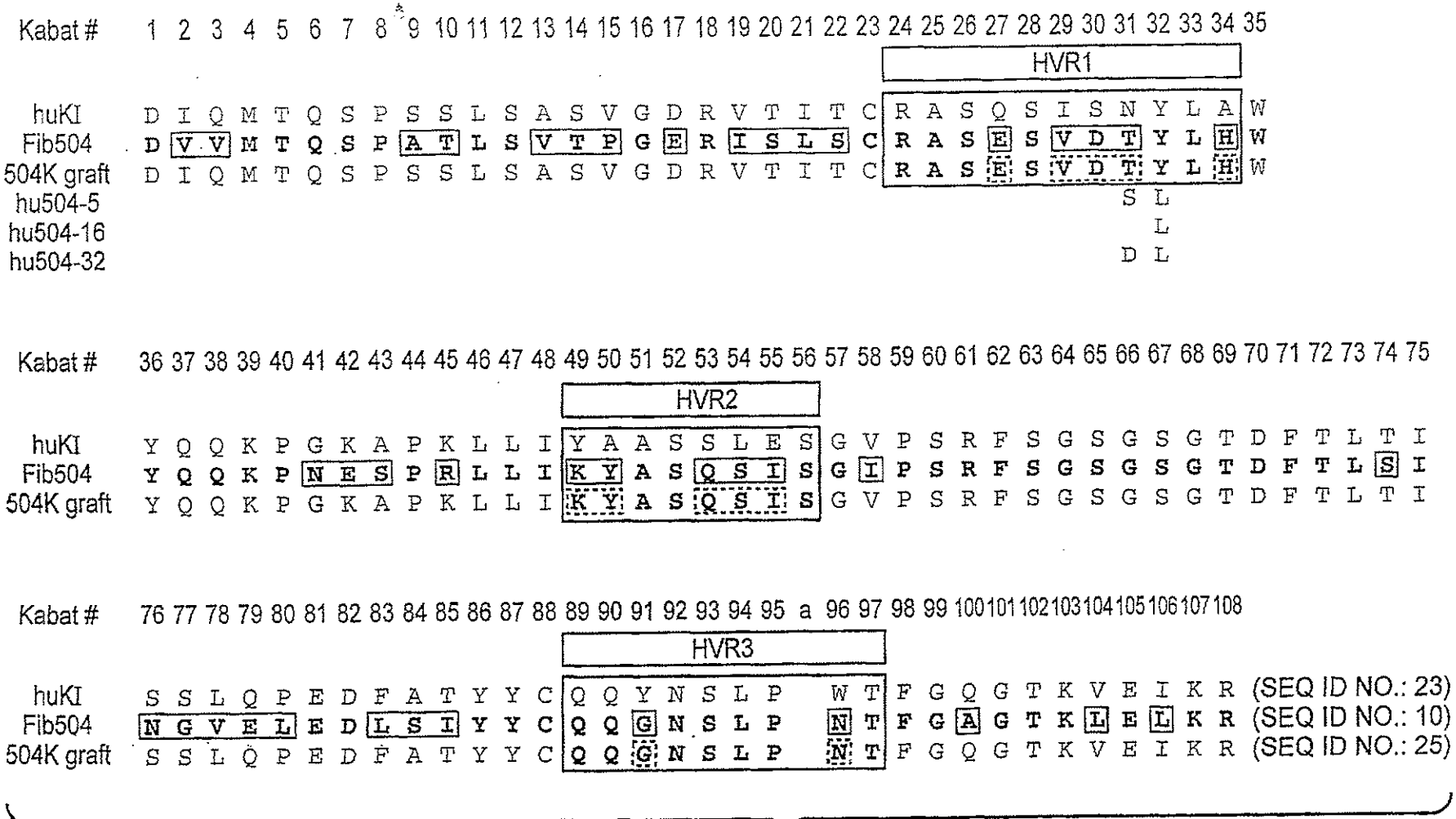

Kabat # 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35
HVR1
huKI D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q S I S N Y L A W
Fib504 D V V M T Q S P A T L S V T P G E R I S L S C R A S E S V D T Y L H W
504K graft D I Q M T Q S P S S L S A S V G D R V T I T C R A S E S V D T Y L H W
hu504-5 S L
hu504-16 L
hu504-32 D L
Kabat # 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75
HVR2
huKI Y Q Q K P G K A P K L L I Y A A S S L E S G V P S R F S G S G S G T D F T L T I
Fib504 Y Q Q K P N E S P R L L I K Y A S Q S I S G I P S R F S G S G S G T D F T L S I
504K graft Y Q Q K P G K A P K L L I K Y A S Q S I S G V P S R F S G S G S G T D F T L T I
Kabat # 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 a 96 97 98 99 100 101 102 103 104 105 106 107 108
HVR3
huKI S S L Q P E D F A T Y Y C Q Q Y N S L P W T F G Q G T K V E I K R (SEQ ID NO.: 23)
Fib504 N G V E L E D L S I Y Y C Q Q G N S L P N T F G A G T K L E L K R (SEQ ID NO.: 10)
504K graft S S L Q P E D F A T Y Y C Q Q G N S L P N T F G Q G T K V E I K R (SEQ ID NO.: 25)

