

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 February 2008 (28.02.2008)

PCT

(10) International Publication Number
WO 2008/024459 A3

(51) International Patent Classification:

C12Q 1/68 (2006.01)

(21) International Application Number:

PCT/US2007/018699

(22) International Filing Date: 24 August 2007 (24.08.2007)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/840,381 24 August 2006 (24.08.2006) US

60/931,439 23 May 2007 (23.05.2007) US

(71) Applicant (for all designated States except US): **GOVT. OF THE USA , AS REPRESENTED BY THE SEC., DEPT. OF HEALTH AND HUMAN SERVICES** [—/US]; 6011 Executive Boulevard, Suite 325, Rockville, MD 20852 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SHILOACH, Joseph** [US/US]; 1717 Mark Lane, Rockville, MD 20852 (US). **JALURIA, Pratik** [US/US]; 4242 E-W Highway, Condo #406, Chevy Chase, MD 20815 (US). **BETEN-BAUGH, Michael** [US/US]; 3400 N. Charles Street, Baltimore, MD 21205 (US).

(74) Agents: **CORLESS, Peter, F.** et al.; Edwards Angell Palmer & Dodge LLP, P.O. Box 55874, Boston, MA 02205 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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

2 October 2008

(15) Information about Correction:

Previous Correction:

see Notice of 31 July 2008

(54) Title: COMPOSITIONS AND METHODS FOR MODIFYING CELLULAR PROPERTIES

(57) Abstract: The invention generally provides compositions and methods for modulating cell properties and enhancing recombinant protein yields. In particular, the compositions and methods provide for cells having altered growth characteristics, including altered adhesion, rate of proliferation, growth to particular cell density, and recombinant protein expression level.



WO 2008/024459 A3

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/018699

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C12Q1/68

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)

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, EMBL, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TANAKA RYOICHI ET AL: "Cloning and expression of the ccdA-associated thiol-disulfide oxidoreductase (catA) gene from Brevibacillus choshinensis: Stimulation of human epidermal growth factor production." JOURNAL OF BIOTECHNOLOGY, vol. 103, no. 1, 12 June 2003 (2003-06-12), pages 1-10, XP002481597 ISSN: 0168-1656 abstract ----- -/--	



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.

* & * document member of the same patent family

Date of the actual completion of the international search

2 June 2008

Date of mailing of the international search report

07/08/2008

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Cornelis, Karen

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/018699

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHANG GIN-WEN ET AL: "Multiple changes in gene expression are associated with normal cell-induced modulation of the neoplastic phenotype" CANCER RESEARCH, vol. 58, no. 19, 1 October 1998 (1998-10-01), pages 4445-4452, XP002481598 ISSN: 0008-5472	1,2
Y	the whole document	3-9
X	NAGATO S ET AL: "DOWNREGULATION OF LAMININ ALPHA4 CHAIN EXPRESSION INHIBITS GLIOMA INVASION IN VITRO AND IN VIVO" INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 117, no. 1, 20 October 2005 (2005-10-20), pages 41-50, XP008054255 ISSN: 0020-7136 the whole document	1,2
X	MILASINCIC DEBRA J ET AL: "Anchorage-dependent control of muscle-specific gene expression in C-2C-12 mouse myoblasts" IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY ANIMAL, vol. 32, no. 2, 1996, pages 90-99, XP002481599 ISSN: 1071-2690 the whole document	1,2
X	WO 2004/007754 A (RIGEL PHARMACEUTICALS INC [US]; HITOSHI YASUMICHI [US]; JENKINS YONCHU) 22 January 2004 (2004-01-22)	39-56
Y	example 25	3-9
X	WO 2005/072470 A (EXELIXIS INC [US]; PLOWMAN GREGORY D [US]; KARIM FELIX D [US]; SWIMMER) 11 August 2005 (2005-08-11) paragraphs [0110] - [0120]	10, 37, 38

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/018699

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:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an 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.:

see annex

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-2 (completely) 3-10,37-56 (partially)

A method for identifying a gene whoses expression modulates cellular adhesion, a method of altering the expression of cdk13 in the cell, a method for modulating cell growth characterisitics by contacting the cell with an agent that modulates the expression of cdk13, a method for altering growth characterisics of a cell by using expression of cdk13, an expression vector comprising cdk13, an expression vector comprising an inhibitory molecule of cdk13, an inhibitory nucleic acid molecule that reduces the expression of cdk13, a cell comprising an expression vector of cdk13 or of an inhibitory nucleic acid, a cell comprising a mutation that alters the expression of cdk13.

2. claims: 26-32 (completely) 3-10,37-56 (partially)

a method of altering the expression of siat7e in the cell, a method for modulating cell growth characterisitics by contacting the cell with an agent that modulates the expression of siat7e, a method for decreasing cell adhesion by expressing siat7e, a method for increasing cell adhesion with an agent that decreases siat7e expression, a method for altering growth characterisics of a cell by using expression of siat7e, an expression vector comprising siat7e, an expression vector comprising an inhibitory molecule of siat7e, an inhibitory nucleic acid molecule that reduces the expression of siat7e, a cell comprising an expression vector of siat7e or of an inhibitory nucleic acid, a cell comprising a mutation that alters the expression of siat7e.

3. claims: 19-25 (completely) 3-10,37-56 (partially)

a method of altering the expression of lama4 in the cell, a method for modulating cell growth characterisitics by contacting the cell with an agent that modulates the expression of lama4, a method for increasing cell adhesion by expressing lama4, a method for increasing cell adhesion with an agent that decreases lama4 expression, a method for altering growth characterisics of a cell by using expression of lama4, an expression vector comprising lama4, an expression vector comprising an inhibitory molecule of lama4, an inhibitory nucleic acid molecule that reduces the expression of lama4, a cell comprising an expression vector of lama4 or of an inhibitory nucleic acid, a cell comprising a mutation that alters the expression of lama4.

Inventions 4-8: claims 3-10,37-56 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

a method of altering the expression of cox15 in the cell, a method for modulating cell growth characteristics by contacting the cell with an agent that modulates the expression of cox15, a method for altering growth characteristics of a cell by using expression of cox15, an expression vector comprising cox15, an expression vector comprising an inhibitory molecule of cox15, an inhibitory nucleic acid molecule that reduces the expression of cox15, a cell comprising an expression vector of cdk13 or of an inhibitory nucleic acid, a cell comprising a mutation that alters the expression of cox15. Analogous for egr1, gas6, map3k9 and gap43.

Invention 9: Claims 11-18, 33-36 (completely), 39-56 (partially)

A method for modulationg recombinant polypeptide expression by a gene selected from cdk13, siat7e, lama4, cox15, egr1, gas6, map3k9 or gap43, or an inhibitory nucleic acid thereof, expression vectors and cells.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/018699

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004007754 A	22-01-2004	AU 2003249284 A1 EP 1576173 A2	02-02-2004 21-09-2005
WO 2005072470 A	11-08-2005	NONE	