A method for treating inflammatory skin disease comprises applying peripheral blood from a patient to an apheresis column loaded with a solid support comprising one or more binding reagents capable of specifically binding to a chemokine receptor or, optionally, the chemokine receptor CCR4, CXCR1, CXCR2, CCR2, CCR6, CCR3, CCR5, CCR1, CCR9 or ChemR23 immobilized directly or indirectly on the support thus removing one or more chemokine receptor, optionally CCR4, CXCR1, CXCR2, CCR2, CCR6, CCR3, CCR5, CCR1, CCR9 and ChemR23 expressing cells from the peripheral blood of the patient or subject. Various companion diagnostic methods and useful binding reagents are also described.
A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K14/52 C07K17/02 A61M1/36 B01J20/32 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

<table>
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<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>Y</td>
<td>DE 10 2005 036505 AI (ADEXTER GMBH [DE]) 1 June 2006 (2006-06-01) paragraphs [0003], [0023], [0026]; claims 16, 29</td>
<td>4,21, 59-66</td>
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<td>Y</td>
<td>Wo 2007/133147 AI (IBD COLUMN THERAPIES INTERNAT [SE]; TH0ERN MAGNUS [SE]; WINQVIST OLA [ ]) 22 November 2007 (2007-11-22) the whole document</td>
<td>4,21, 59-66</td>
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<td>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</td>
<td>1-6, 10, 12, 13, 16-23, 27,29, 30,33, 34,59-66</td>
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</table>

[X] Further documents are listed in the continuation of Box C.  [X] 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

"I" 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.

"A" 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

**Box No. 1**  
**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 and necessary to the claimed invention, the international search was carried out on the basis of:
   
   a. (means)
   - [ ] on paper
   - [x] in electronic form
   
   b. (time)
   - [x] in the international application as filed
   - [ ] together with the international application in electronic form
   - [ ] subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto 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:

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Form PCT/ISA/21 0 (continuation of first sheet (1)) (July 2009)
INTERNATIONAL SEARCH REPORT

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 fee, 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 only by claims Nos.:

   1-6, 10, 12, 13, 16-23, 27, 29, 30, 33, 34, 59-66(al l p arti a lly)

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

1. claims: 1-6, 10, 12, 13, 16-23, 27, 29, 30, 33, 34, 59-66 (all partly)

   A binding reagent capable of specifically binding the CCR4 chemokine receptor, immobilized on a solid support with an apheresis column, and its use for treating inflammatory skin disease

   ---

2. claims: 1-5, 12, 13, 16-22, 29, 30, 33, 34, 59-66 (all partly)

   A binding reagent capable of specifically binding the CXCR1 chemokine receptor, immobilized on a solid support with an apheresis column, and its use for treating inflammatory skin disease

   ---

3. claims: 1-5, 12, 13, 16-22, 29, 30, 33, 34, 59-66 (all partly)

   A binding reagent capable of specifically binding the CXCR2 chemokine receptor, immobilized on a solid support with an apheresis column, and its use for treating inflammatory skin disease

   ---

4. claims: 7, 24 (completely) ; 1-6, 12, 13, 16-23, 29, 30, 33, 34, 59-66 (partly)

   A binding reagent capable of specifically binding the CCR2 chemokine receptor, immobilized on a solid support with an apheresis column, and its use for treating inflammatory skin disease

   ---

5. claims: 8, 9, 14, 25, 26, 31 (completely) ; 1-5, 12, 16-22, 29, 33, 34, 59-66 (partly)

   A binding reagent capable of specifically binding the CCR6 chemokine receptor, immobilized on a solid support with an apheresis column, and its use for treating inflammatory skin disease

   ---

6. claims: 1-5, 10-12, 15-22, 27-29, 32-34, 59-66 (all partly)

   A binding reagent capable of specifically binding the CCR3 chemokine receptor, immobilized on a solid support with an apheresis column, and its use for treating inflammatory skin disease

   ---

7. claims: 1-5, 10-12, 15-22, 27-29, 32-34, 59-66 (all partly)
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 inflammatory skin disease ---

8. claims: 1-5, 10-12, 16-22, 27-29, 33, 34, 59-66 (all partially)

A binding reagent capable of specifically binding the CCR1 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating inflammatory skin disease ---

9. claims: 1-5, 12, 15-22, 29, 32-34, 59-66 (all partially)

A binding reagent capable of specifically binding the CCR9 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating inflammatory skin disease ---

10. claims: 1-5, 12, 16-22, 29, 33, 34, 59-66 (all partially)

A binding reagent capable of specifically binding the ChemR23 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating inflammatory skin disease ---

11. claims: 35-45

Methods of diagnosing inflammatory skin diseases or selecting an effective treatment for the disease comprising determining the levels of CCR4, CXCR1, CXCR2, CCR2, CCR6, CCR3, CCR5, CCR1, CCR9 or ChemR23 ---

12. claims: 46-50

Modified MCP-1 chemokine ---

13. claims: 51-58

Modified MCP-5 chemokine ---

14. claims: 67-71

Modified CCL8 chemokine ---

15. claims: 72-75
Modified CCL5 chemokine

16. claims: 76-80

Modified CCL20 chemokine

17. claims: 81-85

Modified CCL22 chemokine
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<td>Y</td>
<td>ROTTMAN JAMES B ET AL: &quot;Potential role of the chemokine receptors CXCR3, CCR4, and the integrin alphaEbeta7 in the pathogenesis of psoriasis vulgaris&quot;. LABORATORY INVESTIGATION, vol. 81, no. 3, March 2001 (2001-03), pages 335-347, XP002681949, ISSN: 0023-6837, page 343 left-hand column - paragraph 2</td>
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<td>TOMOMI NAKATANI ET AL: &quot;CCR4+ memory CD4+ T lymphocytes are increased in peripheral blood and lesional skin from patients with atopic dermatitis&quot;. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, vol. 107, no. 2, 1 February 2001 (2001-02-01), pages 353-358, XP055035429, ISSN: 0091-6749, DOI: 10.1067/mi.2001.112601 abstract last sentence</td>
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<td>US 2003/215421 AI (MCDONALD JOHN R [CA] ET AL) 20 November 2003 (2003-11-20)</td>
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