



(51) International Patent Classification:

A61K 38/00 (2006.01) *A61P 25/00* (2006.01)
A61P 19/00 (2006.01) *A61P 23/00* (2006.01)
A61P 19/02 (2006.01) *A61P 9/00* (2006.01)
A61P 19/10 (2006.01) *A61P 1/00* (2006.01)

(21) International Application Number:

PCT/US2014/016384

(22) International Filing Date:

14 February 2014 (14.02.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

13/837,005 15 March 2013 (15.03.2013) US

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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, 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, 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, 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, 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))*

(88) Date of publication of the international search report:

20 November 2014

(54) Title: METHODS AND ACELLULAR COMPOSITIONS FOR TREATING INFLAMMATORY DISORDERS

(57) Abstract: Acellular compositions for treating inflammation, comprising two or more of IL1- α , sTNF-R1, sTNF-RII, IGF-I, EGF, HGF, PDGF-AB, PDGF-BB, VEGF, TGF- β 1, and sIL-1RII. Components of the acellular compositions may be derived from biologic materials, such as blood clots and urine. Components may also be obtained from cell cultures.



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/016384

A. CLASSIFICATION OF SUBJECT MATTER		
INV.	A61K38/00	A61P19/00
	A61P23/00	A61P9/00
		A61P1/00
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)		
A61K A61P		
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, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FEIGE U ET AL: "Anti-interleukin-1 and anti-tumor necrosis factor-alpha synergistically inhibit adjuvant arthritis in Lewis rats", CMLS CELLULAR AND MOLECULAR LIFE SCIENCES, BIRKHAUSER VERLAG, HEIDELBERG, DE, vol. 57, no. 10, 1 September 2000 (2000-09-01), pages 1457-1470, XP002229548, ISSN: 1420-682X page 1459, column 1 page 1458, column 2, paragraph 1 abstract ----- -/--	1-9, 11-14
☒ 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 "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		Date of mailing of the international search report
5 June 2014		09/10/2014
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 Rodrigo-Simón, Ana

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/016384

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BENDELE ALISON M ET AL: "COMBINATION BENEFIT OF TREATMENT WITH THE CYTOKINE INHIBITORS INTERLEUKIN-1 RECEPTOR ANTAGONIST AND PEGYLATED SOLUBLE TUMOR NECROSIS FACTOR RECEPTOR TYPE I IN ANIMAL MODELS OF RHEUMATOID ARTHRITIS", ARTHRITIS & RHEUMATISM, J.B. LIPPINCOTT CO, vol. 43, no. 12, 1 December 2000 (2000-12-01), pages 2648-2659, XP009073840, ISSN: 0004-3591, DOI: 10.1002/1529-0131(200012)43:12<2648::AID-NR4>3.0.CO;2-M page 2649, column 1, paragraph 6; tables 1-2 page 2657, column 2, paragraph 3 -----	1-14
X	Caldwell, J.R.; Offenberg, H.; Furst, D.; Lam, N.P.; Jayne, G.; Joh, T.; Davis, M.; Edwards, C.K. III.: "A phase I safety study of combination treatment with pegylated soluble tumor necrosis factor receptor type I (PET STNF-RI) and anakinra (interleukin-1 receptor antagonist, IL-1RA) in patients with rheumatoid arthritis", Prous integrity 12 June 2002 (2002-06-12), pages 1-1, XP002724516, Retrieved from the Internet: URL:https://integrity.thomson-pharma.com/integrity/xmlxsl/pk_ref_list.xml_show_ficha_ref?p_ref_id=675920 [retrieved on 2014-04-22] the whole document -----	1
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/016384

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SOLCHAGA L A ET AL: "HYALURONIC ACID-BASED POLYMERS AS CELL CARRIERS FOR TISSUE-ENGINEERED REPAIR OF BONE AND CARTILAGE", JOURNAL OF ORTHOPAEDIC RESEARCH, ORTHOPAEDIC RESEARCH SOCIETY, US, vol. 17, 1 January 1999 (1999-01-01), pages 205-213, XP002937764, ISSN: 0736-0266, DOI: 10.1002/JOR.1100170209 the whole document	2-9, 11-14
Y	----- SANJAY MEHTA ET AL: "Gentamicin distribution from a collagen carrier", JOURNAL OF ORTHOPAEDIC RESEARCH, vol. 14, no. 5, 1 September 1996 (1996-09-01), pages 749-754, XP055118622, ISSN: 0736-0266, DOI: 10.1002/jor.1100140511 the whole document	2-9, 11-14
A	----- KITAZAWA R ET AL: "INTERLEUKIN-1 RECEPTOR ANTAGONIST AND TUMOR NECROSIS FACTOR BINDING PROTEIN DECREASE OSTEOCLAST FORMATION AND BONE RESORPTION IN OVARECTOMIZED MICE", JOURNAL OF CLINICAL INVESTIGATION, AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, US, vol. 94, no. 6, 1 December 1994 (1994-12-01), pages 2397-2406, XP001095290, ISSN: 0021-9738, DOI: 10.1172/JCI117606 abstract	1-14
A	----- WO 91/08285 A1 (SYNERGEN INC [US]) 13 June 1991 (1991-06-13) page 2, paragraph 2-3; examples 1-4	1-14
A	----- Anonymous: "Arthritis", Mayo Clinic 22 January 2013 (2013-01-22), pages 1-3, XP002724517, Retrieved from the Internet: URL: http://www.mayoclinic.org/diseases-conditions/arthritis/basics/treatment/con-20034095?p=1 [retrieved on 2014-04-24] the whole document	1-14
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/016384

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	K. OKUNISHI ET AL: "Hepatocyte Growth Factor Significantly Suppresses Collagen-Induced Arthritis in Mice", THE JOURNAL OF IMMUNOLOGY, vol. 179, no. 8, 15 October 2007 (2007-10-15), pages 5504-5513, XP055115378, ISSN: 0022-1767, DOI: 10.4049/jimmunol.179.8.5504 abstract -----	1-14
A	DAWSON J ET AL: "Effects of soluble interleukin-1 type II receptor on rabbit antigen-induced arthritis: Clinical, biochemical and histological assessment", RHEUMATOLOGY (OXFORD), vol. 38, no. 5, May 1999 (1999-05), pages 401-406, XP002724518, ISSN: 1462-0324 the whole document -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/016384

Box No. I 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
- ☒ in electronic form
- b. (time)
- ☐ 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:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/016384

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.:

1-14

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: 1-14

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture

2. claims: 15-21

A method for making an acellular composition comprising IL-1ra

3. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of arthritis

4. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of osteolysis

5. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI ; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment tendonitis

6. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of synovitis

7. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of pain

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of traumatic injury

9. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of muscle strain

10. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood, or tissue culture for use in the treatment of peripheral vascular disease

11. claims: 22-29(partially)

A substantially acellular anti-inflammatory cytokine composition comprising IL-1ra and sTNF-RI; wherein at least one of them is derived from urine, clotted blood or from tissue culture for use in the treatment of inflammatory respiratory disease

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2014/016384

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9108285	A1	13-06-1991	
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