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C12N 15/113 (2010.01)

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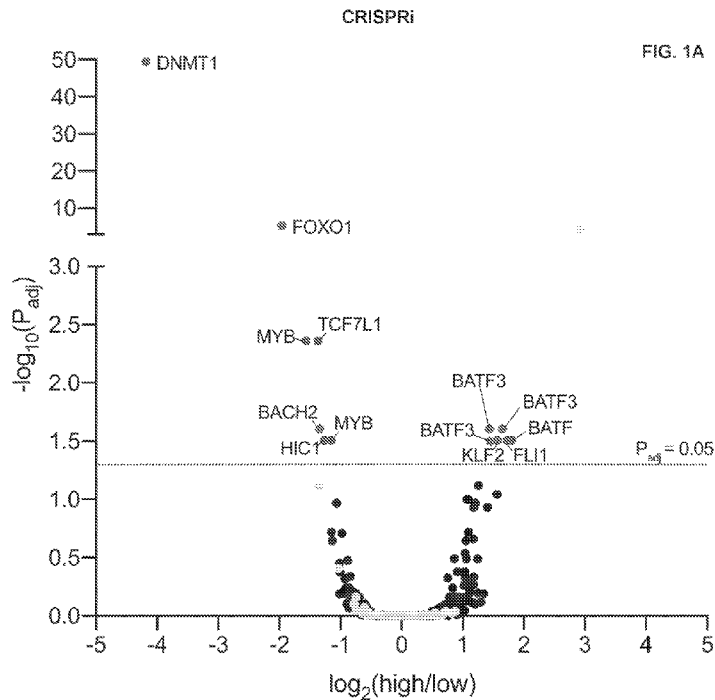
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(54) Title: COMPOSITIONS AND METHODS FOR EPIGENOME EDITING TO ENHANCE T CELL THERAPY



(57) Abstract: Disclosed herein are compositions and methods for modulating T cells. For example, the compositions and methods may be used to increase memory T cells. The compositions and method may be used in combination with Adoptive T Cell Therapy (ACT) to enhance the ACT.



DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT,
LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE,
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- *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))*

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/63297

<p>A. CLASSIFICATION OF SUBJECT MATTER</p> <p>IPC - INV. C12N 5/0783, A61K 35/17, C12N 15/113, C12N 9/22 (2023.01) ADD. C12N 15/85 (2023.01)</p> <p>CPC - INV. C12N 5/0636, A61K 35/17, C12N 15/113, C12N 9/22</p> <p>ADD. C12N 2501/60, C12N 2310/20, C12N 15/85, C12N 2510/00</p> <p>According to International Patent Classification (IPC) or to both national classification and IPC</p>														
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols) See Search History document</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched See Search History document</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) See Search History document</p>														
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>US 2019/0183932 A1 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 20 June 2019 (20.06.2019) para [0028], claims 12, 15, 16</td> <td>1-6</td> </tr> <tr> <td>X</td> <td>WO 2022/038264 A1 (JULIUS-MAXIMILIANS-UNIVERSITAT WURZBURG) 24 February 2022 (24.02.2022) pg 3 para 2, claim 47.</td> <td>31, 32, 35, 36</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	US 2019/0183932 A1 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 20 June 2019 (20.06.2019) para [0028], claims 12, 15, 16	1-6	X	WO 2022/038264 A1 (JULIUS-MAXIMILIANS-UNIVERSITAT WURZBURG) 24 February 2022 (24.02.2022) pg 3 para 2, claim 47.	31, 32, 35, 36			
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.</p>														
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"D" document cited by the applicant in the international application</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td></td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"D" document cited by the applicant in the international application	"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	"E" earlier application or patent but published on or after the international filing date	"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	"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)	"&" document member of the same patent family	"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	
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"P" document published prior to the international filing date but later than the priority date claimed														
<p>Date of the actual completion of the international search</p> <p>17 August 2023</p>		<p>Date of mailing of the international search report</p> <p style="text-align: center; font-size: 1.2em; font-weight: bold;">OCT 18 2023</p>												
<p>Name and mailing address of the ISA/US</p> <p>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300</p>		<p>Authorized officer</p> <p style="text-align: center;">Kari Rodriguez</p> <p>Telephone No. PCT Helpdesk: 571-272-4300</p>												

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/63297

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

a. forming part of the international application as filed.

b. furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),

accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 7-30, 37-53
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.:
Claims 1-6, 31, 32, 35, 36, limited to modulator of BATF3.

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.

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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 1-6, 31-36, drawn to a composition for modulating T cells.

The composition for modulating T cells will be searched to the extent that the gene to be modulated is the first named, BATF3. This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. It is believed that claims 1-6, 31, 32, 35, 36 read on this first named invention and thus these claims will be searched without fee to the extent that they encompass BATF3.

Additional genes to be modulated will be searched upon payment of additional fees. Applicant must specify the claims that encompass any additional elected target gene(s). Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be: DNMT1 (claims 1-6, 33, 34).

The inventions listed as Groups I+ 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:

Among the inventions listed as Groups I+ are the specific genes recited therein. Each invention requires a specific gene, not required by any other inventions.

Common Technical Features:

1. a composition for modulating T cells comprising a modulator of a gene (e.g., BATF3).
2. A DNA targeting composition comprising a Cas9 protein or fusion protein and a guide RNA.

However, said common technical features do not represent a contribution over the prior art, and are disclosed by US 2019/0183932 A1 to The Board of Trustees of the Leland Stanford Junior University (hereinafter "Stanford").

As to common technical feature #1, Stanford discloses a composition for modulating T cells comprising a modulator of a gene (e.g., BATF3) (claim 12; "method of treating a disease or condition in a patient comprising administering to the patient having the disease or condition an effective amount of a composition comprising T cells modified to reduce and/or eliminate expression and/or activity of one or more AP-1 inhibitory complex members"; claim 15; "The method of claim 12, wherein the AP-1 inhibitory complex member is JunB, BATF3, and/or IRF4"; claim 16; "The method of claim 12, wherein the T cells are modified by CRISPR-Cas9, shRNA, siRNA, RNAi").

As to common technical feature #2, Stanford discloses a DNA targeting composition comprising a Cas9 protein or fusion protein and a guide RNA (claim 16; "The method of claim 12, wherein the T cells are modified by CRISPR-Cas9"; para [0028]; "HA-28Z exhausted CAR T cells edited using three independent gRNAs targeting BATF3 all showed increased IL2 production compared to control or ZB2 edited controls").

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

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

Notes:

Claim 36 is written to depend from claim 5, but claim 5 lacks antecedent precedent to "activator". For the purposes of the International Search & Opinion, claim 36 is interpreted to depend from claim 35, which does have antecedent precedent to "activator".

Item 4 (continuation): Claims 7-30, 37-53 are dependent claims and are not drafted according to the second and third sentences of PCT Rule 6.4(a).