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(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,

(54) Title: METHODS OF USING GENETIC MARKERS ASSOCIATED WITH ENDOMETRIOSIS

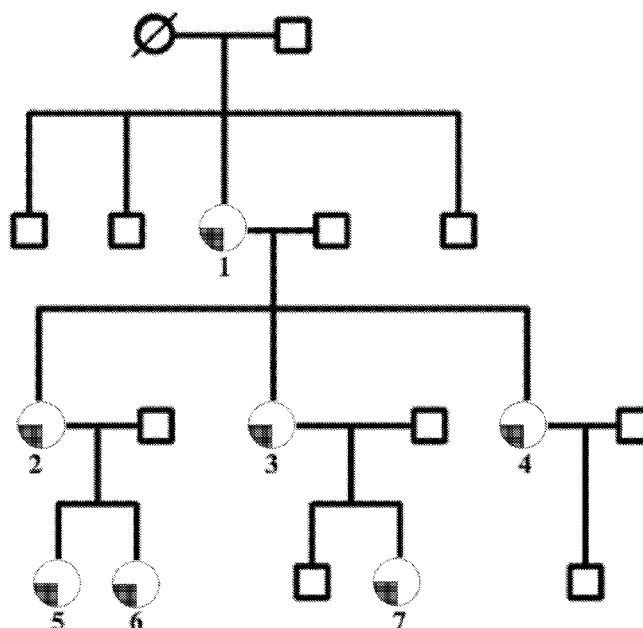


FIG. 1

(57) Abstract: Disclosed herein are methods of using genetic markers associated with endometriosis, for example via a computer-implemented program to predict risk of developing endometriosis, and methods of preventing or treating endometriosis or a symptom thereof. For example, the present disclosure provides a method of testing for endometriosis and treating a subject having at least one genetic mutation in at least one gene of *UGT2B28*, *USP17L2* (alias *DUB3*), and *METTL11B* such that the subject is prevented from developing endometriosis or such that endometriosis in the subject is prevented from progressing. The treatment may be a surgical intervention, a hormone treatment, a pharmaceutical treating, or a combination thereof.





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.

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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))*

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:

02 April 2020 (02.04.2020)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/029218

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/56; A61K 31/566; A61K 39/395; A61P 15/00; C07H 21/04; C12N 15/09 (2020.01)

CPC - A61P 15/00; C07H 21/04; C12N 15/11; C12Q 1/6844; C12Q 1/6883; C12Q 1/6886; C12Q 2600/106; C12Q 2600/156; C12Q 2600/158; C12Q 2600/172; G01N 33/574; G01N 33/57415 (2020.02)

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 435/6.12; 435/6.14; 435/7.1; 506/9; 506/16; 514/170; 536/23.1; 536/24.5 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2014/0235486 A1 (CHAPMAN et al) 21 August 2014 (21.08.2014) entire document	1-3, 8-10, 75-80
Y	US 2015/0368714 A1 (WARD et al) 24 December 2015 (24.12.2015) entire document	1-3, 8-10
Y	US 2007/0172853 A1 (MCCARROLL et al) 26 July 2007 (26.07.2007) entire document	10
Y	US 2008/0305967 A1 (WARD et al) 11 December 2008 (11.12.2008) entire document	25-30, 38-40, 69-72, 75-80, 90-93, 100-103
Y	INNOCENTI et al. "SNP Discovery and Functional Assessment of Variation in the UDP-Glucuronosyltransferase 2B7 (UGT2B7) Gene," Pharmacogenet Genomics, 31 August 2008 (31.08.2008), Vol. 18, No. 8, Pgs. 683-697. entire document	25-30, 38-40, 69-72, 90-93, 100-103
Y	US 2008/0306034 A1 (WARD) 11 December 2008 (11.12.2008) entire document	79, 80
P, X	ALBERTSEN et al. "Whole Exome Sequencing Identifies Hemizygous Deletions in the UGT2B28 and USP17L2 Genes in a Three-Generation Family with Endometriosis," Molecular Medicine Reports, 03 January 2019 (03.01.2019), Vol. 19, No. 3, Pgs. 1716-1720. entire document	1-3, 8-10, 25-30, 38-40, 69-72, 75-80, 90-93, 100-103
P, X	MATALLIOTAKI et al. "Co-Existence of Endometriosis with 13 Non-Gynecological Co-Morbidities: Mutation Analysis by Whole Exome Sequencing," Molecular Medicine Reports, 01 October 2018 (01.10.2018), Vol. 18, No. 6, Pgs. 5053-5057. entire document	1-3, 8-10, 25-30, 38-40, 69-72, 75-80, 90-93, 100-103



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

03 February 2020

Date of mailing of the international search report

03 MAR 2020

Name and mailing address of the ISA/US

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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/029218

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2013/0197056 A1 (HUNTSMAN et al) 01 August 2013 (01.08.2013) entire document	1-3, 8-10, 25-30, 38-40, 69-72, 75-80, 90-93, 100-103
A	WO 2012/071665 A1 (UNIVERSITE LAVAL et al) 07 June 2012 (07.06.2012) entire document	1-3, 8-10, 25-30, 38-40, 69-72, 75-80, 90-93, 100-103
A	WO 2013/049926 A1 (UNIVERSITÉ LAVAL) 11 April 2013 (11.04.2013) entire document	1-3, 8-10, 25-30, 38-40, 69-72, 75-80, 90-93, 100-103
A	— MATALLIOTAKIS et al. "Genetic Association Study in a Three-Generation Family with Seven Members with Endometriosis," Molecular Medicine Reports, 23 August 2017 (23.08.2017), Vol. 16, No. 5, Pgs. 6077-6080. entire document	1-3, 8-10, 25-30, 38-40, 69-72, 75-80, 90-93, 100-103

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/029218

Box No. 1 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:

- a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
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 forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

ISA/225 was mailed on 05 December 2019. No approved electronic sequence listing was submitted in response to the ISA/225.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/029218

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.: 4-7, 11-24, 31-37, 41-68, 73, 74, 81-89, 94-99
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:

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.:

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.