

(10) International Publication Number
WO 2013/041846 A2(43) International Publication Date
28 March 2013 (28.03.2013)

(51) International Patent Classification:

A01K 67/027 (2006.01) *C07K 16/46* (2006.01)
C12N 15/85 (2006.01)

(21) International Application Number:

PCT/GB2012/052298

(22) International Filing Date:

18 September 2012 (18.09.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

1116122.1	19 September 2011 (19.09.2011)	GB
1116120.5	19 September 2011 (19.09.2011)	GB
1203257.9	24 February 2012 (24.02.2012)	GB
1204592.8	15 March 2012 (15.03.2012)	GB
1205702.2	29 March 2012 (29.03.2012)	GB
1208749.0	18 May 2012 (18.05.2012)	GB
1211692.7	2 July 2012 (02.07.2012)	GB

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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, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: MANIPULATION OF IMMUNOGLOBULIN GENE DIVERSITY AND MULTI-ANTIBODY THERAPEUTICS

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
142582	,IGHV1-69*01, H*0101	W	Q	L	V	Q	S	S	A	S	V	K	R	B	G	S	S	V	K	S	S	C	R	A	S		
217566	,IGHV1-69*02, J1086179071	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
599340	,IGHV1-69*03, S759A5	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
883130	,IGHV1-69*04, H*0201	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
867892	,IGHV1-69*05, H*0102	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
122583	,IGHV1-69*06, H*0103	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
828976	,IGHV1-69*07, H*0202	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
814939	,IGHV1-69*08	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
114301	,IGHV1-69*09	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
814370	,IGHV1-69*10	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
814376	,IGHV1-69*11	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
814384	,IGHV1-69*12	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
814214	,IGHV1-69*13	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Alignment of 13 IGHV1-69 alleles showing the variable (V) coding region only. Nucleotides that differ from VH1-69 allele *01 are indicated at the appropriate position whereas identical nucleotides are marked with a dash. Where nucleotide changes result in amino acid differences, the encoded amino acid is shown above the corresponding triplet. Boxed regions correspond to CDR1, CDR2 and CDR3 as indicated.

Figure 5 (part 1 of 4)

(57) Abstract: The invention provides improved non-human vertebrates and non-vertebrate cells capable of expressing antibodies comprising human variable region sequences. The present invention is directed to the provision of long HCDR3s from non-human vertebrates and cells. The present invention is also directed to the provision of novel V, D and J pairings in immunoglobulin heavy and light chain loci. Novel, biased antibody diversities and potentially expanded diversities are provided. The invention also provides for novel and potentially expanded diversity or diversity that is biased towards variable gene usage common to antibodies useful for treating and/or preventing certain diseases or conditions, such as infectious diseases. The invention also provides methods of generating antibodies using such vertebrates, as well as the antibodies per se, therapeutic compositions thereof and uses.



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