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(54) Title: ENGINEERED CHIMERIC NUCLEIC ACID GUIDED NUCLEASE CONSTRUCTS AND USES THEREOF

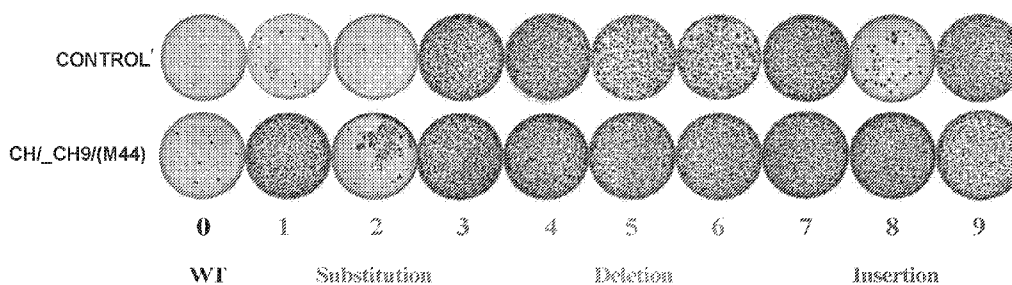


Fig. 4B

(57) Abstract: Embodiments of the present disclosure relate to engineered chimeric nucleic acid guided nucleases for improved targeted gene editing. In certain embodiments, the engineered chimeric nucleic acid guided nucleases can be used for genome editing. In accordance with these embodiments, a targeted genome can be edited by one or more of the engineered chimeric nucleic acid guided nucleases comprising one or more nucleic acid or amino acid constructs represented by one or more of SEQ ID NO:1 to SEQ ID NO:9 or a polypeptide encoded thereof. In certain embodiments, the engineered chimeric nucleic acid guided nucleases can be used to remove, edit, and/or insert genes into a targeted genome. In other embodiments, use of these chimeras can be for producing a targeted result (e.g. removing, editing or replacing a defective gene) in a subject to reduce the onset of or prevent a condition.



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- *with international search report (Art. 21(3))*
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/54872

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C12N 9/22, 15/10, 15/11, 15/52; C12P19/34 (2020.01)

CPC - C12N 9/22, 15/10, 15/11, 15/52; C12P19/34

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 -- A	US 2018/0230461 A1 (THE REGENTS OF THE UNIVERSITY OF COLORADO et al.) 16 August 2018; paragraphs [0007], [0263], [0396]; table 1	13 ----- 1-4, 14-16, 40
A	WO 2018/071672 A1 (THE REGENTS OF THE UNIVERSITY OF COLORADO et al.) 19 April 2018; paragraphs [00154], [00166], [00173], [00257]	1-4, 14-16, 40
A	(GARST, A et al.) Synthetic Construct RNA-Directed Nuclease (MAD7) Gene, Complete CDS. National Center for Biotechnology Information. Genbank Entry. Submitted 14 May 2018 [retrieved on 24 March 2020]. Retrieved from the Internet: <URL: https://www.ncbi.nlm.nih.gov/nuccore/MH347339>; pages 1-2	1-4, 40
A	(PARKS, DH) TPA: Type V CRISPR-Associated Protein Cpf1 [Eubacterium sp.]. National Center for Biotechnology Information. Genbank Entry. Submitted 04 April 2018 [retrieved on 24 March 2020]. Retrieved from the Internet: <URL: https://www.ncbi.nlm.nih.gov/protein/HCF15406>; pages 1-2	14-16

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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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/54872

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.: 7-12, 19-39, 41-43
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:

- Please See within the Next Supplemental Page-

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.:
Group 1+ Claims 1-4, 13-16, 40; SEQ ID NO: 1 (nucleic acid sequence), encoding SEQ ID NO: 33 (amino acid sequence)

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/US19/54872

-Continued from 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 examined, the appropriate additional examination fees must be paid.

Groups I+, Claims 1-6, 13-18, 40, and SEQ ID NO: 1 (nucleic acid sequence), encoding SEQ ID NO: 33 (amino acid sequence) are directed toward engineered chimeric nucleic acid guided nuclease constructs; and polypeptides encoded thereby.

The constructs and polypeptides will be searched to the extent they encompass a construct encompassing SEQ ID NO: 1 (first exemplary nucleic acid sequence), encoding SEQ ID NO: 33 (first exemplary amino acid sequence). Applicant is invited to elect additional nucleic acid sequence(s), with corresponding encoded amino acid sequence(s), with specified SEQ ID NO: for each, or with specified substitution (s) at specified site(s) of a SEQ ID NO:, such that the sequence of each elected species is fully specified (i.e. no optional or variable nucleobases, residues or substituents), and where available as an option within at least one searchable claim, to be searched. Additional nucleic acid and/or amino acid sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1-4 (each in-part), 13-16 (each in-part), and 40 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 1 (nucleic acid sequence), encoding SEQ ID NO: 33 (amino acid sequence). Applicants must specify the searchable claims that encompass any additionally elected nucleic acid and/or amino acid sequence(s). Applicants must further indicate, if applicable, the claims which encompass 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 SEQ ID NO: 2 (nucleic acid sequence), encoding SEQ ID NO: 32 (amino acid sequence).

No technical features are shared between the nucleic acid sequences and/or amino acid sequences of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features including: an engineered chimeric nucleic acid guided nuclease construct comprising, a construct represented by a nucleic acid sequence; and a polypeptide encoded by the nucleic acid sequence; these shared technical features are previously disclosed by WO 2018/071672 A1 to The Regents of the University of Colorado, et al. (hereinafter 'Colorado').

Colorado discloses an engineered chimeric nucleic acid guided nuclease construct (a vector encoding an engineered chimeric nucleic acid guided nuclease (an engineered chimeric nucleic acid guided nuclease construct); abstract, paragraph [00166]) comprising, a construct represented by a nucleic acid sequence (comprising, a construct represented by a nucleic acid sequence; paragraphs [0003], [0009], [00166]); and a polypeptide encoded by the nucleic acid sequence (a polypeptide encoded by the nucleic acid sequence; paragraphs [00154], [00173], [00257]).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Colorado reference, unity of invention is lacking.