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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))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
26 October 2012

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(54) Title: DETECTION OF HUMAN ENDOGENOUS RETROVIRUS EXPRESSION IN CANCER AND NORMAL CELLS

(57) Abstract: The invention relates to human endogenous retrovirus env (HERV-WL) polypeptides, nucleotide sequences, HERV-WL antibodies, methods to detect cancer, and methods to determine the effectiveness of the treatment of cancer.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/27289

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 16/00, G01N 33/53 (2012.01)
USPC - 435/7.1; 530/387.1
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: 435/7.1; 530/387.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 435/6.14, 7.1; 530/388.1, 388.15, 387.1
(keyword limited; terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (PGPB,USPT,USOC,EPAB,JPAB); Google; PubMed
Search terms: HERV-WL, HERV-W, HERV, WL, human endogenous retrovirus, env, envelope, antibody, immunotoxin, tekvkeirdgiqrra, SEQ ID NO:2

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0196754 A1 (DRMANAC et al.) 8 September 2005 (08.09.2005) claims 20, 28; SEQ ID NO:37891; para [0286], [0322], [0339]-[0342], [0364], [0366], [0384], [0386]	1-9
A	US 2010/0074894 A1 (PERRON) 25 March 2010 (25.03.2010)	1-9
A	MARSDEN et al. Short communication: Activating stimuli enhance immunotoxin-mediated killing of HIV-infected macrophages. AIDS Res. Hum. Retroviruses. November 2008 (11.2008), Vol. 24, No. 11, pages 1399-1404	1-9

☐ 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
7 August 2012 (07.08.2012)	16 AUG 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 12/27289

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.: 26-29
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, drawn to an isolated antibody that specifically binds to HERV-WL.

Group II: Claims 10-12, drawn to a method of detecting HERV-WL in a cell.

Group III: Claims 13-20 and 30-33, drawn to a method of detecting or monitoring treatment of a cancer in a subject, and to a kit for diagnosing, prognosis or monitoring the treatment of cancer.

Group IV: Claims 21, 23-24, drawn to an isolated nucleic acid comprising a sequence with identity to SEQ ID NO:1.
----------(Continued 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.:
1-9

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 12/27289

Continuation of Box III - observations where unity of invention is lacking:

Group V: Claims 22-25, drawn to an isolated nucleic acid comprising a sequence that encodes a peptide with identity to SEQ ID NO:2, and to an isolated peptide with identity to SEQ ID NO:2.

The inventions listed as Groups I-V 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 shared technical feature of the inventions listed as Groups I-III is a human endogenous retrovirus env polypeptide (HERV-WL). The shared technical feature of the inventions listed as Groups I-II is an antibody that specifically binds to HERV-WL. This shared technical feature fails to provide a contribution over the prior art, as evidenced by US 2005/0196754 A1 to Drmanac et al. (published 8 September 2005; hereinafter 'Drmanac'). Drmanac discloses an isolated antibody that specifically binds to a polypeptide comprising claimed SEQ ID NO:2 (claim 28 - " antibody that specifically binds to a polypeptide of claim 10 or 20"; claim 20 - "amino acid sequence selected from the group consisting of SEQ ID NO: 30369-60736"; amino acids 432-446 of SEQ ID NO:37891 exhibits 100% identity with SEQ ID NO:2). Drmanac further teaches that SEQ ID NO:37891 is an env protein (see "other information" field in the sequence listing). Although Drmanac does not expressly name the disclosed SEQ ID NO:37891 as a HERV-WL protein, said disclosed env protein is inherently a HERV-WL env protein, based on the 100% sequence identity. In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature.

The shared technical feature of the inventions listed as Groups II and III is the detection of HERV-WL. This shared technical feature fails to provide a contribution over Drmanac. As discussed above, Drmanac disclsoes a polypeptide that exhibits 100% identity to SEQ ID NO:2, which is an epitiope of the HERV-WL polypeptide. Further, Drmanac discloses a method comprising contacting the polypeptide with an isolated antibody that specifically binds to the polypeptide (para [0022] - " contacting the sample with a compound that binds to and forms a complex with the polypeptide"; para [0023] - "monolconal antibodies"); and detecting the presence of a complex of the antibody and polypeptide in the cell (para [0022] - "detecting the formation of the complex such that if a complex is formed, the polypeptide is detected"). 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 antibody that specifically binds to HERV-WL. This special technical feature is not shared by the inventions of Groups III-V.
The special technical feature of the inventions listed as Group II is detection of HERV-WL in a cell. This special technical feature is not shared by the inventions of Groups I and IV-V. The special technical feature of the inventions listed as Group III is the analysis of the level of HERV-WL for making a determination related to cancer. This special technical feature is not shared by the inventions of Groups I -II and IV-V. The special technical feature of the inventions listed as Group IV is a nucleic acid having identity to SEQ ID NO:1 This special technical feature is not shared by the inventions of Groups I-III and V. The special technical feature of the inventions listed as Group V is a polypeptide having identity to SEQ ID NO:2. This special technical feature is not shared by the inventions of Groups I-IV.

Unity of invention exists only when the same or corresponding technical feature is shared by the claimed inventions. Without a shared special technical feature, the inventions of Groups I-V lack unity with one another.