FIG. 1A

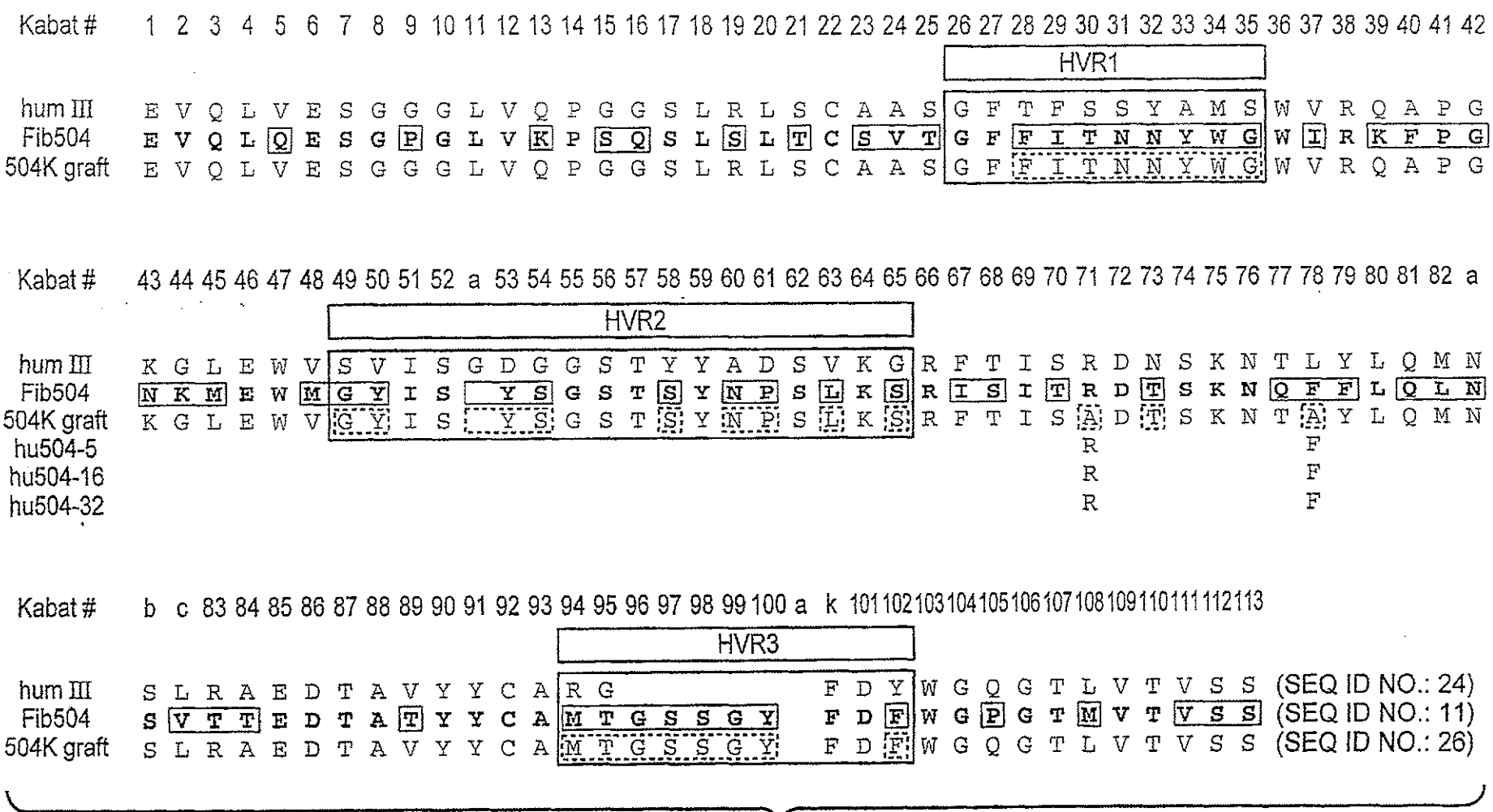

Kabat # 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42
HVR1
hum III E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S S Y A M S W V R Q A P G
Fib504 E V Q L Q E S G P G L V K P S Q S L S L T C S V T G F F I T N N Y W G W I R K F P G
504K graft E V Q L V E S G G G L V Q P G G S L R L S C A A S G F F I T N N Y W G W V R Q A P G
Kabat # 43 44 45 46 47 48 49 50 51 52 a 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 a
HVR2
hum III K G L E W V S V I S G D G G S T Y Y A D S V K G R F T I S R D N S K N T L Y L Q M N
Fib504 N K M E W M G Y I S Y S G S T S Y N P S L K S R I S I T R D T S K N Q F F L Q L N
504K graft K G L E W V G Y I S Y S G S T S Y N P S L K S R F T I S A D T S K N T A Y L Q M N
hu504-5 R F
hu504-16 R F
hu504-32 R F
Kabat # b c 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 a k 101 102 103 104 105 106 107 108 109 110 111 112 113
HVR3
hum III S L R A E D T A V Y Y C A R G F D Y W G Q G T L V T V S S (SEQ ID NO.: 24)
Fib504 S V T T E D T A T Y Y C A M T G S S G Y F D F W G P G T M V T V S S (SEQ ID NO.: 11)
504K graft S L R A E D T A V Y Y C A M T G S S G Y F D F W G Q G T L V T V S S (SEQ ID NO.: 26)

