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(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, 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, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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.

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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR INTRODUCTION OF MACROMOLECULES INTO CELLS

(57) Abstract: Disclosed are novel compositions and methods for introduction of macromolecules and nanoparticles into living cells. The invention includes a polypeptide sequence which when fused to a macromolecule or nanoparticle enhances its introduction into the cell.

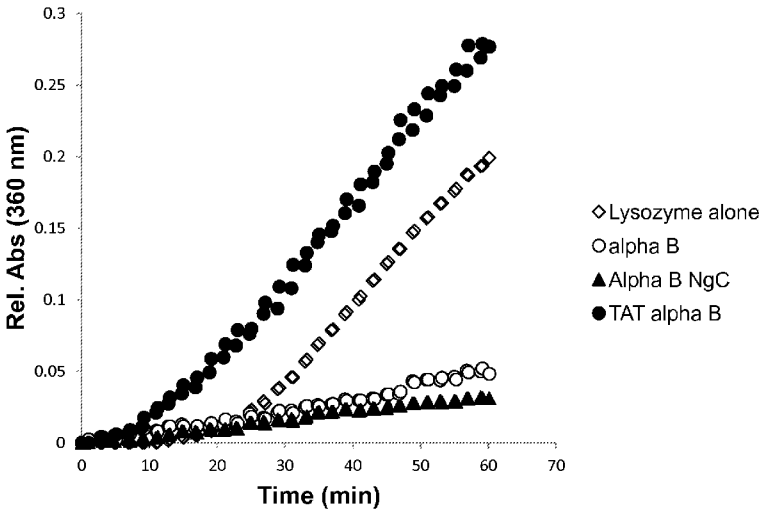

Figure 4

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GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, 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, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
1 May 2014

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/31372

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/385; A61K 39/00 (2012.01)
USPC - 424/194.1
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 39/385; A61K 39/00 (2012.01)
USPC - 424/194.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 424/185.1, 192.1, 193.1
(Text Search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (PGPB, USPT, USOC, EPAB, JPAB) and Google Scholar.
Search Terms: crystallin, HSPB, HSPB$, TAT, penetrat$, transpor$, transduc$, entry, fusion, CRYAA, CRYAB, peptide, HSPB5, ocular, heparin sulfate, PTD, uptake, internaliz$, cataract, retinitis, pigmentosa, retinopathy, macular degeneration, uveitis, administ$, alpha,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WADIA, J.S. et al. Transmembrane delivery of protein and peptide drugs by TAT-mediated transduction in the treatment of cancer. Advanced Drug Delivery Reviews. 19 December 2004, Vol 57, pages 579-596: abstract; pg 582, col 2, para 2 to pg 583, col 1, para 1; pg 584, col 1, para 2; pg 585, col 1, para 1 to col 2, para 2; pg 586, col 1, para 3 to pg 587, col 1, para 2	1-15
Y	TRYBALA, E. et al. Structural and functional features of the polycationic peptide required for inhibition of herpes simplex virus invasion of cells. Antiviral Research. 2004, Vol 62, pages 125-134: abstract; pg 128, col 2, para 1; pg 130, col 1, para 1	1-15
Y	US 2009/0149384 A1 (RAO et al.) 11 June 2009 (11.06.2009) para [0009]-[0011]	4-10 and 12-14
Y	DE JONG, W.W. et al. Alpha crystallin A chain (Heat-shock protein beta-4) (HspB4). Uniprot Accession Number P02489 [online]. 01 May 2005 [retrieved on 27 July 2012]. Retrieved from the Internet: <URL: http://www.uniprot.org/uniprot/P02489.txt?version=58>, pages 1-3: amino acid residues 2-173	8-10
A	US 2003/0148983 A1 (FONTOURA et al.) 07 August 2003 (07.08.2003) entire document.	12-14

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
28 July 2012 (28.07.2012)	10 AUG 2012
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/31372

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 filed or furnished:

   a. (means)

   ☐ on paper

   ☒ in electronic form

   b. (time)

   ☐ in the international application as filed

   ☒ together with the international application in electronic form

   ☐ subsequently to this Authority for the purposes of search

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 in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

GenCore 6.3: SEQ ID NOs: 1-2 and 4