



(51) International Patent Classification:

C07K 14/52 (2006.01) *C07K 17/02* (2006.01)
A61M 1/36 (2006.01) *G01N 33/68* (2006.01)
B01J 20/32 (2006.01)

(21) International Application Number:

PCT/GB2012/051354

(22) International Filing Date:

13 June 2012 (13.06.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/496,352 13 June 2011 (13.06.2011) US

(71) Applicant (for all designated States except US): **ITH IMMUNE THERAPY HOLDINGS** [SE/SE]; Unit L2:04, Karolinska University Hospital Solna, S-171 76 Stockholm (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **COTTON, Graham** [GB/GB]; 18, Dreghorn Park, Edinburgh EH13 9PH (GB). **WINQVIST, Ola** [SE/SE]; Svankarrsvagen 32-F, S-756 53 Uppsala (SE).

(74) Agent: **SPENCER, Matthew**; Verulam Gardens, 70 Gray's Inn Road, London, Greater London WC1X 8BT (GB).

(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, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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, 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, ML, MR, NE, SN, TD, TG).

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:

14 March 2013

(54) Title: TREATING CONDITIONS ASSOCIATED WITH SEPSIS

(57) Abstract: A method for treating sepsis and/or respiratory distress syndrome (RDS) comprises applying peripheral blood from a patient or subject to an apheresis column loaded with a solid support comprising one or more binding reagents capable of specifically binding to a chemokine receptor, optionally the chemokine receptor CCR5, CXCR1, CXCR2, and/or CCR2 immobilized directly or indirectly on the support thus removing one or more chemokine receptor, optionally CCR5, CXCR1, CXCR2, and/or CCR2 expressing cells from the peripheral blood of the patient or subject. Various companion therapeutic methods and useful binding reagents are also described.



INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2012/051354

A. CLASSIFICATION OF SUBJECT MATTER INV. C07K14/52 A61M1/36 B01J20/32 C07K17/02 G01N33/68 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 A61M B01J G01N		
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, BIOSIS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DE 10 2005 036505 A1 (ADEXTER GMBH [DE]) 1 June 2006 (2006-06-01) paragraph [2324]	4,13, 43-50
Y	----- WO 2007/133147 A1 (IBD COLUMN THERAPIES INTERNAT [SE]; THOERN MAGNUS [SE]; WINQVIST OLA [] 22 November 2007 (2007-11-22) claims	4,13, 43-50
Y	----- WO 2010/029317 A2 (IBD COLUMN THERAPIES INTERNAT [SE]; WINQVIST OLA [SE]; COTTON GRAHAM [] 18 March 2010 (2010-03-18) cited in the application the whole document ----- -/-	1-5, 7-14, 16-18, 43-50
☒ 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 "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 21 September 2012		Date of mailing of the international search report 11/01/2013
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 Van der Schaal, C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2012/051354

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.:
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.:

1-5, 7-14, 16-18, 43-50(all partially)

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/GB2012/051354

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/017979 A1 (MACK MATTHIAS [DE] ET AL) 23 January 2003 (2003-01-23) claims 4, 5, 19 -----	4, 13, 43-50
Y	US 2007/092484 A1 (LEVINE ZURIT [IL] ET AL) 26 April 2007 (2007-04-26) paragraphs [0006], [0007], [0032], [0035]; claims 52, 53 -----	1-5, 7-14, 16-18, 43-50
Y	WO 2006/052723 A2 (NEW ENGLAND MEDICAL CENTER INC [US]; KULIOPULOS ATHAN [US]; COVIC LIDJ) 18 May 2006 (2006-05-18) page 68, paragraph 2; examples 7, 15 -----	1-5, 7-14, 16-18, 43-50
Y	F. O. SOUTO ET AL: "Essential Role of CCR2 in Neutrophil Tissue Infiltration and Multiple Organ Dysfunction in Sepsis", AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, vol. 183, no. 2, 15 January 2011 (2011-01-15), pages 234-242, XP055037727, ISSN: 1073-449X, DOI: 10.1164/rccm.201003-04160C abstract -----	1-5, 7-14, 16-18, 43-50
Y	AN J L ET AL: "Immunohistochemical detection of CCR2 and CX3CR1 in sepsis-induced lung injury", FORENSIC SCIENCE INTERNATIONAL, ELSEVIER SCIENTIFIC PUBLISHERS IRELAND LTD, IE, vol. 192, no. 1-3, 20 November 2009 (2009-11-20), pages e21-e25, XP026669683, ISSN: 0379-0738, DOI: 10.1016/J.FORSCIINT.2009.08.007 [retrieved on 2009-09-04] abstract -----	1-5, 7-14, 16-18, 43-50
Y	SPEYER CECILIA L ET AL: "Novel chemokine responsiveness and mobilization of neutrophils during sepsis", AMERICAN JOURNAL OF PATHOLOGY, vol. 165, no. 6, December 2004 (2004-12), pages 2187-2196, XP055037768, ISSN: 0002-9440 page 2194, right-hand column, paragraph 1; figure 1B ----- -/-	1-5, 7-14, 16-18, 43-50

