rule 6.4(a).