FIG. 1B

Humanized Variants of Fib504

HVR-L1 and L2 Substitutions, Fib504•K RF Framework	L1										L2								BIAcore Affinity Assay (nM)
504K-RF Residues	R	A	S	E	S	V	D	T	Y	L	H	K	Y	A	S	Q	S	I	S	11
Variant																				
68	R	A	S	E	S	V	D	T	I	L	H	K	Y	A	S	Q	S	I	S	
74	R	A	S	E	S	V	D	D	L	V	H	K	Y	A	S	Q	S	I	S	
504-32	R	A	S	E	S	V	D	D	L	L	H	K	Y	A	S	Q	S	I	S	3.5
51	R	A	S	E	S	V	D	N	L	L	H	K	Y	A	S	Q	S	I	S	
59	R	A	S	E	S	V	D	P	L	L	H	K	Y	A	S	Q	R	T	S	
504-5	R	A	S	E	S	V	D	S	L	L	H	K	Y	A	S	Q	S	I	S	9
60	R	S	S	D	S	V	D	S	L	V	H	K	Y	A	S	Q	S	I	S	
96	R	A	S	E	D	V	D	T	L	L	H	K	Y	A	S	Q	S	I	S	
83	R	A	S	E	N	V	D	T	L	L	H	K	Y	A	S	Q	S	I	S	
504-16 (8)	R	A	S	E	S	V	D	T	L	L	H	K	Y	A	S	Q	S	I	S	23.4
504-RF (29)	R	A	S	E	S	V	D	T	Y	L	H	K	Y	A	S	Q	S	I	S	132

FIG. 1C

Human Consensus

Light Chain (kappa I)

DIQMTQSPSSLSASVGDRVTITCRASQSISNYLAWYQQKPGKAPKLLIYAASSLES
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSLPWTFGQGTKVEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS
KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 27)

FIG. 2A

Human Consensus

Heavy Chain (subgroup III)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSVISGDGG
STYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAMTGSSGYFDFWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV
HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKT
ISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 28)

FIG. 2B

Fib504 Graft

Light Chain

DIQMTQSPSSLSASVGDRVTITCRASESVDTYLHWYQQKPGKAPKLLIYYASQSIS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGNSLPNTFGQGTKVEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS
KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 29)

FIG. 3A

Fib504 Graft

Heavy Chain

EVQLVESGGGLVQPGGSLRLSCAASGFFITNNYWGWVRQAPGKGLEWVGYISYSGS
TSYNPSLKSRFTISADTSKNTAYLQMNSLRAEDTAVYYCAMTGSSGYFDFWGQGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 30)

FIG. 3B

Fib504K Graft

Light Chain

DIQMTQSPSSLSASVGDRVTITCRASESVDTYLHWYQQKPGKAPKLLIKYASQSIS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGNSLPNTFGQGTKVEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS
KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 31)

FIG. 4A

Fib504K Graft

Heavy Chain

EVQLVESGGGLVQPGGSLRLSCAASGFFITNNYWGWVRQAPGKGLEWVGYISYSGS
TSYNPSLKSRFTISADTSKNTAYLQMNSLRAEDTAVYYCAMTGSSGYFDFWGQGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 30)

FIG. 4B

Fib504K-RF Graft

Light Chain

DIQMTQSPSSLSASVGDRVTITCRASESVDTYLHWYQQKPGKAPKLLIKYASQSIS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGNSLPNTFGQGTKVEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS
KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 31)

FIG. 5A

Fib504K-RF Graft

Heavy Chain

EVQLVESGGGLVQPGGSLRLSCAASGFFITNNYWGWVRQAPGKGLEWVGYISYSGS
TSYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCAMTGSSGYFDFWGQGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 32)

FIG. 5B

Humanized Variant 504.32

Light Chain

DIQMTQSPSSLSASVGDRVTITCRASESVDDLLHWYQQKPGKAPKLLIKYASQSIS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGNSLPNTFGQGTKVEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS
KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 33)

FIG. 6A

Humanized Variant 504.32

Heavy Chain

EVQLVESGGGLVQPGGSLRLSCAASGFFITNNYWGWVRQAPGKGLEWVGYISYSGS
TSYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCAMTGSSGYFDFWGQGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 32)

FIG. 6B

Rat Anti-Mouse Fib504 Variable Domains

Variable Light Chain

DVVMTQSPATLSVTPGERISLSCRASESVDTYLHWYQQKPNESPRLLIKYASQSIS
GIPSRFSGSGSGTDFTLSINGVELEDLSIYYCQQGNSLPNTFGAGTKLELKRADAA
PTVSIFPPSMEQLTSGGATVVCFVNNFYPRDISVKWKIDGSEQRDGVLDSVTDQDS
KDSTYS (SEQ ID NO: 12)

FIG. 9A

Rat Anti-mouse Fib504 Variable Domains

Variable Heavy Chain

EVQLQESGPGLVKPSQSLSLTCSVTGFFITNNYWGWIRKFPGNKMEWMGYISYSGS
TSYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYYCAMTGSSGYFDFWGPGTM
VTVSSAETTAPSVYPLAPGTALKSNSMVTLGCLV (SEQ ID NO: 13)

