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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

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(54) Title: SITE-SPECIFIC MODIFICATION OF THE HUMAN GENOME USING CUSTOM-DESIGNED ZINC FINGER NUCLEASES

(57) Abstract: Disclosed herein are chimeric zinc finger endonucleases useful in disrupting and/or replacing at least a portion of a gene of interest (e.g. CFTR, DMPK, CCR5, TYR or β globin).



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/028739

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N15/62 C12N15/09 C12Q1/68 C12N15/90

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)

C12N C12Q

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 practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, FSTA, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KANDAVELOU K ET AL: "ENGINEERING AND APPLICATIONS OF CHIMERIC NUCLEASES" NUCLEIC ACIDS AND MOLECULAR BIOLOGY, SPRINGER VERLAG, BERLIN, DE, 2004, pages 413-434, XP008071950 ISSN: 0933-1891 the whole document, in particular p.428, paragraph 4.2	1-13, 54-56
X	KANDAVELOU KARTHIKEYAN ET AL: "'Magic" scissors for genome surgery." NATURE BIOTECHNOLOGY. JUN 2005, vol. 23, no. 6, June 2005 (2005-06), pages 686-687, XP002411068 ISSN: 1087-0156 the whole document	1-3, 54-56
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☒ 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 document 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.

G document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/028739

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Y-G KIM ET AL: "Hybrid restriction enzymes: Zinc finger fusions to Fok I cleavage domain" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 93, no. 3, 6 February 1996 (1996-02-06), pages 1156-1160, XP002116423 ISSN: 0027-8424 the whole document	1-3, 54-56
X	URNOV FYODOR D ET AL: "Highly efficient endogenous human gene correction using designed zinc-finger nucleases." NATURE. 2 JUN 2005, vol. 435, no. 7042, 2 June 2005 (2005-06-02), pages 646-651, XP002411069 ISSN: 1476-4687 the whole document	1-3, 54-56
P,X	MANI ET AL: "Design, engineering, and characterization of zinc finger nucleases" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 335, no. 2, 23 September 2005 (2005-09-23), pages 447-457, XP005021916 ISSN: 0006-291X the whole document, in particular Table 1	1-13, 54-56
P,X	DURAI S ET AL: "Zinc finger nucleases: custom-designed molecular scissors for genome engineering of plant and mammalian cells" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 33, no. 18, 26 October 2005 (2005-10-26), pages 5978-5990, XP002403200 ISSN: 0305-1048 the whole document	1-3, 54-56

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/028739

Box 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:

Although claims 6-9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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 fee, this Authority did not invite payment of any additional fee.
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.:

1-3 and 54-56 all partially; 4-13 all completely

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-3 and 54-56 all partially; 4-13 all completely

Method and related compositions for cleaving or disrupting the CFTR gene and the replacement of mutations in said gene associated with cystic fibrosis via homologous recombination under the use of zinc finger nucleases.

2. claims: 1-3 and 54-56 all partially; 14-23 all completely

Method and related compositions for cleaving or disrupting the DMPK gene and the replacement of mutations in said gene associated with myotonic dystrophy via homologous recombination under the use of zinc finger nucleases.

3. claims: 1-3 and 54-56 all partially; 24-39 all completely

Method and related compositions for cleaving or disrupting the CCR5 gene and the replacement of mutations in said gene via homologous recombination under the use of zinc finger nucleases.

4. claims: 1-3 and 54-56 all partially; 40-50 all completely

Method and related compositions for cleaving or disrupting the TYR gene and the replacement of mutations in said gene associated with tyrosinase enzyme activity via homologous recombination under the use of zinc finger nucleases.

5. claims: 1-3 and 54-56 all partially; 51-53 all completely

Method and related compositions for cleaving or disrupting the beta globin gene and the replacement of mutations in said gene associated with sickle cell anemia via homologous recombination under the use of zinc finger nucleases.
