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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 July 2002 (11.07.2002)

PCT

(10) International Publication Number
WO 02/054073 A3

(51) International Patent Classification[7]: G01N 33/569, C12R 1/32

(21) International Application Number: PCT/US02/00309

(22) International Filing Date: 7 January 2002 (07.01.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/260,348 8 January 2001 (08.01.2001) US
60/311,235 9 August 2001 (09.08.2001) US

(71) Applicant *(for all designated States except US)*: **THE GOVERNEMENT OF THE UNITED STATES OF AMERICA as represented by THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, CENTERS FOR DISEASE CONTROL AND PREVENTION** [US/US]; Technology Transfer Office, 4770 Buford Highway (K79), Atlanta, GA 30341 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **QUINN, Frederick, D.** [US/US]; 3243 Wiltshire Drive, Avondale Estates, GA 30002 (US). **BIRKNESS, Kristin, A.** [US/US]; 268 Eighth Street #7, Atlanta, GA 30309 (US). **DESLAURIERS, Manon** [CA/US]; 4006 Northlake Creek Court, Tucker, GA 30084 (US). **KING, Peter** [US/US]; 4709 Wood Creek Drive, Nacogdoches, TX 75961 (US). **BEALL, David, S.** [US/US]; 327 10th Street, Atlantic Beach, FL 32233 (US).

(74) Agent: **HARDING, Tanya, M.**; Klarquist, Sparkman, LLP, Suite 1600, One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).

(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, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, 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 (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
28 August 2003

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.

WO 02/054073 A3

(54) Title: LATENT HUMAN TUBERCULOSIS MODEL, DIAGNOSTIC ANTIGENS, AND METHODS OF USE

(57) Abstract: Provided herein is an *in vitro* granuloma model and methods of its use. Methods of detecting and/or diagnosing latent tuberculosis in a subject are also provided, as are latency-specific antigens (and antibodies thereto), such as α-crystallin, and methods of identifying and using such molecules. Also provided are immunostimulatory compositions, for instance for use in eliciting an immune response in a subject, such as an immune response to a latent tuberculosis infection. Kits for carrying out the provided methods are also described.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/00309

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/569 C12R1/32

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 C12R

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 29132 A (UNIV NEW YORK) 9 July 1998 (1998-07-09) claims 10,12,20	1,2,6
Y	claims 10,12,20 ---	1-13
X	WO 97 26007 A (BERNARDO JOHN ;UNIV BOSTON (US); RAINA JAWAHAR L (US); FENTON MATT) 24 July 1997 (1997-07-24) page 22, line 24 - line 25 ---	1,2
	-/--	

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

[X] 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	Date of mailing of the international search report
6 May 2003	06.06.03

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Cuendet, P

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WILKINSON R J ET AL: "Human T- and B-cell reactivity to the 16kDa alpha-crystallin protein of Mycobacterium tuberculosis." SCANDINAVIAN JOURNAL OF IMMUNOLOGY, vol. 48, no. 4, October 1998 (1998-10), pages 403-409, XP002217751 ISSN: 0300-9475 page 403, right-hand column -page 404, left-hand column, paragraph 1	7
Y	CUNNINGHAM ADAM F ET AL: "Mycobacterial stationary phase induced low oxygen tension: Cell wall thickening and localization of the 16-kilodalton alpha-crystallin homolog." JOURNAL OF BACTERIOLOGY, vol. 180, no. 4, February 1998 (1998-02), pages 801-808, XP002217752 ISSN: 0021-9193 abstract	1-13
X	page 801 page 807, paragraph 3	14-21, 31-33
X	WO 99 02670 A (BARRY CLIFTON E III ;CRANE DEBORAH (US); US HEALTH (US); YUAN YING) 21 January 1999 (1999-01-21) page 13, line 25 -page 14, line 5 page 20 -page 24	14-31
X	YUAN ET AL: "Stationary phase-associated protein expression in Mycobacterium tuberculosis: function of the mycobacterial alpha-crystallin homolog" JOURNAL OF BACTERIOLOGY, WASHINGTON, DC, US, vol. 178, no. 15, 1 August 1996 (1996-08-01), pages 4484-4492, XP002086106 ISSN: 0021-9193 page 4484, right-hand column, paragraph 1 page 4491, left-hand column, paragraph 2	14-31
X	WAYNE LAWRENCE G ET AL: "An in vitro model for sequential study of shiftdown of Mycobacterium tuberculosis through two stages of nonreplicating persistence." INFECTION AND IMMUNITY, vol. 64, no. 6, 1996, pages 2062-2069, XP002240188 ISSN: 0019-9567 cited in the application abstract	14-31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/00309

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 7-11 relate to Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy; nevertheless these claims were searched.

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:

1. [X] 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.

[ ] 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: 1-13

   detecting latent tuberculosis by use of latency-specific binding partners.

2. Claims: 14-33

   in vitro granuloma and its use for screening a tuberculosis drug.

INTERNATIONAL SEARCH REPORT

formation on patent family members

International Application No
PCT/US 02/00309

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9829132 A	09-07-1998	AU 746752 B2	02-05-2002
		AU 5905198 A	31-07-1998
		EP 0952849 A1	03-11-1999
		WO 9829132 A1	09-07-1998
WO 9726007 A	24-07-1997	AU 1750197 A	11-08-1997
		WO 9726007 A1	24-07-1997
WO 9902670 A	21-01-1999	AU 8296498 A	08-02-1999
		EP 0994944 A1	26-04-2000
		WO 9902670 A1	21-01-1999
		US 6403100 B1	11-06-2002