

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

(19) World Intellectual Property

Organization

International Bureau

(43) International Publication Date

18 October 2018 (18.10.2018)



(10) International Publication Number

WO 2018/189020 A3

(51) International Patent Classification:

A61K 31/202 (2006.01) A61K 31/51 (2006.01)

A61P 25/28 (2006.01) A61K 31/592 (2006.01)

A61K 31/14 (2006.01) A61K 31/593 (2006.01)

A61K 31/4415 (2006.01)

(21) International Application Number:

PCT/EP2018/058701

(22) International Filing Date:

05 April 2018 (05.04.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/484,119 11 April 2017 (11.04.2017) US

62/484,156 11 April 2017 (11.04.2017) US

17193916.8 29 September 2017 (29.09.2017) EP

PCT/EP2017/074731

29 September 2017 (29.09.2017) EP

62/580,574 02 November 2017 (02.11.2017) US

PCT/EP2017/082148

11 December 2017 (11.12.2017) EP

(71) Applicant: NESTEC S.A. [CH/CH]; Avenue Nestlé 55, 1800 VEVEY (CH).

(72) Inventors: BOWMAN, Gene; Chemin du Boschet 8B, 1025 ST-SULPICE (CH). HUDRY-LABBE, Julie; Chemin de la Cabolettaz 11, 1066 EPALINGES (CH). SCHMITT, Jeroen Antonius Johannes; Chemin du Général Voruz 13, 1510 Moudon (CH). BOSCHAT, Corina; Route du Jorat 112, 1000 LAUSANNE (CH). RIEKER, Claus; Rue du Centre 158, 1025 ST-SULPICE (CH).

(74) Agent: CHAUTARD, Cécile; Centre de Recherche Nestlé, Case postale 44, Vers-chez-les-Blanc, 1000 LAUSANNE 26 (CH).

(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).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

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:

18 April 2019 (18.04.2019)

(54) Title: OMEGA-3 FATTY ACID, HOMOCYSTEINE AND VITAMIN D LEVELS TO IDENTIFY AND ATTENUATE COGNITIVE AGING IN INDIVIDUALS

(57) Abstract: A method for identifying pre-disposition to cognitive decline in a subject, the method comprising determining levels of: (a) omega-3 fatty acids, and vitamin D or a metabolite thereof; (b) omega-3 fatty acids, and homocysteine; (c) vitamin D or a metabolite thereof, and homocysteine; or (d) omega-3 fatty acids, vitamin D or a metabolite thereof, and homocysteine, independently in one or more samples obtained from the subject.



WO 2018/189020 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2018/058701

A. CLASSIFICATION OF SUBJECT MATTER INV. A61K31/202 A61P25/28 A61K31/14 A61K31/4415 A61K31/51 A61K31/592 A61K31/593 ADD. 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) A61K 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) EPO-Internal, WPI Data, BIOSIS, CHEM ABS Data, EMBASE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015/086625 A1 (MILLER RAYMOND A [US]) 26 March 2015 (2015-03-26) claims 1,15,19 -----	9-11, 13-21
X	US 2014/271844 A1 (MILLER RAYMOND A [US]) 18 September 2014 (2014-09-18) paragraphs [0071], [0101] examples 10-20,6,65,70-75 -----	9-11, 13-21
X	WO 2010/143053 A1 (ENERGY4LIFE AG [CH]; ROHNER MARKUS [CH]) 16 December 2010 (2010-12-16) examples 7,8 -----	9,11, 13-21
X	US 2002/182196 A1 (MCCLEARY EDWARD LARRY [US]) 5 December 2002 (2002-12-05) paragraph [0177] paragraph [0001] - paragraph [0003] ----- -/-	9,11, 13-21
☒ 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 14 March 2019		Date of mailing of the international search report 22/03/2019
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Bonzano, Camilla

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2018/058701

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2016/207794 A1 (NESTEC SA [CH]) 29 December 2016 (2016-12-29) claims 1,4,5 paragraph [0034] paragraph [0086] - paragraph [0087] -----	9,11, 13-21
X	WO 2015/140545 A1 (ISIS INNOVATION [GB]) 24 September 2015 (2015-09-24) claims 1,22,23,28 page 24, line 20 - line 35 page 32, paragraph 1 -----	9,11, 13-21
Y	WO 2014/122290 A1 (CENTRE NAT RECH SCIENT [FR]; UNIV PARIS DIDEROT PARIS 7 [FR]; UNIV PAR) 14 August 2014 (2014-08-14) page 16, paragraph 4 - page 17, paragraph 1 -----	12
Y	WO 02/03074 A1 (AXIS SHIELD ASA [NO]; COCKBAIN JULIAN [GB]; OERNING LARS [NO]) 10 January 2002 (2002-01-10) page 4, paragraph 2 page 8; example 1 -----	12
X	WO 2011/143587 A1 (NITROMEGA CORP [US]; MILLER RAYMOND [US]) 17 November 2011 (2011-11-17) claims 1,6 example 24 paragraph [0159] -----	9-11, 13-21
X	WO 2017/004436 A2 (UNIV CALIFORNIA [US]) 5 January 2017 (2017-01-05) paragraph [0324]; example 2 paragraph [0328]; table 6 claims 1,59-66 paragraph [0234] -----	9-21
X	BARBERGER-GATEAU P: "Nutrition and brain aging: How can we move ahead?", EUROPEAN JOURNAL OF CLINICAL NUTRITION, NATURE PUBLISHING GROUP, GB, vol. 68, no. 11, 13 November 2014 (2014-11-13), pages 1245-1249, XP009503472, ISSN: 0954-3007, DOI: 10.1038/EJCN.2014.177 -----	1-11, 13-21
Y	abstract page 1246, paragraph 1 -----	12
	-/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2018/058701