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2012/051354

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BOSSINK A W J ET AL: "Plasma Levels of the Chemokines Monocyte Chemotactic Protein-1 and -2 Are Elevated in Human Sepsis", BLOOD, AMERICAN SOCIETY OF HEMATOLOGY, US, vol. 86, no. 10, 15 November 1995 (1995-11-15), pages 3841-3847, XP002963170, ISSN: 0006-4971 abstract, last sentence -----	1-5, 7-14, 16-18, 43-50

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2012/051354

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 102005036505 A1	01-06-2006	NONE	
WO 2007133147 A1	22-11-2007	AU 2007250552 A1 CA 2651883 A1 CN 101443041 A EA 200802086 A1 EP 2021025 A1 JP 2009536944 A KR 20090007642 A SG 171684 A1 US 2009192434 A1 WO 2007133147 A1 ZA 200809429 A	22-11-2007 22-11-2007 27-05-2009 30-06-2009 11-02-2009 22-10-2009 19-01-2009 29-06-2011 30-07-2009 22-11-2007 26-08-2009
WO 2010029317 A2	18-03-2010	AU 2009290694 A1 CA 2736632 A1 CN 102186880 A EA 201100452 A1 EP 2331568 A2 JP 2012501708 A KR 20110057222 A US 2011224645 A1 WO 2010029317 A2	18-03-2010 18-03-2010 14-09-2011 30-12-2011 15-06-2011 26-01-2012 31-05-2011 15-09-2011 18-03-2010
US 2003017979 A1	23-01-2003	US 2003017979 A1 US 2005191702 A1	23-01-2003 01-09-2005
US 2007092484 A1	26-04-2007	NONE	
WO 2006052723 A2	18-05-2006	AU 2005304963 A1 AU 2010202328 A1 BR PI0517058 A CA 2586344 A1 CN 101094866 A EP 1814911 A2 EP 2380904 A1 JP 2008519039 A JP 2012176985 A US 2008214451 A1 WO 2006052723 A2	18-05-2006 01-07-2010 30-09-2008 18-05-2006 26-12-2007 08-08-2007 26-10-2011 05-06-2008 13-09-2012 04-09-2008 18-05-2006

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-5, 7-14, 16-18, 43-50(all partially)

A binding reagent capable of specifically binding the CCR5 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating sepsis and/or respiratory distress syndrome

2. claims: 1-5, 7-14, 16-18, 43-50(all partially)

A binding reagent capable of specifically binding the CCR5 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating sepsis and/or respiratory distress syndrome

3. claims: 1-5, 7-14, 16-18, 43-50(all partially)

A binding reagent capable of specifically binding the CXCR2 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating sepsis and/or respiratory distress syndrome

4. claims: 6, 15(completely); 1-5, 7-14, 16-18, 43-50(partially)

A binding reagent capable of specifically binding the CCR2 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating sepsis and/or respiratory distress syndrome

5. claims: 19-29

Methods of diagnosing sepsis and/or respiratory distress syndrome or selecting a suitable treatment for the disease comprising determining the levels of CCR5, CXCR1, CXCR2 and/or CCR2

6. claims: 30-34, 66-71

Modified CCL2/MCP-1 chemokine

7. claims: 35-42

Modified MCP-5 chemokine

8. claims: 51-55

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Modified CCL8/MCP-2 chemokine

9. claims: 56-61

Modified CXCL8 chemokine

10. claims: 62-65

Modified CCL5 chemokine