FIG. 9B

kv1 Z DIQMTQSPSSLSASVGDRVTITC -L1- WYQQKPGKAPKLLIY -L2- GVPSRFSGSGSGTDFTLTISSLQP

kv1 X DIQMTQSPSSLSASVGDRVTITC -L1- WYQQKPGKAPKLLI -L2- GVPSRFSGSGSGTDFTLTISSLQP

kv2 DIVMTQSPLSLPVTPGEPASISC -L1- WYLQKPGQSPQLLIY -L2- GVPDRFSGSGSGTDFTLKISRVEA

kv3 EIVLTQSPGTLSLSPGERATLSC -L1- WYQQKPGQAPRLLIY -L2- GIPDRFSGSGSGTDFTLTISRLEP

kv4 DIVMTQSPDSLAVSLGERATINC -L1- WYQQKPGQPPKLLIY -L2- GVPDRFSGSGSGTDFTLTISSLQA

FIG. 7A

kv1 Z EDFATYYC -L3- FGQGTKVEIK SEQ ID NO.: 14

kv1 X EDFATYYC -L3- FGQGTKVEIK SEQ ID NO.: 15

kv2 EDVGVYYC -L3- FGQGTKVEIK SEQ ID NO.: 16

kv3 EDFAVYYC -L3- FGQGTKVEIK SEQ ID NO.: 17

kv4 EDVAVYYC -L3- FGQGTKVEIK SEQ ID NO.: 18

FIG. 7B

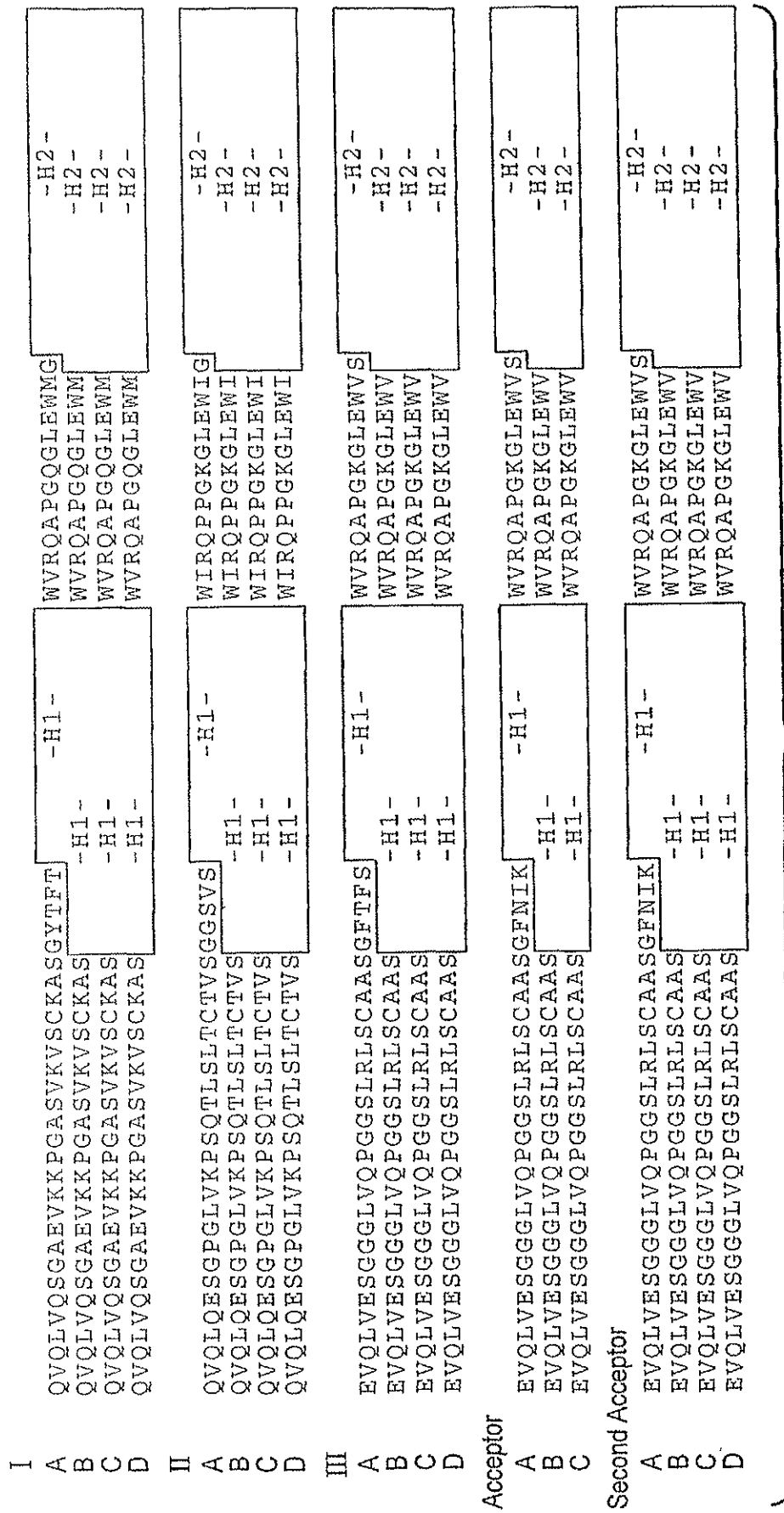

I
A QVQLVQSGAEVKKPGASVKVSCKASGYTFT -H1- WVRQAPGQGLEWMG -H2-
B QVQLVQSGAEVKKPGASVKVSCKAS -H1- WVRQAPGQGLEWM -H2-
C QVQLVQSGAEVKKPGASVKVSCKAS -H1- WVRQAPGQGLEWM -H2-
D QVQLVQSGAEVKKPGASVKVSCKAS -H1- WVRQAPGQGLEWM -H2-
II
A QVQLQESGPGLVKPSQTLSLTCTVSGGSVS -H1- WIRQPPGKGLEWIG -H2-
B QVQLQESGPGLVKPSQTLSLTCTVS -H1- WIRQPPGKGLEWI -H2-
C QVQLQESGPGLVKPSQTLSLTCTVS -H1- WIRQPPGKGLEWI -H2-
D QVQLQESGPGLVKPSQTLSLTCTVS -H1- WIRQPPGKGLEWI -H2-
III
A EVQLVESGGGLVQPGGSLRLSCAASGFTFS -H1- WVRQAPGKGLEWVS -H2-
B EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
C EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
D EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
Acceptor
A EVQLVESGGGLVQPGGSLRLSCAASGFNIK -H1- WVRQAPGKGLEWVS -H2-
B EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
C EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
Second Acceptor
A EVQLVESGGGLVQPGGSLRLSCAASGFNIK -H1- WVRQAPGKGLEWVS -H2-
B EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
C EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
D EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-

