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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:
21 February 2013

(54) Title: COMPOSITIONS AND METHODS FOR TREATING RENAL DISEASE

(57) Abstract: Compositions and methods are disclosed herein for treating or reducing the symptoms of a renal disease, such as focal segmental glomerulosclerosis (FSGS), hypertensive end-stage kidney disease (ESKD), and HIV-associated nephropathy (a distinct form of FSGS, also termed collapsing glomerulopathy). The compositions include the common variant of APOL1 and fragments thereof, as well as antibodies and fragments thereof that bind and neutralize pathogenic APOL1, nucleic acid molecules that encode the common variant of APOL1 and fragments thereof, and other compounds that bind and neutralize pathogenic APOL1. The methods of the invention include administering one or more of the compositions of the invention to a subject having or at risk of developing renal disease.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/39145

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 38/00, 31/7088; C12N 15/113 (2012.01)
USPC - 514/15.4, 44R, 44A
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 38/00, 31/7088; C12N 15/113 (2012.01)
USPC - 514/15.4, 44R, 44A

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)
WEST, PatBase, Google Scholar, GenCore 6.3
search terms: APO-L, APOL, APOL1, apolipoprotein L1, apolipoprotein L-1, apolipoprotein L, FSGS4, APOLI, apolipoprotein LI, apo-l1, Apolipoprotein-LI, kidney, renal, glomerulosc$, anti, antibod$, inhibi$, antagon$, reduc$, down, silenc$, APO-L4, APOL4, APOLIV,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	WO 2011/020865 A1 (PAYS et al.) 24 February 2011 (24.02.2011) para [0001]; [0002]; [0004]-[0010]; [0035]; [0042]; [0043].	1-3, 6, 7, 11, 12, 15, 16, 19, 20 ---------- 4, 5, 8, 9, 13, 14, 21-23
X	US 2010/0120781 A1 (NEAMATI) 13 May 2010 (13.05.2010) para [0020]; [0026]; [0029]; [0122]; [0123].	1
Y	US 2009/0162333 A1 (PAYS et al.) 25 June 2009 (25.06.2009) para [0013]; [0014]; [0026]; [0027]; [0033]; [0035].	4, 5, 8, 9, 13, 14, 21-23
Y	Gibson et al., "The human serum resistance associated gene is ubiquitous and conserved in Trypanosoma brucei rhodesiense throughout East Africa" Infection, Genetics and Evolution; 2002; Vol. 1, No. 3; pg. 207-214. p. 207, 1st para; Fig. 2; AJ345057.	13, 14

☐ 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
12 November 2012 (12.11.2012)	07 DEC 2012
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

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/39145

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.: 10, 17, 18, 24-38, 43, 49, 50, 59, 61-62
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 1-9, 11-16, and 19-23, directed to a method of treating or reducing the likelihood of development of a renal disease comprising administering to a subject in need thereof a composition comprising an agent that decreases a deleterious effect of a pathogenic APOL1.

- 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.:
1-9, 11-16, and 19-23

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

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Continuation of Box III: Lack of Unity of Invention

Group II: claims 39-42, 44-48, and 51-58, directed to an isolated agent that decreases a deleterious effect of a pathogenic APOL1 in a subject, wherein said agent is selected from a fragment of a common APOL1, a nucleic acid molecule encoding said common APOLI fragment, a nucleic acid molecule that decreases the level of APOL1 polypeptide expression, wherein preferably said nucleic acid molecule is an antisense nucleic acid molecule or a ribonucleic acid interference molecule (RNAi), an anti-APOL1 antibody or fragment thereof, wherein said an anti-APOL1 antibody or fragment thereof binds to, and preferably neutralizes a pathogenic APOL1, an APOL1-binding polypeptide or fragment thereof that binds to, and preferably neutralizes, said pathogenic APOL1, but not a common APOL1, and a nucleic acid molecule that encodes said APOL1-binding polypeptide or fragment thereof.

Group III: claim 60, directed to a method of treating or reducing the likelihood of development of a renal disease comprising the step of extracorporeally contacting all or a portion of the blood or plasma from a subject with a composition comprising an agent that decreases a deleterious effect of a pathogenic APOL1.

The inventions listed as Groups I - III 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 special technical features of the claims of Groups I-III are disclosed in the Group descriptions, above.

The only common technical element shared by all of the above groups is that they are related to decreasing deleterious effects of pathogenic APOL1. Groups I and III share the common technical elements of a method of treating or reducing the likelihood of development of a renal disease comprising administering to a subject in need thereof a composition comprising an agent that decreases a deleterious effect of a pathogenic APOL1. These common technical elements do not represent an improvement over the prior art of US 2010/0120781 A1 to Neamati, which teaches a method of treating or reducing the likelihood of development of a renal disease (para [0026] ? 'renal cancer'), comprising administering to a subject in need thereof a composition comprising an agent that decreases a deleterious effect of APOL1 (para [0026], [0029] ? 'apolipoprotein L', and [0122]-[0123]). Neamati does not specifically recite wherein the APOL1 is pathogenic. However, since Neamati teaches wherein the use of an effective amount of a compound (para [0020]) treats cancer (para [0020]), while reducing expression of the APOL1 (para [0029]), it would have been obvious to a person skilled in the art that the APOL1 was involved in the pathology of the disease, and to therefore consider the APOL1 to be "pathogenic".

Therefore, the inventions of Groups I-III lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.