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[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	V	K	V	S	C	R	A	S			
217566	,IGHV1-69*02, J1086179071	C	N	S	T	S	C	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
599340	,IGHV1-69*03, S759A5																										
883130	,IGHV1-69*04, H*0201																										
867892	,IGHV1-69*05, H*0112																										
122583	,IGHV1-69*06, H*0101																										
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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