FIG. 8A

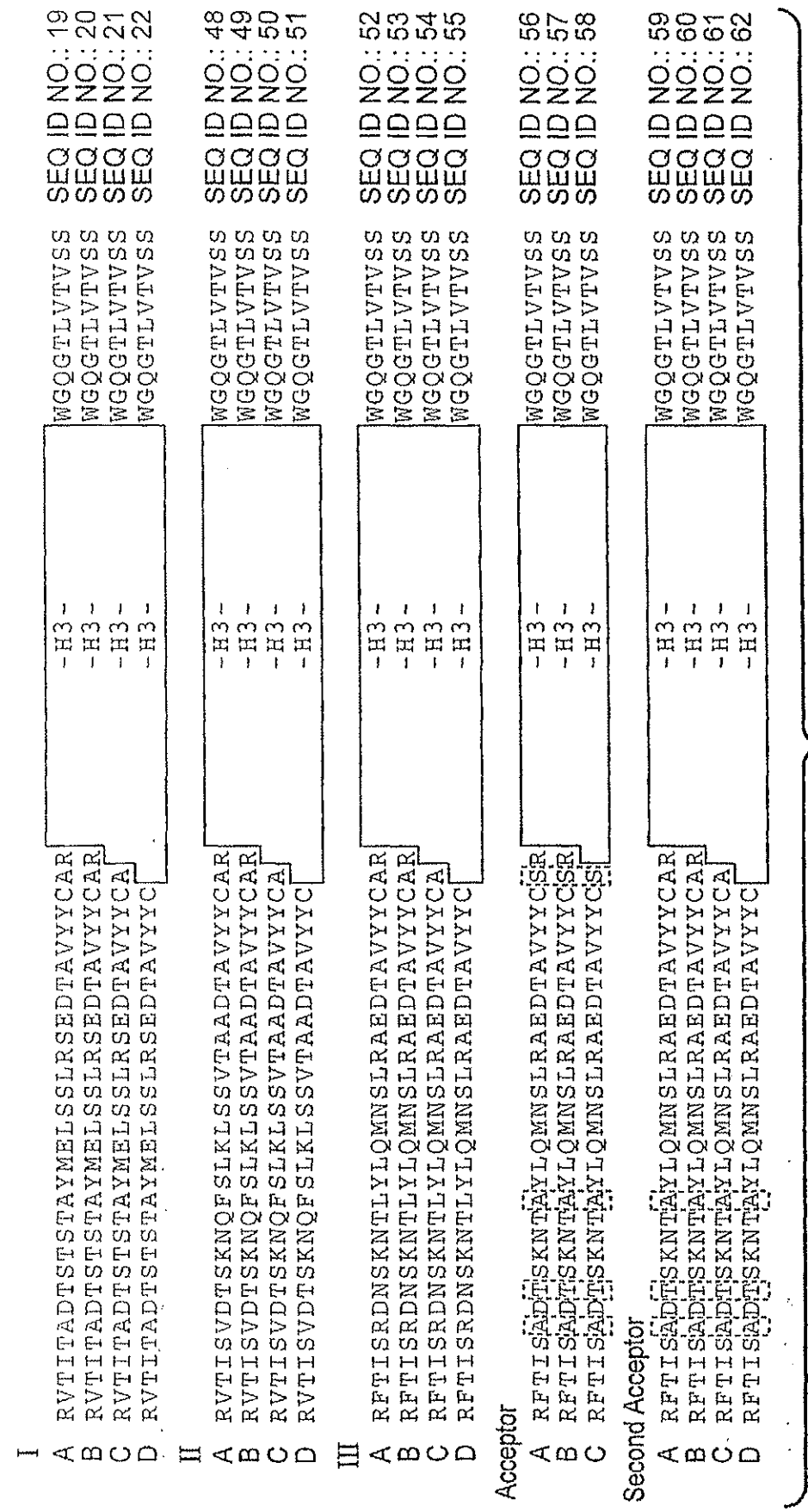

I
A RVTITADTSTSTAYMELSSLRSEDTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 19
B RVTITADTSTSTAYMELSSLRSEDTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 20
C RVTITADTSTSTAYMELSSLRSEDTAVYYCA -H3- WGQGTLVTVSS SEQ ID NO.: 21
D RVTITADTSTSTAYMELSSLRSEDTAVYYC -H3- WGQGTLVTVSS SEQ ID NO.: 22
II
A RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 48
B RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 49
C RVTISVDTSKNQFSLKLSSVTAADTAVYYCA -H3- WGQGTLVTVSS SEQ ID NO.: 50
D RVTISVDTSKNQFSLKLSSVTAADTAVYYC -H3- WGQGTLVTVSS SEQ ID NO.: 51
III
A RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 52
B RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 53
C RFTISRDNSKNTLYLQMNSLRAEDTAVYYCA -H3- WGQGTLVTVSS SEQ ID NO.: 54
D RFTISRDNSKNTLYLQMNSLRAEDTAVYYC -H3- WGQGTLVTVSS SEQ ID NO.: 55
Acceptor
A RFTISADTSKNTAYLQMNSLRAEDTAVYYCSR -H3- WGQGTLVTVSS SEQ ID NO.: 56
B RFTISADTSKNTAYLQMNSLRAEDTAVYYCSR -H3- WGQGTLVTVSS SEQ ID NO.: 57
C RFTISADTSKNTAYLQMNSLRAEDTAVYYCS -H3- WGQGTLVTVSS SEQ ID NO.: 58
Second Acceptor
A RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 59
B RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS SEQ ID NO.: 60
C RFTISADTSKNTAYLQMNSLRAEDTAVYYCA -H3- WGQGTLVTVSS SEQ ID NO.: 61
D RFTISADTSKNTAYLQMNSLRAEDTAVYYC -H3- WGQGTLVTVSS SEQ ID NO.: 62

