(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 September 2016 (09.09.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/140923 A3

(51) International Patent Classification:
C09K 11/00 (2006.01) *B82Y 15/00* (2011.01)
G01N 21/62 (2006.01) *A61K 49/00* (2006.01)
G01N 33/532 (2006.01)

(21) International Application Number:
PCT/US2016/020106

(22) International Filing Date:
29 February 2016 (29.02.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/127,376 3 March 2015 (03.03.2015) US

(71) Applicant: **UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL** [US/—]; 225 Franklin Street, 12th Floor, Boston, MA 02100 (US).

(72) Inventors: **HAN, Gang**; 6 Hearthside Circle, Shrewsbury, MA 01545 (US). **LI, Zhangjun**; Green Drive, Apt. 22 (I), Shrewsbury, MA 01545 (US).

(74) Agent: **ZHANG, Yin, Philip**; Milstein Zhang & Wu LLC, 2000 Commonwealth Ave., Suite 400, Newton, MA 02466 (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, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, 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))*

(88) Date of publication of the international search report:
13 October 2016

WO 2016/140923 A3

(54) Title: HOMOGENEOUS PERSISTENT LUMINESCENCE NANOCRYSTALS AND METHODS OF PREPARATION AND APPLICATION THEREOF

(57) Abstract: This invention provides a groundbreaking approach to PLNPs and their preparation. In particular, the synthetic methodology disclosed herein fundamentally differs from the traditional solid-state annealing reactions that require extreme and harsh reaction conditions. In one unique aspect of the invention, a simple, one-step mesoporous template method utilizing mesoporous silica nanoparticles (MSNs) is disclosed that affords *in vivo* rechargeable NIR-emitting mesoporous PLNPs with uniform size and morphology. In another unique aspect of the invention, the novel synthetic approach is based on aqueous-phase chemical reactions conducted in mild conditions, resulting in uniform and homogeneous PLNPs with desired size control (*e.g.*, sub-10 nm).

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/20106

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C09K 11/00; G01N 21/62; G01N 33/532; B82Y 5/00; B82Y 15/00; A61K 49/00 (2016.01)
CPC - B82Y 5/00; B82Y 15/00; C09K 11/08; C01P 2004/64; G01N 33/587; G01N 21/64; A61K 51/1244
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) - C09K 11/00; G01N 21/62; G01N 33/532; B82Y 5/00; B82Y 15/00; A61K 49/00 (2016.01)
CPC - B82Y 5/00; B82Y 15/00; C09K 11/08; C01P 2004/64; G01N 33/587; G01N 21/64; A61K 51/1244

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Patents and non-patent literature (classification, keyword; search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, Google Scholar (NPL), Google Patents; search terms: persistent luminescence nanoparticles, mesoporous, porous, mesopores, reaction, reacting, uniform, homogenous, silica, defined size, morphology, template, surface area, m2/g, NIR-emitting, nm, hydrothermal reaction, aqueous phase, temperature, particle size

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Li et al., "In Vivo Repeatedly Charging Near-Infrared-Emitting Mesoporous SiO2/ZnGa2O4:Cr3+ Persistent Luminescence Nanocomposites" Adv. Sci., Vol. 2, No. 3 (09 February 2015) [online] [retrieved on 11 July 2016]. Retrieved from the Internet <URL: http://onlinelibrary.wiley.com/doi/10.1002/advs.201500001/epdf> pg 1-3, 5-6	1-3
X	Hang et al., "Long lasting behavior of Gd2O2S:Eu3+ phosphor synthesized by hydrothermal routine" Materials Chemistry and Physics, Vol. 107, No. 1, pp 142-147 (2008) pg 143, 145	10-12
A	US 2014/0371575 A1 (MALDINEY et al.) 18 December 2014 (18.12.2014) entire document	1-3, 10-12
A	EP 1 431 352 A1 (NANOSOLUTIONS GMBH) 23 June 2004 (23.06.2004) entire document	10-12
A	US 2004/0014060 A1 (HOHEISEL et al.) 22 January 2004 (22.01.2004) entire document	10-12
A	Byrappa et al., "Hydrothermal technology for nanotechnology" Prog. Cryst. Growth Charact. Mater., Vol. 53, No. 2, pp 117-166 (2007) entire document	10-12
A, P	Li et al., "Long persistent phosphors--fundamentals to applications" Chem. Soc. Rev., Vol. 45, No. 8, pp 2090-2136 (03 February 2016) entire document	1-3, 10-12

☐ 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
11 July 2016	09 SEP 2016
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: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/20106

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.: 4-9, 13-16, 20-26
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:
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 1-3 and 10-12, drawn to a method for preparing mesoporous persistent luminescence nanoparticles, comprising providing mesoporous silica nanoparticles having mesopores of defined size and morphology; and reacting precursors to form persistent luminescent nanoparticles templated by the mesopores of the mesoporous silica nanoparticles.

Group II: Claims 17-19, drawn to rechargeable persistent luminescence nanocomposites comprising doped zinc gallates $ZnGa_2O_4$:Cr having particle sizes of less than about 1000 nm and having specific surface area from about 50 m^2/g to about 600 m^2/g, wherein the persistent luminescence nanocomposites is capable of NIR-emitting in the range of 650 nm and 900 nm after multiple emission and recharge cycles.

- Please see extra sheet for continuation -

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.:
1-3, 10-12

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. Observations where unity of invention is lacking---

The inventions listed as Groups I-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:

Special Technical Features

Group II does not require providing mesoporous silica nanoparticles having mesopores of defined size and morphology; and reacting precursors to form persistent luminescent nanoparticles templated by the mesopores of the mesoporous silica nanoparticles, as required by Group I.

Groups I and III do not require conducting a hydrothermal chemical reaction in an aqueous phase, as required by Group II.

Group I does not require persistent luminescence nanocomposites comprising doped zinc gallates $ZnGa_2O_4$:Cr having particle sizes of less than about 1000 nm and having specific surface area from about 50 m^2/g to about 600 m^2/g, wherein the persistent luminescence nanocomposites is capable of NIR-emitting in the range of 650 nm and 900 nm after multiple emission and recharge cycles, as required by Group II

Shared Common Features

Groups I-II share the technical feature of persistent luminescence nanoparticles and uniform and homogenous persistent luminescence nanoparticles and mesoporous persistent luminescence nanoparticles.. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is disclosed by the article entitled "In Vivo Repeatedly Charging Near-Infrared-Emitting Mesoporous $SiO_2/ZnGa_2O_4$:Cr^{3+} Persistent Luminescence Nanocomposites" by Li et al. (hereinafter "Li"). Li teaches persistent luminescence nanoparticles (pg 1, abstract; "ZGC PL nanoparticles"; pg 2, col 1; "NIR-persistent-luminescent mesoporous nanocomposites") and uniform (pg 5, col 2; "ZGC PL nanoparticles with uniform morphology") and homogenous (pg 2, col 2; "homogeneous distribution") persistent luminescence nanoparticles and mesoporous persistent luminescence nanoparticles (pg 2, col 1; "NIR-persistent-luminescent mesoporous nanocomposites").

Groups I-II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

NOTE: Claims 4-9, 13-16, 20-26 are determined unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).