

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
1 August 2002 (01.08.2002)

PCT

(10) International Publication Number
WO 02/059604 A3

(51) International Patent Classification⁷: **G01N 33/564**,
A61K 39/00, A61P 25/00

(21) International Application Number: PCT/GB02/00330

(22) International Filing Date: 25 January 2002 (25.01.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/264,404 26 January 2001 (26.01.2001) US
60/331,647 20 November 2001 (20.11.2001) US

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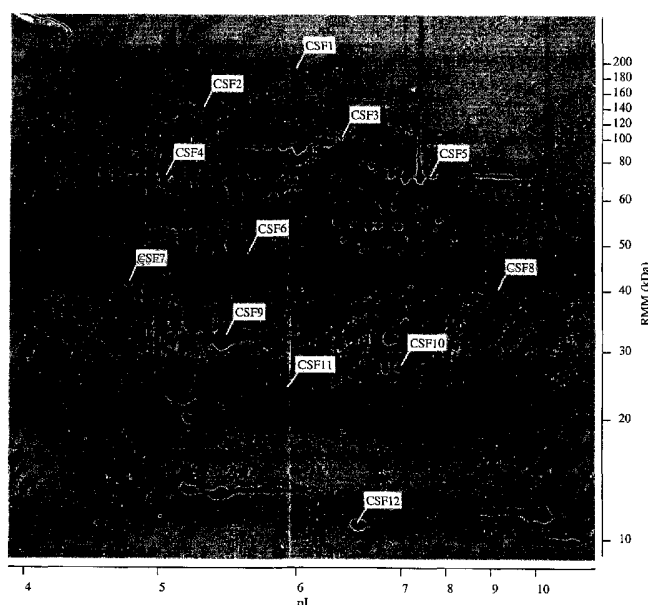
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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent

[Continued on next page]

(54) Title: DIAGNOSIS AND TREATMENT OF MULTIPLE SCLEROSIS



(57) Abstract: The present invention provides methods and compositions for screening, diagnosis and prognosis of Multiple Sclerosis, for monitoring the effectiveness of Multiple Sclerosis treatment, identifying patients most likely to respond to a particular therapeutic treatment and for drug development. Multiple Sclerosis-Associated Features (MSFs), detectable by two-dimensional electrophoresis of body fluid e.g. cerebrospinal fluid are described. The invention further provides Multiple Sclerosis-Associated Protein Isoforms (MSPIs) detectable in body fluid e.g. cerebrospinal fluid, preparations comprising isolated MSPIs, antibodies immunospecific for MSPIs, and kits comprising the aforesaid.



WO 02/059604 A3



(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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

3 July 2003

(15) Information about Correction:

Previous Correction:

see PCT Gazette No. 47/2002 of 21 November 2002, Section II

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.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 02/00330

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/564 A61K39/00 A61P25/00

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 G01N A61K

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, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HARRINGTON MICHAEL G ET AL: "Identification of a brain-specific human cerebrospinal fluid glycoprotein, beta-trace protein." APPLIED AND THEORETICAL ELECTROPHORESIS, vol. 3, no. 5, 1993, pages 229-234, XP009003878 ISSN: 0954-6642 abstract page 233, column 2, paragraph 2; figures 1-3 --- -/-	1-39

☒ 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

15 January 2003

Date of mailing of the international search report

30.04.03

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 02/00330

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HIRAOKA ATSUSHI ET AL: "Capillary-zone electrophoretic analyses of the proteins and amino acid components in cerebrospinal fluid of central nervous system diseases." BIOLOGICAL & PHARMACEUTICAL BULLETIN, vol. 16, no. 10, 1993, pages 949-952, XP001121494 ISSN: 0918-6158 abstract page 952, column 1, line 20 -column 2, line 2 ---	1-39
X	MELEGOS D N ET AL: "Prostaglandin D Synthase Concentration in Cerebrospinal Fluid and Serum of Patients with Neurological Disorders" PROSTAGLANDINS, BUTTERWORTH, STONEHAM, MA, US, vol. 54, no. 1, 1 July 1997 (1997-07-01), pages 463-474, XP004087867 ISSN: 0090-6980 abstract page 469, paragraph 2 -page 470, paragraph 1; table 4 page 471, paragraph 3 ---	1-39
X	BOLLENGIER F: "CYSTATIN C ALIAS POST-GAMMA-GLOBULIN A MARKER FOR MULTIPLE SCLEROSIS" JOURNAL OF CLINICAL CHEMISTRY AND CLINICAL BIOCHEMISTRY, vol. 25, no. 9, 1987, pages 589-594, XP009003893 ISSN: 0340-076X abstract ---	1-39
X	MARIA ASSUNTA LAURENZI ET AL: "OLIGOCLONAL IGG AND FREE LIGHT CHAINS IN MULTIPLE SCLEROSIS DEMONSTRATED BY THIN-LAYER POLYACRYLAMIDE GEL ISOELECTRIC FOCUSING AND IMMUNOFIXATION" ANNALS OF NEUROLOGY, BOSTON, US, vol. 8, no. 3, September 1980 (1980-09), pages 241-247, XP001105807 ISSN: 0364-5134 the whole document ---	1-39
A	ROHLFF C: "PROTEOMICS IN MOLECULAR MEDICINE: APPLICATIONS IN CENTRAL NERVOUS SYSTEMS DISORDERS" ELECTROPHORESIS, WEINHEIM, DE, vol. 21, 2000, pages 1227-1234, XP000944098 ISSN: 0173-0835 the whole document --- -/--	1-39

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 02/00330

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PAGE M J ET AL: "Proteomics: a major new technology for the drug discovery process" DRUG DISCOVERY TODAY, ELSEVIER SCIENCE LTD, GB, vol. 4, no. 2, February 1999 (1999-02), pages 55-62, XP002217224 ISSN: 1359-6446 the whole document ---	1-39
A	WO 99 41612 A (JOHNSON PHILIP J ; OXFORD GLYCOSCIENCES UK LTD (GB); MOYSES CHRISTO) 19 August 1999 (1999-08-19) the whole document -----	1-39

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 02/00330

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:

Although claims 19-22, 26-31, 37 and 38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 II Observations where unity of invention is lacking (Continuation of item 2 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 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.:

1-39 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ 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:

Invention 1: 1-39 (partially)

Method for diagnosis of multiple sclerosis using the feature/isoform MSF-1/MSPI-1 as marker; antibodies against said marker and a kit comprising said antibodies; pharmaceutical composition comprising said marker or said antibodies; A method for screening for agents that interact with said marker; Use of said antibody, said marker or said modulating agent for treating multiple sclerosis.

Inventions 2-311: 1-39 (partially)

Method for diagnosis of multiple sclerosis using the features/isoforms MSF-2 to MSF-325/MSPI-2 to 325.2 as markers; antibodies against said markers and a kit comprising said antibodies; pharmaceutical composition comprising said markers or said antibodies; A method for screening for agents that interact with said markers; Use of said antibodies, said markers or said modulating agents for treating multiple sclerosis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 02/00330

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9941612	A	19-08-1999	
		AU 2534999 A	30-08-1999
		CA 2321160 A1	19-08-1999
		CN 1295668 T	16-05-2001
		EP 1055126 A1	29-11-2000
		WO 9941612 A1	19-08-1999
		HU 0101285 A2	28-08-2001
		JP 2002503813 T	05-02-2002
		PL 342365 A1	04-06-2001
		ZA 9901184 A	15-08-2000