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C12N 15/113 (2010.01)

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(71) Applicant: **THE JOHNS HOPKINS UNIVERSITY** [US/US]; Technology Ventures, 3400 N. Charles Street, Clark 106, Baltimore, MD 21218 (US).

(72) Inventors: **LUPOLD, Shawn, E.**; 2302 Mount Hebron Dr., Ellicott City, MD 21042 (US). **HATANO, Koji**; 6705 Maple Leaf Ct. 102, Baltimore, MD 21209 (US). **KUMAR, Binod**; 302 Stevenson Lane, Apt. C5, Baltimore, MD 21204 (US). **DEWEESE, Theodore, L.**; 610 East Seminary Avenue, Towson, MD 21286 (US).

(74) Agents: **CORLESS, Peter, F.** et al.; Mintz Levin Cohn Ferris Glovsky and Popeo, P.C., One Financiel Center, Boston, MA 02111 (US).

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Published:

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(88) Date of publication of the international search report:
5 January 2017

(54) Title: SENSITIZING AGENT FOR CANCER CHEMOTHERAPY AND RADIATION THERAPY AND USES THEREOF

FIG. 1A

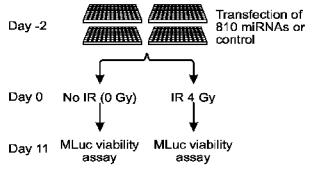


FIG. 1B

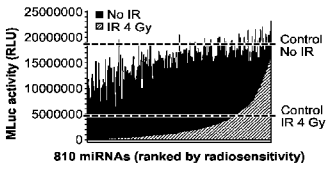


FIG. 1C

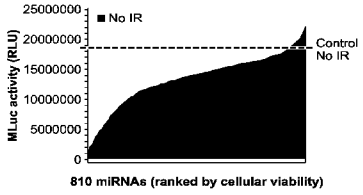
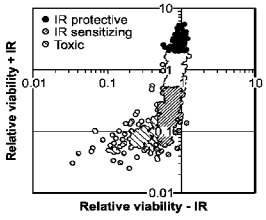


FIG. 1D



(57) Abstract: The present disclosure provides compositions and methods whereby specific microRNA (miRNA) is utilized as a means to sensitize cancer cells to radiation or chemotherapy.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/23065

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12Q 1/68; C12N 15/113; A61K 5/10 (2016.01)
CPC - A61K 31/7105, 48/005; C12N 15/113
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) Classifications: C12Q 1/68; C12N 15/113; A61K 5/10; CPC Classifications: A61K 31/7105, 48/005; C12N 15/113

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); USPTO Web Page; Google; Google Scholar; EBSCO: Entrez Pubmed; Science Direct; Search terms -- 'radiation sensitizer', microRNA, miR-744, miR-890, activator, mimic, chemotherapy, brachytherapy

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2008/0119436 A1 (SLACK, FJ et al.) May 22, 2008: abstract; paragraphs [0018], [0019], [0046]-[0047], [0128], [0136], [0158], [0202], [0207]; claim 1	1, 10-11, 16, 23-24, 29, 32 ---------- 12-15, 25-28, 30-31
Y	WO 2014/129895 A1 (STICHTING VU-VUMC) August 28, 2014; page 1, lines 17-27; page 6, line 31 -- page 7, line 3; page 10, lines 7-12; page 13, lines 16-20; page 34, lines 20-26; figure 6	12, 13, 25-26, 30-31
Y	US 2009/0289181 A1 (WICKMAN, G) November 26, 2009; paragraphs [0054], [0086]; figure 7	14-15, 27-28
A	US 2010/0216139 A1 (GALOS, D et al.) August 26, 2010; paragraphs [0024], [0025], [0076]	2-6, 17-21
A	US 2013/0331433 A1 (THIBONNIER, M) December 12, 2013; paragraphs [0012], [0252]	8
A	US 2015/0024486 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) January 22, 2015; paragraph [0052], [0163]	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 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
1 September 2016 (01.09.2016)	14 SEP 2016
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

International application No.
PCT/US16/23065

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:

-***-Continued Within the Next Supplemental Box-***-

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.:
1-6, 8-21, 23-32; SEQ ID NO: 734

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 application No.
PCT/US16/23065

-***-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 1-32 and SEQ ID NO: 734 are directed toward methods of increasing sensitivity to ionizing radiation (IR) therapy or chemotherapy in a patient in need thereof, the method comprising: administering to the patient in need thereof a composition comprising an miRNA, miRNA mimetic, or activator of miRNA; and a composition therefor.

The methods and composition will be searched to the extent they encompass SEQ ID NO: 734 (first exemplary miRNA sequence). Applicant is invited to elect additional miRNA(s), with specified SEQ ID NO: for each, to be searched. Additional miRNA sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1-6, 8-21 and 23-32 encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 734 (miRNA sequence). Applicants must specify the claims that encompass any additionally elected miRNA sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. 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 an miRNA encompassing SEQ ID NO: 764 (first exemplary elected miRNA sequence).

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

Groups I+ share the technical features including: a composition for increasing sensitization to ionizing radiation (IR) comprising an miRNA; miRNA mimetic, activator of miRNA, or mixture thereof; a method of increasing sensitivity to ionizing radiation (IR) therapy or chemotherapy in a patient in need thereof, the method comprising: administering to the patient in need thereof a composition comprising an miRNA, miRNA mimetic, activator of miRNA, or mixture thereof; a method of increasing sensitivity to IR therapy or chemotherapy in a tumor cell, the method comprising: contacting the tumor cell with a composition comprising an miRNA, miRNA mimetic, activator of miRNA, or mixture thereof, thereby increasing sensitivity to IR therapy or chemotherapy.

However, these shared technical features are previously disclosed by WO 2014/129895 A1 to Stichting Vu Vumc (hereinafter 'Stichting').

Stichting discloses a composition (a composition; page 16, lines 9-10) for increasing sensitization to ionizing radiation (IR) (for increasing sensitization to ionizing radiation (IR); page 6, lines 19-29) comprising an miRNA (comprising miRNA; page 6, line 31 - page 7, line 5); a method of increasing sensitivity to ionizing radiation (IR) therapy in a patient in need thereof (a method of increasing sensitivity to ionizing radiation (IR) therapy in a patient in need thereof; page 6, line 31-page 7, line 33), the method comprising: administering to the patient in need thereof a composition comprising an miRNA (the method comprising: administering to the patient in need thereof a composition comprising an miRNA; page 6, line 31-page 7, line 33; page 16, lines 30-33); a method of increasing sensitivity to IR therapy in a tumor cell (a method of increasing sensitivity to IR therapy in a tumor cell; page 6, line 31 - page 7, line 5; page 7, lines 14-16), the method comprising: contacting the tumor cell with a composition comprising an miRNA (the method comprising: contacting the tumor cell with a composition comprising an miRNA; page 6, line 19 - page 7, line 5), thereby increasing sensitivity to IR therapy (thereby increasing sensitivity to IR therapy; page 6, line 31 - page 7, line 5).

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