(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 10 November 2005 (10.11.2005)

(10) International Publication Number WO 2005/105844 A3

(51) International Patent Classification⁷:

C07K 16/00

(21) International Application Number:

PCT/EP2005/004893

(22) International Filing Date: 4 May 2005 (04.05.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

04010702.1 5 May 2004 (05.05.2004) EP

(71) Applicant (for all designated States except US): MI-CROMET AG [DE/DE]; Staffelseestrasse 2, 81477 München (DE).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): RAUM, Tobias [DE/DE]; c/o Micromet AG, Staffelseestr. 2, 81477 München (DE). HENCKEL, Julia [DE/DE]; c/o Micromet AG, Staffelseestr. 2, 81477 München (DE). KRIN-NER, Eva [DE/DE]; c/o Micromet AG, Staffelseestr. 2, 81477 München (DE). MITTELSTRASS, Silke [DE/DE]; c/o Micromet AG, Staffelseestr. 2, 81477 München (DE). WOLF, Andreas [DE/DE]; c/o Micromet AG, Staffelseestr. 2, 81477 München (DE).
- (74) Agent: DEHMEL, Albrecht; Dehmel & Bettenhausen, Herzogspitalstr. 11, 80331 München (DE).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

(88) Date of publication of the international search report: 26 January 2006

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: PREPARATION OF SCFV ANTIBODY FRAGMENTS

(57) Abstract: The invention relates to methods of preparing antibody fragments. The invention further relates to antibody fragments prepared by said methods. The invention further relates to antibody variable regions comprised in antibody fragments producible by said methods.

International Application No
PCT/EP2005/004893

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K16/00

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) $IPC \ 7 \ C07K$

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 practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE CHINGWEI V ET AL: "Bivalent antibody phage display mimics natural immunoglobulin." JOURNAL OF IMMUNOLOGICAL METHODS. JAN 2004, vol. 284, no. 1-2, January 2004 (2004-01), pages 119-132, XP004485591 ISSN: 0022-1759 page 120, right-hand column; figure 1	1-15

Σ Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
 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 document 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 24 October 2005 Name and mailing address of the ISA	Date of mailing of the international search report 02/11/2005 Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Le Flao, K

International Application No
PCT/EP2005/004893

	tion) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
X	PACK P ET AL: "Miniantibodies: use of amphipathic helices to produce functional, flexibly linked dimeric FV fragments with high avidity in Escherichia coli." BIOCHEMISTRY. 18 FEB 1992, vol. 31, no. 6, 18 February 1992 (1992-02-18), pages 1579-1584, XP002026334 ISSN: 0006-2960 page 1580, left-hand column, last paragraph - right-hand column, paragraph 2; figure 1	1-15	
X	NERI D ET AL: "Targeting by affinity-matured recombinant antibody fragments of an angiogenesis associated fibronectin isoform." NATURE BIOTECHNOLOGY. NOV 1997, vol. 15, no. 12, November 1997 (1997-11), pages 1271-1275, XP002124779 ISSN: 1087-0156 page 1274, left-hand column, last paragraph - right-hand column, paragraph 1	1 -15	
X	PACK P ET AL: "Tetravalent miniantibodies with high avidity assembling in Escherichia coli." JOURNAL OF MOLECULAR BIOLOGY. 10 FEB 1995, vol. 246, no. 1, 10 February 1995 (1995-02-10), pages 28-34, XP000607470 ISSN: 0022-2836 page 28, right-hand column	1-15	
X	PACK P ET AL: "Improved bivalent miniantibodies, with identical avidity as whole antibodies, produced by high cell density fermentation of Escherichia coli." BIO/TECHNOLOGY (NATURE PUBLISHING COMPANY) NOV 1993, vol. 11, no. 11, November 1993 (1993-11), pages 1271-1277, XP000608190 ISSN: 0733-222X page 1271 - page 1275; figure 1	1-15	
A	HOLT L J ET AL: "Domain antibodies: proteins for therapy" TRENDS IN BIOTECHNOLOGY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 11, November 2003 (2003-11), pages 484-490, XP004467495 ISSN: 0167-7799 the whole document	1-15	

International Application No
PCT/EP2005/004893

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
A	CLACKSON T ET AL: "MAKING ANTIBODY FRAGMENT USING PHAGE DISPLAY LIBRARIES" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 352, 15 August 1991 (1991-08-15), pages 624-628, XP001019232 ISSN: 0028-0836 the whole document	1-15			
4	US 6 265 150 B1 (LOGTENBERG TON ET AL) 24 July 2001 (2001-07-24) column 2, line 31 - column 6, line 67	1-15			
A	SBLATTERO D ET AL: "EXPLOITING RECOMBINATION IN SINGLE BACTERIA TO MAKE LARGE PHAGE ANTIBODY LIBRARIES" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 18, no. 1, January 2000 (2000-01), pages 75-80, XP000891515 ISSN: 1087-0156 the whole document	1-15			

International Application No
PCT/EP2005/004893

			101/11/2003/004093	
Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 6265150	B1 24-07-2001	NONE		
			•	
		•		