FIG. 8B

Comparison of VH Framework Sequences

	Framework Region H3							
	71	72	73	74	75	76	77	78
hu subgroup I	A	D	T	S	T	S	T	A
hu subgroup II	V	D	T	S	K	N	Q	F
hu subgroup III	R	D	N	S	K	N	T	L
Herceptin	A	D	T	S	K	N	T	A
Fib504	R	D	T	S	K	N	Q	F
Fib504-RL	R	D	T	S	K	N	T	L
Fib404-RF	R	D	T	S	K	N	T	F

FIG. 10A

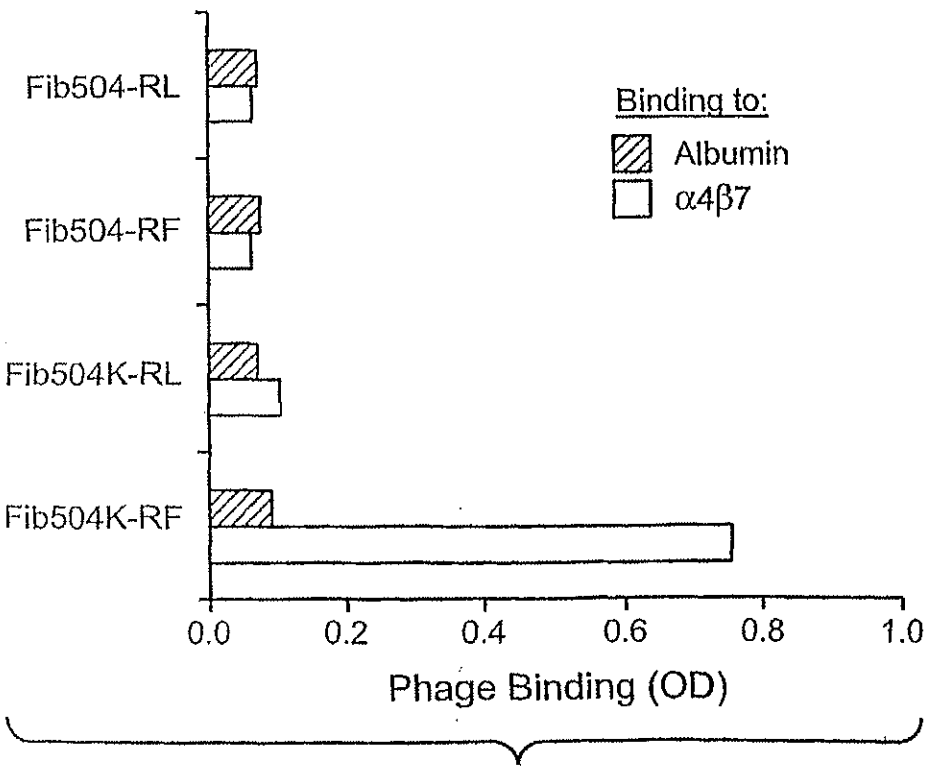


FIG. 10B

FIG. 11A

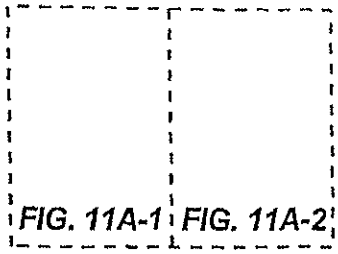


FIG. 11A-1

		504.16	Human Consensus	Codon	Amino Acids Encoded	Amino Acids Observed				
HVR-L1		R	R							
	25	A	A							
		S	S							
	27	E	Q	SAA	EQ	E	Q			
		S	S							
	29	V	I	RTT	VI	V	I			
		D	S	KMT	DSAY	D	S	A		
	31	T	N	RAC	DN	D	N			
		L	Y	YWC	LYFH	L				
	33	L	L							
		H	A	SMC	HADP	H				
HVR-L2	49	K	Y	WAW	KYNZ	K	N			
		Y	A	KMC	YADS	Y				
	51	A	A							
		S	S							
	53	Q	S	YMG	QSPZ	Q	S			
		S	L	TYG	SL	S	L			
	55	I	E	RWA	IEKV	I	E	K	V	
		S	S							
HVR-L3	89	Q	Q							
		Q	Q							
	91	G	Y	KRT	GYDC	G				
		N	N							
	93	S	S							
		L	L							
	95	P	P							
		N	W	WRS	NWYRSZ	N	W	Y	R	S
	97	T	T							

NOTE: Z is a stop codon. The most frequently observed amino acid is boxed.

		504.16	Human Consensus	Codon	Amino Acids Encoded	Amino Acids Observed				
HVR-H1	26	G	G							
		F	F							
	28	F	T	WYC	F I T S	F				
		I	F	WTC	I F	I				
	30	T	S	ASC	T S	T				
		N	S	ARC	N S	N				
	32	N	Y	WAC	N Y	N				
		Y	A	KMT	Y A D S	Y				
	34	W	M	WKG	W M R L	W				
		G	S	RGC	G S	G				
HVR-H2	49	G	S	RGC	G S	G				
		Y	V	KWT	Y V D F	Y	V	D	F	
	51	I	I							
		S	S							
	53	Y	G	KRT	Y G C D	Y				
		S	G	RGC	S G	S	G			
	55	G	G							
		S	S							
	57	T	T							
		S	Y	TMT	S Y	S	Y			
	59	Y	Y							
		N	A	RMC	N A D T	N	A	D	T	
	61	P	D	SMT	P D A H	P	D	A	H	
		S	S							
	63	L	V	STG	L V	L	V			
		K	K							
	65	S	G	RGC	S G	S	G			
HVR-H3	93	A	A							
		M	R	AKG	M R	M				
	95	T	G	RSC	T G A S	T				
		G								
	97	S								
		S								
	99	G								
		Y								
		F	F							
	101	D	D							
		F	Y	TWC	F Y	F	Y			

