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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))*

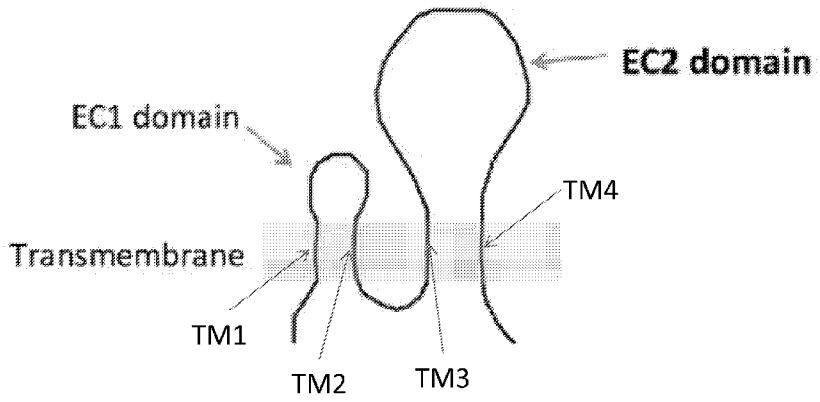
— *with (an) indication(s) in relation to deposited biological material furnished under Rule 13bis separately from the description (Rules 13bis.4(d)(i) and 48.2(a)(viii))*

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

(88) Date of publication of the international search report:
31 December 2014

(54) Title: HYBRIDOMA CLONES AND MONOCLONAL ANTIBODIES TO CD9

FIG. 1



(57) Abstract: The present invention is directed to a monoclonal antibody that recognizes human CD9 in its native form. The invention is also directed to a hybridoma cell line that produces the monoclonal antibody, and exosome isolation kits using the antibody.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 16/00, C12P 21/08, A61K 39/395, A61K 39/00, C12N 5/00, C12N 5/02 (2014.01)
CPC - A61K 38/00, C07K 14/47, C07K 2319/00, C07K 16/18, C07K 14/705, A61K 35/14
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)
CPC- A61K 38/00, C07K 14/47, C07K 2319/00, C07K 16/18, C07K 14/705, A61K 35/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC- A61K 39/00, A61K 48/00, C07K 14/4715, A61K 2039/505, A61K 39/0006, C07K 16/2896, C07K 2316/96, C07K 2317/24
USPC- 530/387.9,530/389.7,530/389.1,424/172.1,424/174.1,424/9.1,424/9.5,424/130.1,424/133.1,424/143.1,424/155.1,435/325

Electronic data base consulted during the international search.(name of data base and, where practicable, search terms used)
PubWEST(PGPB,USPT,USOC,EPAB,JPAB); PatBase, Google Scholar: The Translational Genomics Research Institute; Azorsa, David O, tetraspanin, CD9, anti-CD9 antibody, large extracellular loop, extracellular domain, EC2, TM3, TM4, Z9.1, Z9.2, anti-CD9 mAb, CD9 antigen, ALMA.1, human CD9, GST-CD9 fusion, 5H9 antigen, BA2, BTCC-1

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2011/0195027 A1 (Park, et al.) 11 August 2011 (11.08.2011) para [0144], [0085]; claims 1, 2; SEQ ID NO: 36	1, 2, 4-8, 10-12 --- 3, 9
Y	Jefferis, et al. Human immunoglobulin allotypes: Possible implications for immunogenicity. MAbs 2009, 1(4): 332-338; pg 2, col 2, pg 4, col 2	3, 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
06 October 2014 (06.10.2014)	05 NOV 2014

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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

INTERNATIONAL SEARCH REPORT

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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:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/30797

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:
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.

Group I: claims 1-12, drawn to a monoclonal antibody having the same epitope specificity as a monoclonal antibody produced by a hybridoma cell line selected from the group consisting of Z9.1 and Z9.2 (claims 1-6), and an isolated monoclonal antibody produced by a hybridoma cell line selected from the group consisting of Z9.1 and Z9.2 (claims 7-12).

Group II: claims 13-19, drawn to a method of making an isolated monoclonal antibody produced by a hybridoma cell line selected from the group consisting of Z9.1 and Z9.2 (claims 13-16); and an exosome purification kit comprising at least one container containing said monoclonal antibody (claims 17-19).

********** See Supplemental Sheet to continue **********

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.:
1-12

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.

********** Supplemental Sheet **********

In Continuation of Box III. Observations where unity of invention is lacking:

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
The inventions of Group I do not include the shared or common technical feature of a method of making an isolated monoclonal antibody produced by a hybridoma cell line selected from the group consisting of Z9.1 and Z9.2 (claims 13-16); or an exosome purification kit comprising at least one container containing said monoclonal antibody (claims 17-19), as required by Group II.

Common Technical Features
The inventions of Groups I-II share the technical feature of a monoclonal antibody having the same epitope specificity as a monoclonal antidoby produced by a hybridoma cell line selected from the group consisting of Z9.1 and Z9.2. However, this shared technical feature does not represent a contribution over prior art as being anticipated by US 2011/0195027 A1 to Park, et al. (11 August 2011) (hereinafter "Park") as follows:

Park discloses a monoclonal antibody binding to CD9-ECL2, i.e the large extracellular loop of CD9 (Park, claim 2, "The human antibody according to claim 1, wherein the antibody recognizes the peptide fragment represented by SEQ. ID. NO: 36 in CD9 extracellular loop 2 domain (CD9-ECL2) as an epitope"; para [0144], "10E4 antibody ... recognizes the peptide fragment represented by SEQ. ID. NO: 36 (KEVFDN) in CD9-ECL2 as an epitope", wherein Park's SEQ ID NO:36 is 100% identical to amino acids 74-80 of Applicant's SEQ ID NO:2).

Park does not specifically disclose that 10E4 monoclonal antibody has the same epitope specificity as monoclonal antibody Z9.1 or Z9.2. However, said limitation is inherently present in Park, as evidenced by Applicant, disclosing that monoclonal antibodies Z9.1 and Z9.2 bind to Applicant's SEQ ID NO:2, i.e. large extracellular loop of CD9 (instant application, claim 6, "The monoclonal antibody of claim 1, wherein the monoclonal antibody specifically binds to the amino acid sequence of SEQ ID N0:2"). As Park's 10E4 antibody binds to an epitope within Applicant's epitope of SEQ ID NO:2, it follows that Park does inherently disclose a monoclonal antibody having the same epitope specificity as a monoclonal antibodies Z9.1 and Z9.2.

As said technical feature was known in the art at the time of the invention, this cannot be considered special technical feature that would otherwise unify the groups.

Groups I-II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.