



(51) International Patent Classification:

C12N 9/22 (2006.01)

G01N 33/577 (2006.01)

C07K 16/18 (2006.01)

(21) International Application Number:

PCT/US2019/068373

(22) International Filing Date:

23 December 2019 (23.12.2019)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/784,032 21 December 2018 (21.12.2018) US

62/812,743 01 March 2019 (01.03.2019) US

(71) Applicant: **BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM** [US/US]; 210 West 7th St., Austin, TX 78701 (US).

(72) Inventor: **ARUR, Swathi**; c/o The University of Texas, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030 (US).

(74) Agent: **BYRD, Marshall P.**; Parker Highlander PLLC, 1120 So. Capital of Texas Highway, Bldg. One, Suite 200, Austin, TX 78746 (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, DJ, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, 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))
- with sequence listing part of description (Rule 5.2(a))

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

23 July 2020 (23.07.2020)

(54) Title: PHOSPHORYLATED DICER ANTIBODY AND METHODS OF USE THEREOF

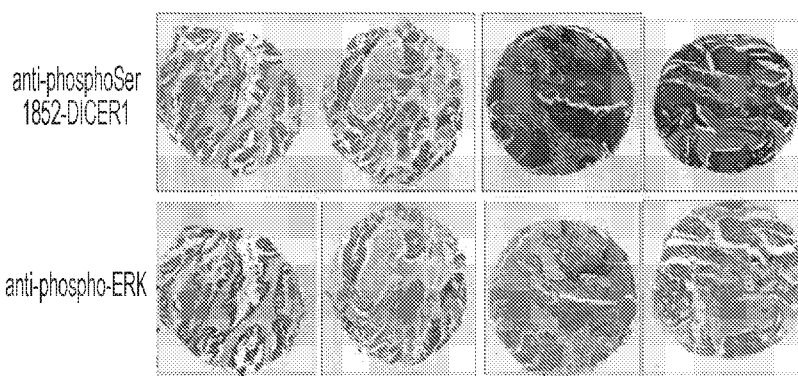


FIG. 1B

(57) Abstract: Provided herein are phosphorylated Dicer 1 (pDicer1) antibodies, including those that selectively bind Serine 1728 and/or Serine 1852. Further provided herein are methods of treating cancer by administering the pDicer1 antibodies alone or in combination with other therapies.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/68373

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C12N 9/22; C07K 16/18; G01N 33/577 (2020.01)

CPC - C12N 9/22; C07K 16/18; G01N 33/577

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	(ARYAL, N) Phosphorylation Impairs Dicer1 Function to Accelerate Aging and Tumorigenesis In Vivo. Doctor of Philosophy Dissertation [online]. The University of Texas, MD Anderson Cancer Center UTHealth, Graduate School of Biomedical Sciences. 2018; Retrieved from the Internet: <URL: https://pdfs.semanticscholar.org/94b6/2f2e5a82024d6a0ad3d28fe13211be16ffaa.pdf >; abstract; page 5, 2nd paragraph; page 14, 1st paragraph; page 60, 2nd paragraph	52-53
Y	(NICHOLSON, RH et al.) Molecular characterization of a mouse cDNA encoding Dicer, a ribonuclease III ortholog involved in RNA interference. Mammalian Genome. February 2002, Vol. 13, No. 2; pages 67-83; abstract; pages 74, 75, 84; DOI: 10.1007/s00335-001-2119-6	52-53
Y	(STRAUSBERG, RL et al.) Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences. Proceedings of the National Academy of Sciences of the USA. 24 December 2002, Epub 11 December 2002, Vol. 99, No. 26; pages 16899-16906; page 16904; DOI: 10.1073/pnas.242603899.	52-53
Y -- A	(DRAKE, M et al.) A Requirement for ERK-Dependent Dicer Phosphorylation in Coordinating Oocyte-to-Embryo Transition in C. elegans. Developmental Cell. 8 December 2014, Vol. 31, No. 5; pages 614-628; page 615, 2nd column, 2nd paragraph; page 622, 2nd column, 1st paragraph; page 626, 1st column, 4th paragraph; Fig. 7E, H; DOI: 10.1016/j.devcel.2014.11.004	1-2, 4/1-2, 8 ----- 3, 4/3, 5-6
Y	US 2013/0203079 A1 (MERCK PATENT GESELLSCHAFT MIT BESCHRANKTER HAFTUNG) 8 August 2013; paragraph [0022]	1-2, 4/1-2, 8



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

Date of the actual completion of the international search

6 April 2020 (06.04.2020)

Date of mailing of the international search report

11 JUN 2020

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. 571-273-8300

Authorized officer

Shane Thomas

Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/68373

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 2011/0300156 A1 (VERPLOEGEN, S et al.) 8 December 2011; paragraphs [0042], [0203], [0204]	3, 4/3, 5-6, 14-15
A	US 2016/0355599 A1 (CYTOMX THERAPEUTICS, INC.) 8 December 2016; paragraphs [0007], [0016]	3, 4/3, 5-6, 14-15
A	US 2014/0199301 A1 (ERDAG, B et al.) 17 July 2014; abstract; paragraphs [0044], [0048]	3, 4/3, 5-6, 14-15
A	(BURGER, K et al.) Nuclear re-localization of Dicer in primary mouse embryonic fibroblast nuclei following DNA damage. PLoS Genetics. 2 February 2018, Vol. 14, No. 2; pages 1-18; DOI: 10.1371/journal.pgen.1007151	1-3, 4/1-3, 5-6, 8, 14-15, 52-53
A	(BURGER, K et al.) Nuclear phosphorylated Dicer processes double-stranded RNA in response to DNA damage. The Journal of Cell Biology. 7 August 2017, Epub 22 June 2017, Vol. 216, No. 8; pages 2373-2389; DOI: 10.1083/jcb.201612131	1-3, 4/1-3, 5-6, 8, 14-15, 52-53

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/68373

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/US19/68373

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.: 7, 9-13, 16-39, 47-51
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.:
Claims 1-6, 8, 14-15, and 52-53; directed toward an isolated monoclonal antibody, wherein the antibody specifically binds phosphorylated human Dicer1 (pDicer1) at Serine 1728 and/or Serine 1852.

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/US19/68373

****-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.

Group I, Claims 1-6, 8, 14-15, and 52-53 are directed toward an isolated monoclonal antibody, wherein the antibody specifically binds phosphorylated human Dicer1 (pDicer1) at Serine 1728 and/or Serine 1852.

Group II, Claims 40-46 are directed toward a mouse whose genome comprises a phospho-mimetic Dicer1.

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 Group I include an antibody that binds phosphorylated human Dicer1, not present in Group II; the special technical features of Group II include a mouse whose genome comprises a phospho-mimetic Dicer1, not present in Group I.

Groups I and II share the technical features including: a phosphorylated Dicer1.

However, these shared technical features are previously disclosed by the publication entitled 'Nuclear phosphorylated Dicer processes double-stranded RNA in response to DNA damage' by Burger, et al. (hereinafter 'Burger').

Burger discloses a phosphorylated Dicer1 (pDicer1) (Dicer phosphorylated at residues S1728 and S1852 (phosphorylated Dicer1); abstract).

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