FIG. 11A-2

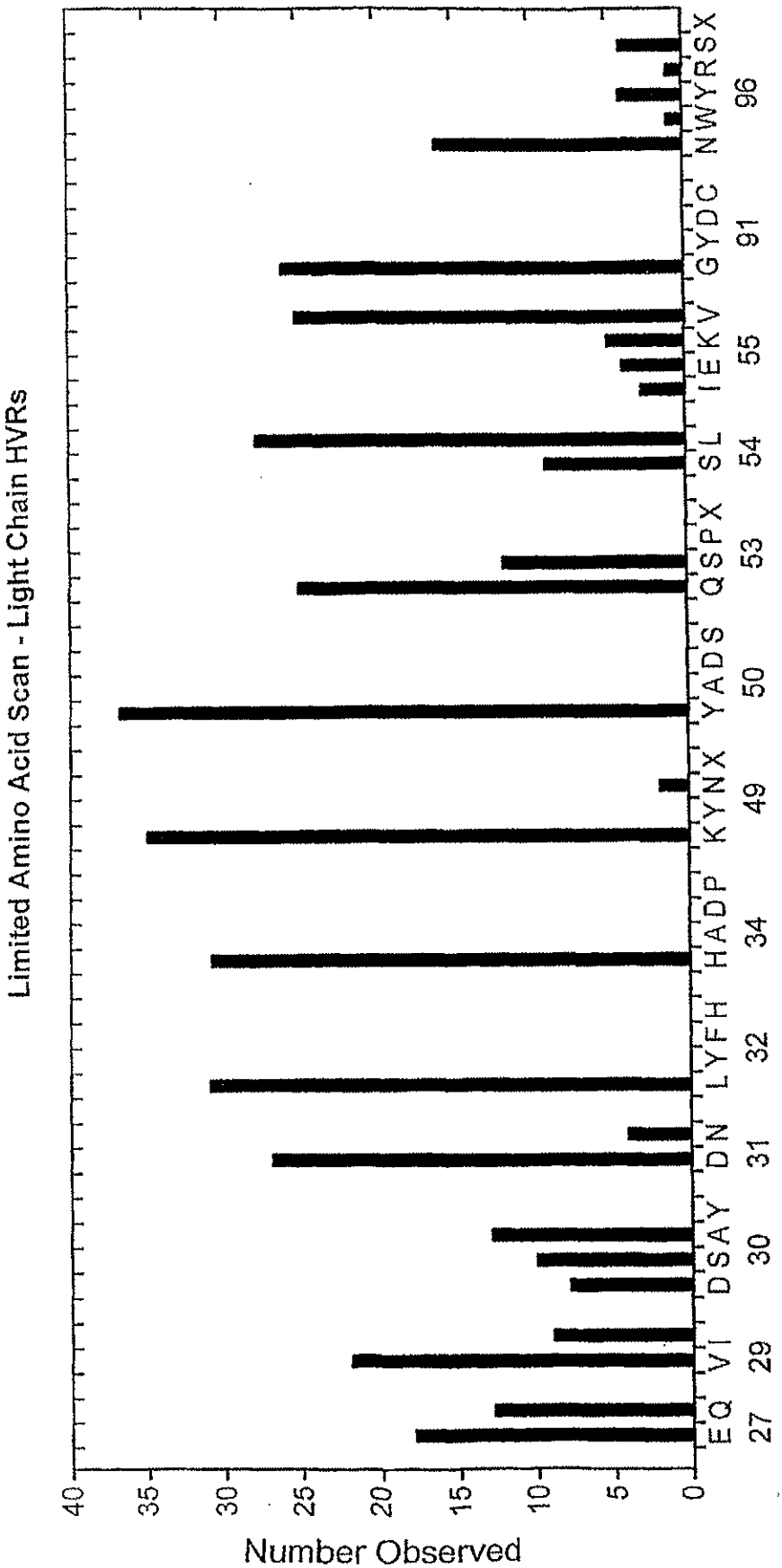

Limited Amino Acid Scan - Light Chain HVRs
Number Observed
0
5
10
15
20
25
30
35
40
EQ VI DSAY DN LYFH HADP KYNX YADS QSPX SL IEKV GYDC NWYRSX
27 29 30 31 32 34 49 50 53 54 55 91 96

