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

(19) World Intellectual Property Organization

1 October 2009 (01.10.2009)

International Bureau

(43) International Publication Date





(10) International Publication Number WO 2009/117791 A3

(51) International Patent Classification:

(21) International Application Number:

PCT/BE2009/000021

(22) International Filing Date:

C12Q 1/68 (2006.01)

30 March 2009 (30.03.2009)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/072,200 28 March 2008 (28.03.2008)

US

(71) Applicant (for all designated States except US):

KATHOLIEKE UNIVERSITEIT LEUVEN [BE/BE];

K.U. Leuven R&D, Minderbroedersstraat 8A - bus 5105,

B-3000 Leuven (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): RUTGEERTS, Paul [BE/BE]; Hertogenveld 3, B-3052 Blanden (BE). SCHUIT, Frans [BE/BE]; Dijlestraat 14, B-3140 Keerbergen (BE).

(74) Agent: KATHOLIEKE UNIVERSITEIT LEUVEN; K.U. Leuven R&D, Minderbroedersstraat 8A, bus 5105, B-3000 Leuven (BE).

(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, BR, BW, BY, BZ, CA, CH, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (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, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

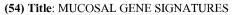
Declarations under Rule 4.17:

of inventorship (Rule 4.17(iv))

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))
- with sequence listing part of description (Rule 5.2(a))
- (88) Date of publication of the international search report: 14 April 2011





(57) Abstract: Infliximab (IFX) is effective treatment for Crohn's disease (CD) and ulcerative colitis (UC) not responding to standard therapy. 30-40% of patients do not improve and response is often incomplete. The aim of this study is to identify mucosal gene signatures predictive of response to EFX using high-density oligonucleotide arrays. Eight UC patients and 12 CD patients showed healing. In UC, only one probe set was differentially expressed in responders compared with non-responders, ie IL-13Ral-pha2. At PAM analysis 2 probe sets, representing IL-13Ralpha2 and IL-I I, separated IBD responders from non-responders with an overall misclassification error rate of 0.046 (2/43), with 100% sensitivity and 91.3 % specificity. The IL-13Ralpha2 probe set was a top-ranked probe set in all our analyses using both LIMMA and PAM strategies. Our gene array studies of mucosal biopsies identified IL-13Ralpha2 in IBD as a predictor of (non-)response to IFX.

INTERNATIONAL SEARCH REPORT

International application No PCT/BE2009/000021

A. CLASSIFICATION OF SUBJECT MATTER INV. C12Q1/68 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) C12Q

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, BIOSIS, MEDLINE, EMBASE, WPI Data

C. DOCUMI	ENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where appropriate, of t	he relevant passages	Relevant to claim No.	
Х	WO 2008/028044 A2 (CENTOCOR I XILIN [US]; SONG XIAO-YU [US] 6 March 2008 (2008-03-06) page 25 - pages 31,39; exampl	1-15		
A	WO 2004/107240 A1 (THIESEN HA [DE]; KEKOW JOERN [DE]; GUTHK [DE]; KOC) 9 December 2004 (2) the whole document	1-15		
A	WO 2007/135568 A2 (INST NAT SANTE RECH MED [FR]; SABLIER JEAN-PHILIPPE [FR]; DAVEAU MARYV) 29 November 2007 (2007-11-29) the whole document		1-15	
A	EP 1 172 444 A1 (CONARIS RES [DE]) 16 January 2002 (2002-0 the whole document		1-15	
X Furtl	her documents are listed in the continuation of Box C.	X See patent family annex.		
"A" docume consid "E" earlier of filing d "L" docume which citation "O" docume other r "P" docume	ategories of cited documents: ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international late ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or means ent published prior to the international filing date but the priority date claimed	"T" later document published after the interpriority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the coannot be considered novel or cannot involve an inventive step when the document of particular relevance; the coannot be considered to involve an involve and to comment is combined with one or moments, such combination being obvious in the art. "&" document member of the same patent the same pate	the application but cory underlying the laimed invention be considered to comment is taken alone laimed invention ventive step when the re other such docusts to a person skilled	
	actual completion of the international search	Date of mailing of the international sea	•	
8 February 2011		17/02/2011	17/02/2011	
Name and r	mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040,	Authorized officer Botz, Jürgen		

INTERNATIONAL SEARCH REPORT

International application No
PCT/BE2009/000021

0/0	POOLINE NEED TO BE BELEVANT		900021
C(Continua	•	I	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Rele	vant to claim No.
A	CHARLES P ET AL: "Regulation of cytokines, cytokine inhibitors, and acute-phase proteins following anti-TNF-alpha therapy in rheumatoid arthritis.", JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) 1 AUG 1999 LNKD- PUBMED:10415055, vol. 163, no. 3, 1 August 1999 (1999-08-01), pages 1521-1528, XP002620410, ISSN: 0022-1767 the whole document		1-15
X,P	ARIJS I ET AL: "Mucosal gene signatures to predict response to infliximab in patients with ulcerative colitis", GUT, vol. 58, no. 12, December 2009 (2009-12), pages 1612-1619, XP002620412, ISSN: 0017-5749 the whole document		1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/BE2009/000021

06-03-2008 09-12-2004	US AU	2009054253 A1 2003304165 A1	26-02-2009 21-01-2005
09-12-2004	AU	2003304165 A1	21-01-2005
29-11-2007	CA EP EP US	2652087 A1 1857559 A1 2019872 A2 2009252740 A1	29-11-2007 21-11-2007 04-02-2009 08-10-2009
16-01-2002	US	2003099943 A1	29-05-2003
	16-01-2002	US	US 2009252740 A1