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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))

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))

(88) Date of publication of the international search report:

23 November 2023 (23.11.2023)

(54) Title: POLYPEPTIDES AND METHODS OF USE

(57) Abstract: The invention features polypeptides containing nuclear localization sequences that can be used to deliver polynucleotides to a cell. The polypeptides can be formulated with a polynucleotide and a lipid.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 47/64, A61K 47/69 (2023.01)

ADD. C12N 15/87, A61K 31/713 (2023.01)

CPC - INV. A61K 47/64, A61K 47/6455, A61K 47/6929

ADD. C07K 2319/00, C07K 2319/09, C12N 15/87

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 2022/0090141 A1 (MOLECULAR TRANSFER, INC.) 24 March 2022 (24.03.2022) para [0011]; [0026]; [0032]-[0036]; [0040]-[0049]; [0053]; [0063]; [0067]-[0074]; [0078]-[0087]; [0191]; Table 1, SEQ ID NOS: 1, 93	1-6, 9-15, 40-48, 63-70 ----- 16-23
Y	US 2015/0314011 A1 (THE QUEEN'S UNIVERSITY OF BELFAST) 05 November 2015 (05.11.2015) para [0030]-[0041]; [0046]-[0049]; SEQ ID NO: 1	16-23
A	KANG et al., Peptide-based gene delivery vectors. Journal of Materials Chemistry B. 2019; Vol 7, No 11, pp: 1824-41. full document	1-6, 9-23, 40-48, 63-70

☐ 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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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:

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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.:
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:
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.

--continued on extra 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 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.:
1-6, 9-23, 40-48, 63-70, limited as discussed on extra sheet

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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--continued from: Box No. III Observations where unity of invention is lacking--

Group I+, claims 1-70 79-119, directed to a composition comprising: (a) a polypeptide comprising a DNA condensing polypeptide and a nuclear localization sequence (NLS). The composition will be searched to the extent that the composition/polypeptide encompasses a polypeptide wherein the NLS comprises the amino acid sequence PKKKRKV (SEQ ID NO: 1), the DNA condensing polypeptide comprises an amphipathic alpha helix, wherein the DNA condensing polypeptide comprises the amino acid sequence of WEARLARALARARHLARALARALRACEA (SEQ ID NO: 9), and the lipid is a phospholipid. The first named invention was determined based on this being the first listed NLS sequence (claim 6), the first listed DNA condensing polypeptide type of alpha helix (claim 16) and sequence (claims 19-22), and the first listed lipid (claim 48). 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, 9-23, 40-48, 63-70 encompass this first named invention, and thus these claims will be searched without fee to the extent that the NLS comprises SEQ ID NO: 1, the DNA condensing polypeptide comprises an amphipathic alpha helix, sequence SEQ ID NO: 9, and the lipid is a phospholipid. Additional polypeptide DNA condensing polypeptide(s), NLS sequence(s), and/or lipid(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected polypeptide DNA condensing polypeptide(s), NLS sequence(s), and/or lipid(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. An exemplary election would be where the NLS comprises the amino acid sequence PAAKRVKL (SEQ ID NO: 2), the DNA condensing polypeptide comprises SEQ ID NO: 9, and the lipid is a phospholipid, (claims 1-5, 7, 9-23, 40-48, 63-70).

[note, claim 27 is not included in the first embodiment or the exemplary election of Group I+ because SEQ ID NO: 9 lacks a DNA binding domain]

Group II, claims 71-78, 120-127, directed to a method of introducing a polynucleotide into a target cell.

The inventions listed as Groups I+ and II do not relate to a single special technical feature 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 or consisting of a polypeptide comprising a DNA condensing polypeptide and a NLS, that is not required by Group II.

Group II has the special technical feature of a method of introducing a polynucleotide into a target cell, that is not required by Group I+.

The inventions of Group I+ each include the special technical feature of a different polypeptide element(s)/domain(s)/sequence(s), and is considered a distinct technical feature.

Common technical features

The inventions of Groups I+-II share the common technical feature of a composition comprising: (a) a polypeptide comprising [A]-[B], wherein: [A] is a DNA condensing polypeptide; and [B] is a nuclear localization sequence (NLS); (b) a polynucleotide; and (c) a lipid.

No technical features are shared between the polypeptide amino acid sequences of Group I+ and accordingly these groups lack unity a priori.

Additionally, even if the inventions listed as Group I+ were considered to share the technical features of including: a composition comprising: (a) a polypeptide comprising [A]-[B], wherein: [A] is a DNA condensing polypeptide; and [B] is a nuclear localization sequence (NLS); (b) a polynucleotide; and (c) a lipid; these shared technical features are previously disclosed by the prior art, as further discussed below.

The feature shared by Groups I+ and II, and the feature shared by the inventions listed as Group I+ are disclosed by US 2022/0090141 A1 to Molecular Transfer, Inc. (24 March 2022), (hereinafter "MTI").

MTI teaches a composition comprising: (a) a polypeptide comprising [A]-[B], wherein: [A] is a DNA condensing polypeptide; and [B] is a nuclear localization sequence (NLS); (b) a polynucleotide; and (c) a lipid (para [0011] "Disclosed herein are transfection complexes comprising at least one cell surface ligand; at least one helper lipid component; and a transfection enhancer"; [0026] "The binding molecule is capable of noncovalently binding to nucleic acid. The binding molecule is also capable of covalently linking to a cell binding adhesion sequence, a nuclear localization sequence and/or a fusion agent. The binding molecule can include...cationic peptides"; [0032] "Transfection agent as used herein may optionally include at least one or more of the transfection compounds optionally in combination with one or more helper lipids, one or more pegylated lipids, optionally one or more targeting moieties, optionally one or more nuclear localization sequences...optionally one or more condensing agents"; [0087] the nucleic acid binding moieties also serve as transfection enhancers when bound to nucleic acids, or alternatively serve as condensing agents. Suitable nucleic acid condensing peptides include...In some embodiments, multimers of these peptides are also synthesized and used as condensing agents. In some embodiments, nuclear localization sequences are also used as condensing agents").

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

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