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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, 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.

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- (88) **Date of publication of the international search report:**
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(54) **Title:** FOLLISTATIN-LIKE-PROTEIN-1 AS A BIOMARKER FOR INFLAMMATORY DISORDERS

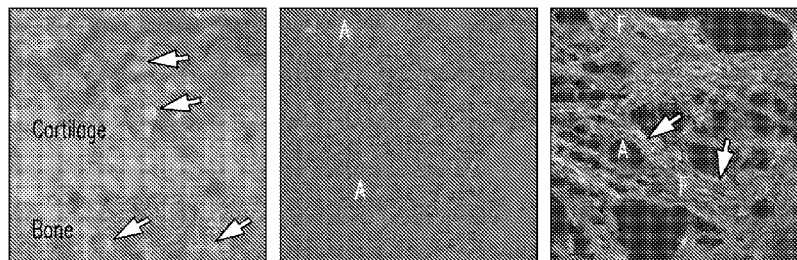


FIG. 1A FIG. 1B FIG. 1C

(57) **Abstract:** The present invention relates to methods and compositions for diagnosis of inflammatory disorders, and in non-limiting embodiments, of inflammatory disorders associated with elevated interleukin -1 β ("IL-1 β "), based on increased levels of follistatin-like protein 1 ("FSTL-1"). In particular non-limiting embodiments, the invention further provides for methods of identifying subjects with systemic onset juvenile idiopathic arthritis ("SOJIA") who are at increased risk for developing macrophage activation syndrome ("MAS") comprising detecting, in said subjects, hyper-increased levels of FSTL-1. In additional non-limiting embodiments, the invention provides for methods of identifying subjects with Kawasaki disease who are at increased risk of developing aortic aneurysms comprising detecting, in said subjects, hyper-increased levels of FSTL-1.

WO 2012/019099 A3

A. CLASSIFICATION OF SUBJECT MATTER*G01N 33/68(2006.01)i, G01N 33/53(2006.01)i*

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)

G01N 33/68; G01N 33/53; G01N 33/50

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords: FSTL-1, juvenile idiopathic arthritis, macrophage activation syndrome, kawasaki disease

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2009-097424 A1 (UNIVERSITY OF PITTSBURGH-OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION et al.) 06 August 2009 See Abstract; Pages 6,23,24,30-34; Claims 1-4	8-10
Y	KELLY, A and RAMANAN, A.V., `Recognition and Management of Macrophage Activation Syndrome in Juvenile Arthritis`, Curr Opin Rheumatol., vol.19, no.5, pp.477-481, September 2007 See Abstract; Page 477	8-10
Y	RAVELLI, A. et al. `Preliminary Diagnostic Guidelines for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis`, The Journal of Pediatrics, vol.146, pp.598-604, May 2005 See Abstract	8-10
Y	BLEESING, J. et al. `The Diagnostic Significance of Soluble CD163 and Soluble Interleukin-2 Receptor α -Chain in Macrophage Activation Syndrome and Untreated New-Onset Systemic Juvenile Idiopathic Arthritis`, Arthritis and Rheumatism, vol.56, no.3, pp.965-971, March 2007 See Abstract	8-10

 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

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"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

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Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/046742

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SURESH, N. and SANKAR, J., 'Macrophage Activation Syndrome: A Rare Complication of Incomplete Kawasaki Disease', Annals of Tropical Paediatrics, vol.30, pp.61-64, March 2010 See Abstract	8-10
Y	SIMONINI, G. et. al., 'Macrophage Activation Syndrome/Hemophagocytic Lymphohistiocytosis and Kawasaki Disease', Pediatr Blood Cancer, vol.55, pp.591, 7 June 2010 See Abstract	8-10

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.: 1-7,11,12
because they relate to subject matter not required to be searched by this Authority, namely:

The subject matter of claims 1-7,11,12 relates to a diagnostic method which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

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.: 12
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:

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.:

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

Information on patent family members

International application No.

PCT/US2011/046742

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009-097424 A1	06.08.2009	US 2011-0045507 A1	24.02.2011