



(51) International Patent Classification:
A61K 39/395 (2006.01) A61K 39/00 (2006.01)

(21) International Application Number:
PCT/US2014/041441

(22) International Filing Date:
7 June 2014 (07.06.2014)

(25) Filing Language:
English

(26) Publication Language:
English

(30) Priority Data:
61/832,434 7 June 2013 (07.06.2013) US
61/926,539 13 January 2014 (13.01.2014) US

(71) Applicant: DUKE UNIVERSITY [US/US]; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US).

(72) Inventors: PATZ, Jr., Edward F.; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). CAMPA, Michael J.; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). GOTTLIN, Elizabeth; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). HAYNES, Barton F.; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). LIAO, Hua-Xin; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). MOODY, M., Anthony; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US).

(74) Agent: YEH, Sansun; Michael Best & Friedrich LLP, 100 East Wisconsin Avenue, Suite 3300, Milwaukee, WI 53202-4108 (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, LT, 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.

[Continued on next page]

(54) Title: INHIBITORS OF COMPLEMENT FACTOR H

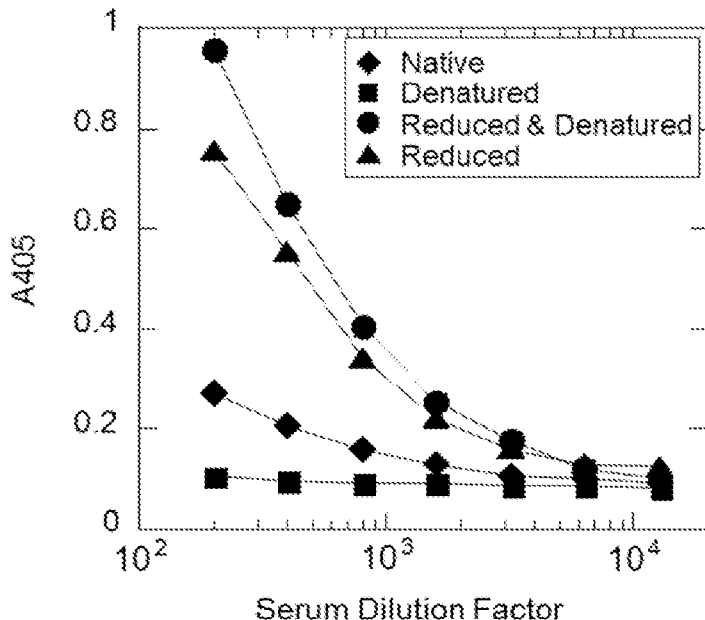


Fig. 1

(57) Abstract: Disclosed herein are Complement factor H (CFH) inhibitors, such as anti-CFH antibodies and small molecules, and methods of using said inhibitors.

WO 2014/197885 A3

(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, 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:

12 March 2015

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/41441

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 39/395, A61K 39/00 (2014.01) CPC - A61K 38/00, A61K 2039/505 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) - A61K 39/395, A61K 39/00 (2014.01) A61K 38/00, A61K 2039/505 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 424/139.1, 424/138.1, 424/141.1, 424/155.1, 424/178.1 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST; PatBase; Google Scholar search terms - complement factor, factor H, CFH, AHUS1, ARMD4, FH, inhibi\$, antagon\$, short consensus repeats, short consensus repeat, SCR, 19, SCR19, cancer, proliferat*, cancer*, tumor, tumor*, reduced, reduced form, anti, antibod*		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	Amornsiripanitch, Nita, et al. "Complement factor H autoantibodies are associated with early stage NSCLC." <i>Clinical Cancer Research</i> 16.12 (2010): 3226-3231. abstract, pg 3227, col 2, para 1, pg 3229, col 1, para 1	1-4 ----- 5, 6, 33, 34
Y	US 2011/0229497 A1 (THURMAN et al.) 22 September 2011 (22.09.2011) para [0043]; [0221]; SEQ ID NO: 8.	5, 6
Y	US 2007/0020647 A1 (HAGEMAN et al.) 25 January 2007 (25.01.2007) para [0015]; [0037]; [0074]; [0085]; [0103]; [0370]; claims 34, 45; Fig. 3.	33, 34
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 22 December 2014 (22.12.2014)	Date of mailing of the international search report 12 JAN 2015	
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. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/41441