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BOWMAN GENE ET AL: "Nutrient biomarker patterns and cognitive decline in older adults", THE FASEB JOURNAL, FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, US, vol. 28, no. 1, Suppl. S, 31 March 2014 (2014-03-31), page 124.6, XP009503473, ISSN: 0892-6638 the whole document -----	1-8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2018/058701

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 additional 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 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.:

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21(partially)

Method to identify pre-disposition to cognitive decline in a subject by determining the levels of (a) omega-3 fatty acids, and vitamin D or a metabolite thereof; more particularly of (d) omega-3 fatty acids, vitamin D or a metabolite thereof, and homocysteine, and use for reducing or preventing cognitive decline and for improving cognitive ability in a subject of the combination of (a') the omega-3 fatty acid with vitamin D or a metabolite thereof, more particularly of (d') omega-3 fatty acids, vitamin D or a metabolite thereof, and the agent capable of reducing plasma homocysteine levels.

2. claims: 1-6, 8-21(all partially)

Method to identify pre-disposition to cognitive decline in a subject by determining the levels of (b) omega-3 fatty acids and homocysteine; and use for reducing or preventing cognitive decline and for improving cognitive ability in a subject of the combination of (b') the omega-3 fatty acid with an agent capable of reducing plasma homocysteine levels.

3. claims: 1-5, 7-21(all partially)

Method to identify pre-disposition to cognitive decline in a subject by determining the levels of (c) vitamin D or a metabolite thereof, and homocysteine and use for reducing or preventing cognitive decline and for improving cognitive ability in a subject of the combination of (c') the vitamin D or metabolite thereof with an agent capable of reducing plasma homocysteine levels.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2018/058701

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2015086625	A1	26-03-2015	AU 2009334476 A1 21-07-2011
		CA 2748743 A1 08-07-2010	
		CA 2929998 A1 08-07-2010	
		CN 102307464 A 04-01-2012	
		CN 104288138 A 21-01-2015	
		EP 2384114 A1 09-11-2011	
		JP 2012513774 A 21-06-2012	
		SG 172826 A1 29-08-2011	
		US 2010166918 A1 01-07-2010	
		US 2015086625 A1 26-03-2015	
		WO 2010078504 A1 08-07-2010	
US 2014271844	A1	18-09-2014	NONE
WO 2010143053	A1	16-12-2010	EP 2440201 A1 18-04-2012
		US 2012148685 A1 14-06-2012	
		WO 2010143053 A1 16-12-2010	
US 2002182196	A1	05-12-2002	NONE
WO 2016207794	A1	29-12-2016	AU 2016281870 A1 23-11-2017
		BR 112017025664 A2 07-08-2018	
		CA 2987033 A1 29-12-2016	
		CN 107708446 A 16-02-2018	
		EP 3310349 A1 25-04-2018	
		JP 2018528160 A 27-09-2018	
		US 2016367509 A1 22-12-2016	
		WO 2016207794 A1 29-12-2016	
WO 2015140545	A1	24-09-2015	EP 3119389 A1 25-01-2017
		US 2018169048 A1 21-06-2018	
		WO 2015140545 A1 24-09-2015	
WO 2014122290	A1	14-08-2014	FR 3002044 A1 15-08-2014
		WO 2014122290 A1 14-08-2014	
WO 0203074	A1	10-01-2002	AT 302416 T 15-09-2005
		AU 5861401 A 14-01-2002	
		DE 60112758 T2 29-06-2006	
		DK 1297342 T3 19-12-2005	
		EP 1297342 A1 02-04-2003	
		ES 2249432 T3 01-04-2006	
		JP 2004502940 A 29-01-2004	
		PT 1297342 E 31-10-2005	
		US 2004014230 A1 22-01-2004	
		WO 0203074 A1 10-01-2002	
WO 2011143587	A1	17-11-2011	BR 112012027915 A2 23-10-2018
		CN 102843922 A 26-12-2012	
		EP 2568826 A1 20-03-2013	
		JP 2013526865 A 27-06-2013	
		US 2011280852 A1 17-11-2011	
		US 2014017219 A1 16-01-2014	
		WO 2011143587 A1 17-11-2011	
WO 2017004436	A2	05-01-2017	NONE