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C12Q 1/68 (2006.01) *G01N 33/15* (2006.01)
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- (71) Applicant (for all designated States except US): **TUFTS MEDICAL CENTER, INC.** [US/US]; 800 Washington Street, Boston, Massachusetts 02111 (US).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): **BUCHSBAUM, Rachel J.** [US/US]; 53 Allen Road, Winchester, Massachusetts 01890 (US).
- (74) Agent: **GUTERMAN, Sonia K.**; Lawson & Weitzen, LLP, 88 Black Falcon Avenue, Suite 345, Boston, Massachusetts 02210 (US).
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[Continued on next page]

(54) Title: METHODS AND KITS FOR MODULATING TUMOR INVASIVENESS AND METASTATIC POTENTIAL

(57) Abstract: Methods and kits for evaluating invasive potential and metastatic potential of cancers by assessing Tiam1 expression levels in fibroblasts in the microenvironments surrounding tumors are provided.

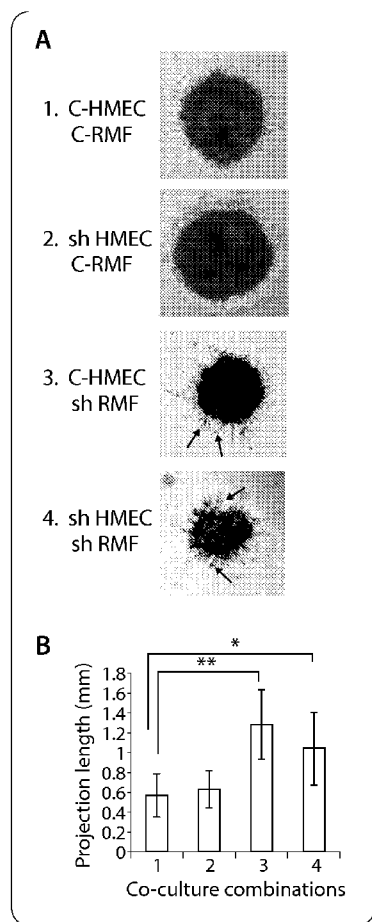


Fig. 3



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, 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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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:

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

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27 September 2012

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/046546**A. CLASSIFICATION OF SUBJECT MATTER***G01N 33/574(2006.01)i, C12Q 1/68(2006.01)i, G01N 33/68(2006.01)i, G01N 33/15(2006.01)i*

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)

G01N 33/574; A61K 39/395; C12N 5/06; A61K 45/00; A61K 48/00; A61K 31/7052; C12Q 1/68

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords:cancer, tumor, neoplasm, Tiam1, invasiveness, metastasis, epithelial, fibroblast

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	R ENGERS et al. Prognostic relevance of Tiam1 protein expression in prostate carcinomas. The British journal of cancer. 2009, vol. 95, no. 8, pp. 1081-1086 See the whole document	1-9
A	JP 2008-308407 A (DAI ICHI SEIYAKU CO., LTD.) 25 December 2008 See the whole document	1-9
A	SUSAN FUGETT ABU-ABSI et al. Three-dimensional co-culture of hepatocytes and stellate cells. Cytotechnology. 2004, vol. 45, no. 3, pp. 125-140 See the whole document	1-9
A	YOSHIRO OTSUKI et al. Tumor metastasis suppressor nm23H1 regulates Rac1 GTPase by interaction with Tiam1. Proceedings of the National Academy of Sciences of the United States of America. 2001, vol. 98, no. 8, pp. 4385-4390 See the whole document	1-9
A	US 2004-0048254 A1 (ALEXANDER OLEK et al.) 11 March 2004 See the whole document	1-9



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 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

29 JUNE 2012 (29.06.2012)

Date of mailing of the international search report

09 JULY 2012 (09.07.2012)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Kim Jeong Hee

Telephone No. 82-42-481-3344



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/046546**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 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 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.:
1-9

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.

(Continuation of Box No. III)

OTSUKI, Y. et al. 'Tumor metastasis suppressor nm23H1 regulates Rac1 GTPase by interaction with Tiam1', PNAS, April 2001, Vol. 98, No. 8, pp. 4385-4390.

This International Searching Authority found several inventions in this application, as follows:

Group I: Methods for evaluating potential invasiveness or modulating metastatic potential of epithelial cell cancer (Claims 1-9).

Group II: Methods for screening compounds to identify an agent that modulates invasiveness of epithelial cell cancer (Claims 10-17).

Group III: Methods of using a three-dimensional spheroid cell culture for prognosis of epithelial cancer or a method of assessing an agent for modulating invasiveness of epithelial cell (Claims 18-25).

Group IV: Kits for evaluating potential invasiveness or metastatic potential of epithelial cell cancer (Claims 26-38).

Group V: Methods for evaluating metastatic potential, modulating metastatic potential of epithelial cell cancer, screening method, or counseling method (Claims 39-46).

Group VI: Methods for screening compounds to identify an agent that modulates invasiveness of epithelial cell cancer (Claims 47-54).

The common technical feature among Group I - Group VI is 'to evaluate potential invasiveness or metastatic potential of epithelial cell cancer by detecting Tiam1 expression level'.

However, OTSUKI, Y. et al. discloses that Tiam1 expression level is a useful indicator of the metastatic potential of tumor cell (see Fig. 2, p.4390 left column). Thus, the common technical feature is not considered to contribute over the prior art as a whole and the present application does not meet the requirements of unity of invention (Rule 13.1 PCT).

In this case the first named invention that will be searched without additional fees is Group I. In order for other inventions to be examined, the appropriate additional examination fees must be paid and the desired inventions clearly identified.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/046546

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2009-0324587 A1 (NEAL CLIFFORD GOODWIN et al.) 31 December 2009 See the whole document	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

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