

(43) International Publication Date
29 December 2016 (29.12.2016)

(51) International Patent Classification:

A61K 38/16 (2006.01) A61K 38/03 (2006.01)
A61K 49/14 (2006.01)

(21) International Application Number:

PCT/US2016/039431

(22) International Filing Date:

24 June 2016 (24.06.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/185,527	26 June 2015 (26.06.2015)	US
62/185,529	26 June 2015 (26.06.2015)	US
62/239,743	9 October 2015 (09.10.2015)	US
62/239,739	9 October 2015 (09.10.2015)	US
62/322,724	14 April 2016 (14.04.2016)	US
62/354,642	24 June 2016 (24.06.2016)	US

(71) Applicant: **FRED HUTCHINSON CANCER RE-SEARCH CENTER** [US/US]; 1100 Fairveiw Avenue North, Seattle, WA 98109 (US).

(72) Inventors: **OLSON, James**; 4733 Lake Washington Boulevard South, Seattle, WA 98199 (US). **STRAND, Andrew, David**; 5003 21st Avenue Sw, Seattle, WA 98106 (US). **GIRARD, Emily, June**; 16724 Woodside Drive Se, Renton, WA 98058 (US). **STRONG, Roland**; 1700 North Northlake Way #209, Seattle, WA 98103 (US). **MEHLIN, Christopher**; 2806 Nw 61st Street, Seattle, WA 98107 (US). **CORRENTI, Colin**; 5846 57th Avenue Ne, Seattle, WA 98105 (US). **MHYRE, Andrew, James**; 7709 Ne 201st Place, Kenmore, WA 98028 (US). **BRUSNIAK, Mi-young**; 2905 208th Place Sw, Lynnwood, WA 98036 (US). **SOTTERO, Theo**; 13724 Midvale Avenue N, Unit B, Seattle, WA 98133 (US).

(74) Agents: **HOLZAPFEL, Keli** et al.; Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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))

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

2 March 2017

(54) Title: THERAPEUTIC PEPTIDES AND METHODS OF USE THEREOF

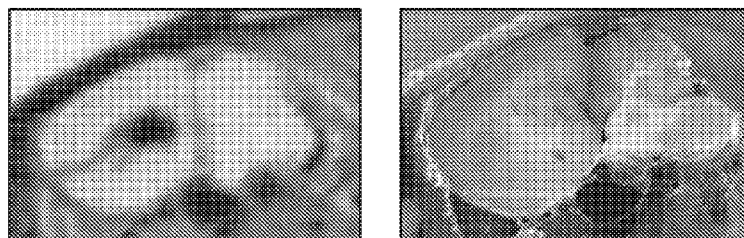


FIG. 33A

(57) Abstract: Peptides that home, distribute to, target, are directed to, or accumulate in tumors, cancers, or diseased cells are disclosed. Peptides that cross the blood brain barrier and home, distribute to, target, are directed to, or accumulate in the brain and in a specific region of the brain are also disclosed. Pharmaceutical compositions and uses for peptides or peptide-active agent complexes comprising such peptides are additionally disclosed. Such compositions can be formulated for targeted or untargeted delivery of a drug to a target region, tissue, structure or cell. Targeted compositions of the disclosure can deliver peptide or peptide-active agent complexes to target regions, tissues, structures or cells targeted by the peptide.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/39431

Box No. 1 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:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☒ furnished subsequent to the international filing date for the purposes of international search only:
 - ☒ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/39431

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.: 13-113
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 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.:
Groups I+, Claims 1, 5; SEQ ID NO: 198 (peptide); Exemplary election: SEQ ID NO: 199 (peptide)

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

International application No.

PCT/US16/39431

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/16, 49/14, 38/03 (2016.01)

CPC - A61K 38/16, 49/14, 38/03

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)

IPC(8): A61K 38/16, 49/14, 38/03, 39/395, 51/08, 51/00, 47/48; C07K 16/28, 16/30, 14/00, 7/08 (2016.01)

CPC: A61K 38/16, 49/14, 38/03, 47/48315, 47/48338, 49/0032, 49/0043, 49/0056, 49/085, 49/146, 51/088

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 practicable, search terms used)

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Lens sequence search database; Google Scholar; Pubmed; EBSCO; NCBI database; therap*, peptide, target*, delivery

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/0179560 A1 (FRED HUTCHINSON CANCER RESEARCH CENTER) 26 June 2014; paragraph [0064]; figure 9	1, 5
A	US 2013/0028836 A1 (SENTISSI, A et al.) 31 January 2013; whole document	1, 5
A	US 2006/0088899 A1 (ALVAREZ, VL et al.) 27 April 2006; whole document	1, 5

☐ 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 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

Date of the actual completion of the international search

08 November 2016 (08.11.2016)

Date of mailing of the international search report

13 JAN 2017

Name and mailing address of the ISA/

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Shane Thomas

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US16/39431

---Continued from Box No. 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, 5, 9 and SEQ ID NO: 198 are directed toward a peptide.

The peptide will be searched to the extent that it encompasses SEQ ID NO: 198 (first exemplary peptide sequence). Applicant is invited to elect additional peptide(s), with specified SEQ ID NO: for each, to be searched. Additional peptide sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part) and 5 (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: 198 (peptide sequence). 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 a peptide encompassing SEQ ID NO: 199 (first exemplary elected peptide sequence).

Groups II+, Claims 2-4, 6-8, 10-12 and SEQ ID NO: 1 are directed toward a peptide.

The peptide can be searched to the extent that it encompasses SEQ ID NO: 1 (first exemplary peptide sequence). Applicant is invited to elect additional peptide(s), with specified SEQ ID NO: for each, to be searched. Additional peptide sequence(s) can be searched upon the payment of additional fees. It is believed that claims 2 (in-part), 3 (in-part), 4 (in-part), 6 (in-part), 7 (in-part), 8 (in-part), 10 (in-part), 11 (in-part) and 12 (in-part) encompass this first named invention and thus these claims can be searched with payment of a fee for the search of Groups II+ to the extent that they encompass SEQ ID NO: 1 (peptide sequence). 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 of Groups II+ to be searched/examined. An exemplary election would be a peptide encompassing SEQ ID NO: 2 (first exemplary elected peptide sequence).

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: the special technical features of Groups I+ include SEQ ID NO: 198, not present in any of Groups II+; the special technical features of Groups II+ include SEQ ID NO: 1, not present in any of Groups I+.

No technical features are shared between the sequences of Groups I+ and, accordingly, these groups lack unity a priori. No technical features are shared between the sequences of Groups II+ and, accordingly, these groups lack unity a priori.

Groups I+ and II+ share the technical features including: a peptide comprising a sequence. Groups I+ share the technical features including: a peptide comprising a sequence. Groups II+ share the technical features including: a peptide comprising a sequence.

However, these shared technical features are previously disclosed by US 2014/0179560 A1 to Fred Hutchinson Cancer Research Center (hereinafter 'Fred').

Fred discloses a peptide comprising a sequence (a peptide comprising a sequence; paragraph [0045]).

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