Box No. I 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 filed or furnished:

a. (means)

on paper

in electronic form

b. (time)

in the international application as filed

together with the international application in electronic form

subsequently to this Authority for the purposes of search

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 in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

The electronic sequence listing submitted in response to the PCT/ISA/225 issued on 02 July 2014 is acknowledged; however, it was a partial e-sequence listing containing only SEQ ID NOs 1-3, and it does not comply with the standard provided for in Annex C of the Administrative Instructions for the remaining sequences. Therefore, the international search was not carried out on the basis of that non-compliant electronic sequence listing for any non-compliant electronic sequence listing, i.e. SEQ ID NO 4+.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/41441

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.: 15-19, 26-32, 35-52
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 defined 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, 33 and 34 directed to an isolated antibody or antibody fragment which immunospecifically binds to the complement factor H (CFH) protein, wherein the binding of the antibody or antibody fragment to CFH protein is sensitive to the reduced form of CFH protein, or a method of treating a subject having cancer.

Group II, claims 9-14, directed to an isolated antibody or antibody fragment which immunospecifically binds to the CFH protein, wherein said antibody has an equilibrium dissociation constant (K_d) of between about 1.00 x 10⁻¹⁰ M to about 1.00 x 10⁻¹⁵ M, wherein said antibody has an off-rate (k_d) of between about 1.00 x 10⁻⁴ s⁻¹ to about 1.00 x 10⁻⁹ s⁻¹, and wherein said antibody has on-rate (k_a) of between about 1.00 x 10³/M-s⁻¹ to about 1.00 x 10⁸/M-s⁻¹.

--continued on first extra sheet attached hereto--

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, 33, 34

- 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 14/41441

continuation of Box No III:

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:

Special technical features

Group I has the special technical feature of wherein the binding of the antibody or antibody fragment to CFH protein is sensitive to the reduced form of CFH protein, or a method of treating a subject having cancer, the method comprising administering a therapeutic compound, wherein the therapeutic compound binds to short consensus repeat (SCR) 19 of a reduced form of CFH, that is not required by Group II.

Group II has the special technical feature of wherein said antibody has an equilibrium dissociation constant (K_d) of between about 1.00×10^{-10} M to about 1.00×10^{-15} M, wherein said antibody has an off-rate (k_d) of between about 1.00×10^{-4} s⁻¹ to about 1.00×10^{-9} s⁻¹, or wherein said antibody has on-rate (k_a) of between about 1.00×10^3 M⁻¹s⁻¹ to about 1.00×10^8 M⁻¹s⁻¹, that is not required by Group I.

Common technical features:

Groups I and II share the common technical feature of an isolated antibody or antibody fragment which immunospecifically binds to the CFH protein. However, this shared technical feature does not represent a contribution over prior art, because this shared technical feature is anticipated by US 2012/0003225 A1 to Patz et al., (hereinafter Patz).

Patz teaches an isolated antibody or antibody fragment which immunospecifically binds to the CFH protein (para [0017] 'an antibody against Complement Factor H (CFH)').

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Groups I and II lack unity of invention defined under PCT Rule 13.

Notes:

Claims 15-19, 26-32 and 35-52 have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Claims 7, 8 and 20-25 have been found to be unsearchable. The electronic sequence listing submitted in response to the PCT/ISA/225 issued on 02 July 2014 is acknowledged; however, it was a partial e-sequence listing containing only SEQ ID NOs 1-3, and it does not comply with the standard provided for in Annex C of the Administrative Instructions for the remaining sequences. Therefore, the international search was not carried out on the basis of that non-compliant electronic sequence listing for any non-compliant electronic sequence listing, i.e. SEQ ID NO 4+. Consequently, claims 7, 8 and 20-25 have been found to be unsearchable.