

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
6 March 2003 (06.03.2003)

PCT

(10) International Publication Number
WO 2003/018774 A3

(51) International Patent Classification⁷: **A61K 39/00**,
39/40, 39/42, C07K 16/08, 16/12, 16/28

(21) International Application Number:
PCT/US2002/028227

(22) International Filing Date: 28 August 2002 (28.08.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/315,539 29 August 2001 (29.08.2001) US
60/388,355 13 June 2002 (13.06.2002) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
5 February 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: THERAPEUTIC USES OF COMPLEMENT RECEPTOR 2

(57) **Abstract:** The present invention is directed to an immune complex composition, and a method of using that complex to enhance an in vivo immune response against a preselected target antigen. The immune complexes of the present invention comprise a monoclonal antibody specific for binding to complement receptor (CR2) site on B lymphocytes linked to a target antigen. As shown in Fig. SA-SD immune complexes bound to monkey B cells are removed in concert with loss of CR2. Figs. SA and SB demonstrate the % A1488 HB135 and % APhCy CD21 positive cells, out of the doubly positive FE CD20/PerCF CD45 population over time, after injection of A1488 labeled HB135 (an anti-CR2 antibody, administration indicated by first arrow) followed by injection of rabbit anti-mouse IgG (administration indicated by the second arrow). Figs. SC and SD are plots of the molecules of equivalent soluble fluorochrome (MESF) values for these populations.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/28227

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/00, 39/40, 39/42; C07K 16/08; 16/12, 16/28

US CL : 424/ 136.1, 144.1, 147.1, 150.1; 530/387.3, 388.22, 388.3, 388.4

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)

U.S. : 424/ 136.1, 144.1, 147.1, 150.1; 530/387.3, 388.22, 388.3, 388.4

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)
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TAYLOR, R.P. et al. Clearance of blood-borne pathogens mediated through bispecific monoclonal antibodies bound to the primate erythrocyte complement receptor. Cancer Immunology Immunotherapy. 1997, Vol. 45, pages 152-155, see entire document.	1-14
A	LINDORFER, M.A. et al. B cell complement receptor 2 transfer reaction. J. Immunol. 1 2003, Vol. 170, pages 3671-3678, especially Abstract.	1-14

☐ 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 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	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search

29 September 2003 (29.09.2003)

Date of mailing of the international search report

12 DEC 2003

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/28227

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim 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. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation 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 fee, this Authority did not invite payment of any additional fee.
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.: 1-14

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

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, claim(s) 1-14, drawn to a bi-specific antibody complex comprising a first antibody that binds to CR2 linked to a second antibody that binds to a target antigen and a method of enhancing in vivo immune response using same.

Group II, claim(s) 15-23, drawn to an immune complex comprising an antibody that binds to CR2 linked to a target antigen.

Group III, claim(s) 24-31, drawn to a method of enhancing in vivo immune response using an immune complex comprising an antibody that binds to CR2 and a target antigen.

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 linked complex of Group I is composed of two antibodies, one that binds complement receptor 2 and a second which binds a target antigen. The linked complex of Group II is composed of an antibody to CR2 and a target antigen. Accordingly, the complexes of Groups I and II are materially different molecules. Equally, the complex used in the method of Group I is materially different from the complex used in the method of Group III. Accordingly, the groups are not so linked by a common feature so as to constitute a single inventive concept.

Continuation of B. FIELDS SEARCHED Item 3:

WEST; STN ONLINE: Medline, Embase, Biosis, Scisearch

terms: complement, receptor, CR2, bispecific