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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 August 2011 (11.08.2011)

PCT

(10) International Publication Number
WO 2011/097031 A3

(51) **International Patent Classification:**
C12N 9/14 *(2006.01)*

(21) **International Application Number:**
PCT/US20 11/000210

(22) **International Filing Date:**
4 February 201 1 (04.02.201 1)

(25) **Filing Language:** English

(26) **Publication Language:** English

(30) **Priority Data:**

61/337,489	4 February 2010 (04.02.2010)	US
61/337,488	4 February 2010 (04.02.2010)	US
61/337,528	4 February 2010 (04.02.2010)	**us**

(71) **Applicant** *(for all designated States except US):* **THE SCRIPPS RESEARCH INSTITUTE** [US/US]; 10550 North Torrey Pines Road, La Jolla, CA 92037 (US).

(72) **Inventors; and**

(75) **Inventors/ Applicants** *(for US only):* **SCHIMMEL, Paul** [US/US]; 9822 La Jolla Farms Road, La Jolla, CA 92037 (US). **YANG, Xiang-lei** [CN/US]; 491 3 Coach Horse Court, San Diego, CA 92130 (US). **SLIKE, Bonnie** [US/US]; 8872 E. Town and Country Blvd., Ellicot City, Maryland 21043 (US). **XU, Xiaoling** [CN/US]; 7665 Palmilla Drive, Apt. 5208, San Diego, California 92122 (US). **GUO, Min** [US/US]; 1061 Vinter Blvd., Palm Beach Gardens, Florida 33410 (CN).

(74) **Agents: FITTING, Thomas** et al; The Scripps Research Institute, 10550 North Torrey Pines Road, TPC-8, La Jolla, CA 92037 (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, 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, 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, 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.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available):* ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, 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, 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:**
6 October 20 11

WO 2011/097031 A3

(54) **Title:** MONOMERIC FORMS OF HUMAN AMINOACYL-TRNA SYNTHETASES HAVING NON-CANONICAL BIOLOGICAL ACTIVITIES

(57) **Abstract:** Isolated monomelic aminoacyl-tRNA synthetase polypeptides and polynucleotides having non-canonical biological activities are provided, as well as compositions and methods related thereto.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/00210

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12N 9/14 (2011.01)
USPC - 435/193
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)
USPC: 435/193

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC:435/193,195,183; 530/350 (text search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Electronic data bases: PubWEST (JPAB, EPAB, PGPB, USPT); Google Scholar, GenCore sequence search (AA)
Search terms: Amino acyl- tRNA synthetase (AARS), tyrosyl-tRNA synthetase (YRS or TyrRS); tryptophanyl-tRNA synthetase (WRS or TrpRS); lysyl-tRNA synthetase (KRS or LysRS), non-canonical, monomer, cytokine activity, inflammatory, VE-cadherin, HIV

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- A	KOVALESKI et al., In vitro characterization of the interaction between HIV-1 Gag and human lysyl-tRNA synthetase. J Biol Chem, 14 July 2006, Vol 281, No 28, Pages 9449-9456. Especially abstract, pg 19451 fig 1, pg 19452 fig 2C	1-6, 17-20, 27 --- 7-16, 28-34, 38
A	US 2009/0227662 A1 (SCHIMMEL et al.) 10 September 2009 (10.09.2009). Especially para [0046], [0195], sheet 17 fig 15, sheet 22 fig 20.	7-12, 28-34
A	KISE et al., A short peptide insertion crucial for angiostatic activity of human tryptophanyl-tRNA synthetase. Nature Struc Mol Bio, February 2004, Vol 11, No 2, Pages 149-156. Especially abstract, pg 150 fig 1B.	13-16, 38
A	KAPOOR et al., Mutational separation of aminoacylation and cytokine activities of human tyrosyl -tRNA synthetase. Chem Biol, 29 May 2009, Vol 16, No 5, Pages 531-539. Especially abstract.	1-12, 28-34
A	LINK et al., Discovery of aminoacyl-tRNA synthetase activity through cell-surface display of noncanonical amino acids. Proc Nat Acad Sci, 5 July 2006, Vol 103, No 27, Pages 10180-10185. Especially abstract.	1-6
A	HOU et al., Sequence determination and modeling of structural motifs for the smallest monomeric aminoacyl-tRNA synthetase. Proc Nat Acad Sci, 1 February 1991, Vol 88, No 3, Pages 976-980. Especially pg 979 right col para 1.	1-6

☐ 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
22 July 2011 (22.07.2011)	12 AUG 2011

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/00210

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.: 21"26 . 35_37 . 39_73_and 77
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. Ill **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:

Group I: Claims 1-20, 27-34, and 38, drawn to an isolated aminoacyl-tRNA synthetase polypeptide.

Group II: Claims 74-76 and 78, drawn to compounds or methods of identifying a compound that specifically binds to an aminoacyl-tRNA synthetase polypeptide, or one or more of its binding partners.

—please see continuation on 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 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.:
1-20, 27-34, and 38

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/US 11/00210

Continuation of:
Box No. Ill Observations where unity of invention is lacking

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 invention of Group I does not share a special technical feature with the invention of Group II. Aminoacyl-tRNA synthetase polypeptide that are monomeric in form is known in the art, as evidenced by the article entitled "Sequence determination and modeling of structural motifs for the smallest monomeric aminoacyl-tRNA synthetase" by Hou et al. (Proc Natl Acad Sci U S A. 1 February 1991, Vol 88, No 3, pp 9767980). Hou discloses a monomeric aminoacyl-tRNA synthetase polypeptide (abstract). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature.

Further, the special technical feature of the inventions listed as Group I is an aminoacyl-tRNA synthetase that exhibits non-canonical biological activity. This special technical feature is not shared by the inventions of Group II. The special technical feature of the inventions listed as Group II is a compound that specifically binds to an aminoacyl-tRNA synthetase or to one or more of its binding partners. This special technical feature is not shared by the inventions of Group I.

Unity of invention exists only when the same or corresponding technical feature is shared by the claimed inventions. With out a shared special technical feature, the inventions of Groups I and II lack unity with one another.