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[Continued on next page]

(54) Title: ANTIBODIES SPECIFICALLY BINDING HLA-DR AND THEIR USES

(57) Abstract: The present invention relates antibodies or antigen-binding fragments thereof specifically binding HLA-DR, polynucleotides encoding the antibodies or fragments, and methods of making and using the foregoing.

mAb	HCDR1					SEQ ID NO:
	Sequence					
DR4B117	S	Y	S	I	H	39
DR4B30	S	D	W	I	G	40
DR4B127	S	Y	Y	I	H	41
DR4B98	S	Y	Y	I	H	41
Genus	S	X <sub>1</sub>	X <sub>2</sub>	I	X <sub>3</sub>	73

SEQ ID NO: 73

SX<sub>1</sub>X<sub>2</sub>IX<sub>3</sub>; wherein  
X<sub>1</sub> is Y or D;  
X<sub>2</sub> is S, W or Y; and  
X<sub>3</sub> is H or G.

**FIG. 1**

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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, 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, 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.

**(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, ST, 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).

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

**(88) Date of publication of the international search report:**  
10 August 2017

**INTERNATIONAL SEARCH REPORT**

International application No  
PCT/US2016/067235

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. C07K16/28  
ADD.

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)  
C07K

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)  
EPO-Internal, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	G. L. DENARDO: "Direct Antilymphoma Effects on Human Lymphoma Cells of Monotherapy and Combination Therapy with CD20 and HLA-DR Antibodies and 90Y-Labeled HLA-DR Antibodies", CLINICAL CANCER RESEARCH, vol. 11, no. 19, 1 October 2005 (2005-10-01), pages 7075s-7079s, XP055358537, US ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-1004-0008 abstract, introduction -----	1-57
Y	EP 1 369 431 A1 (KIRIN BREWERY [JP]) 10 December 2003 (2003-12-10) paragraphs [0005], [0022] - paragraph [0025]; claim 1 ----- -/--	1-57

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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  3 July 2017	Date of mailing of the international search report  13/07/2017
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Heder, Andreas
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2016/067235

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2013/138241 A1 (JANSSEN BIOTECH INC [US]) 19 September 2013 (2013-09-19) page 58; claims 1-3, 5; sequence 207 -----	1-57
Y	WO 2012/047583 A2 (JANSSEN BIOTECH INC [US]; KEHOE JOHN [US]; LEE JENNIFER [US]; ORT TATI) 12 April 2012 (2012-04-12) page 10; claim 2; table 1; sequence 5 -----	1-57
Y	WO 2005/058251 A2 (DENDREON CORP [US]) 30 June 2005 (2005-06-30) claim 12; examples 2, 3 -----	1-57
Y	WO 2015/057906 A1 (JANSSEN BIOTECH INC [US]) 23 April 2015 (2015-04-23) page 87; table 22; sequence 33 -----	1-57
Y	US 9 163 083 B2 (ALMAGRO JUAN CARLOS [US] ET AL) 20 October 2015 (2015-10-20) sequence 60 -----	1-57

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2016/067235

## 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:

see additional 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 an 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.:  
  
32, 33(completely); 1-31, 34-57(partially)
  
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.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 32, 33(completely); 1-29, 34-57(partially)

HLA-DR binding antibody or antibody fragment as specified in subinventions 1.1 and 1.2, and uses thereof

1.1. claims: 32(completely); 1-29, 34-57(partially)

HLA-DR binding antibody or antibody fragment which competes for HLA-DR binding with an antibody having a VH of SEQ ID NO: 58, and a VL of SEQ ID NO: 61, said antibody having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B127 (see Tabs. 8-14), and uses thereof

1.2. claims: 33(completely); 1-29, 34-57(partially)

HLA-DR binding antibody or antibody fragment having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B98 (see Tabs. 8-14), and uses thereof

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2-8. claims: 1-31, 34-57(all partially)

HLA-DR binding antibody or antibody fragment which competes for HLA-DR binding with an antibody having (j) a VH and VL of SEQ ID NO: 56 and 60, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B117, (k) a VH and VL of SEQ ID NO: 57 and 61, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B30, (l) a VH and VL of SEQ ID NO: 137 and 61, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B78, (m) a VH and VL of SEQ ID NO: 138 and 61, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B70, (n) a VH and VL of SEQ ID NO: 139 and 61, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B38, (o) a VH and VL of SEQ ID NO: 140 and 142, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B33, or (p) a VH and VL of SEQ ID NO: 141 and 61, having the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences of antibody DR4B22 (see Tabs. 8-14), and uses thereof

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9. claims: 1-29, 34-57(all partially)

Further groups of inventions relating to HLA-DR binding antibodies or antibody fragments which compete for HLA-DR binding with an antibodies having a VH and a VL as recited under inventions 1-8, but wherein the HCDR1, 2, and 3, and LCDR1, 2, and 3 sequences are not those recited under inventions 1-8, and uses thereof

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/067235

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