FIG. 11B

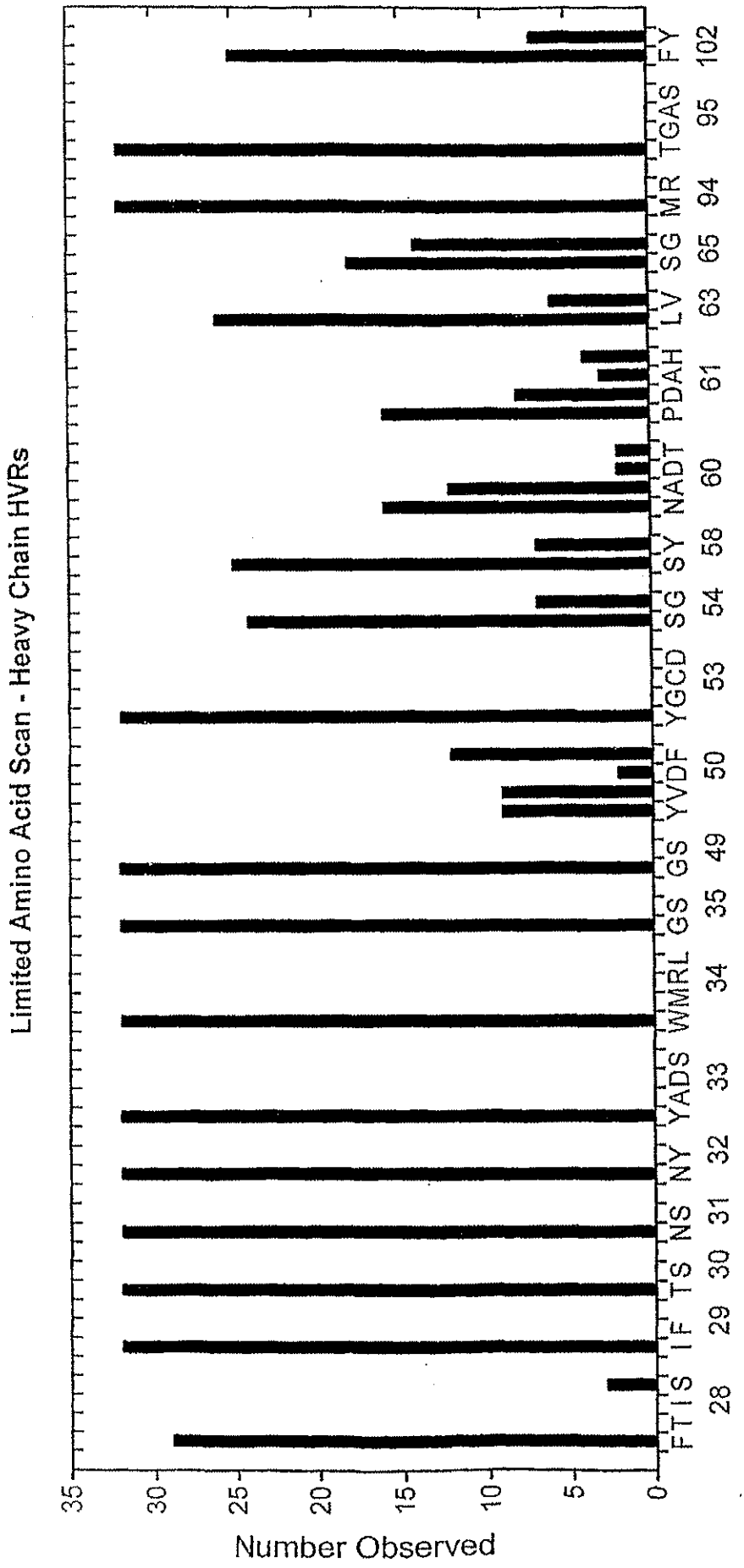

Limited Amino Acid Scan - Heavy Chain HVRs
Number Observed
0
5
10
15
20
25
30
35
FT 28
IS
IF 29
TS 30
NS 31
NY 32
YADS 33
WMRL 34
GS 35
GS 49
YVDF 50
YGCD 53
SG 54
SY 58
NADT 60
PDAH 61
LV 63
SG 65
MR 94
TGAS 95
FY 102

FIG. 11C

	Amino Acid Position	Amino Acid — Number of Times Observed												
HVR-L1	A25	**A 64**	G 2	S 11	T 7	Y 9								
	S26	G 4	I 2	K 3	N 8	P 1	Q 1	R 7	**S 61**	T 6				
	E27	A 6	D 8	**E 60**	G 2	H 1	I 1	K 4	L 1	N 2	Q 5	R 1	V 2	
	S28	A 1	D 1	G 7	H 1	I 1	K 1	N 9	P 3	R 7	**S 56**	T 4	V 1	Y 1
	V29	A 11	G 6	I 3	K 1	L 9	M 6	Q 1	R 1	**V 55**				
	D30	A 3	**D 59**	E 9	G 3	H 3	I 1	K 1	L 1	N 6	P 1	S 1	T 2	V 3
	D31	**D 77**	E 13	G 2	N 1									
	L32	I 1	**L 88**	M 4										
	L33	A 1	I 5	**L 64**	M 1	V 22								
	H34	F 1	**H 87**	Y 4	S 1									
HVR-L3	N96	A 2	F 6	H 1	I 3	**L 47**	M 3	N 2	R 2	S 2	T 4	V 2	W 16	Y 3
HVR-H3	M94	A 1	E 3	G 1	**M 48**	Q 10	R 24	S 8						

NOTE: The most frequently observed amino acid is boxed.

FIG. 12

FIG. 13

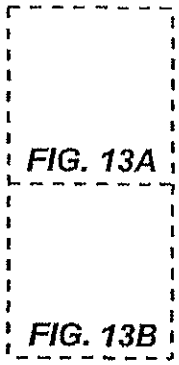


FIG. 13A

		All Observed Changes Rat Fib504	Human Consensus	All Observed Amino Acids	Limited Scan	Amino Acids Observed Broad Scan	Soft Random (Changes to 504)
CDR-L1		R	R				
	25	A	A	AGSTV		AGSTV	S
		S	S	GIKNPQRST		GIKNPQRST	
	27	E	Q	ADEGHIKLNQRV	EQ	ADEGHIKLNQRV	D
		S	S	ADGHIKNPRSTVY		ADGHIKNPRSTVY	DN
	29	V	I	AGIKLMQRV	VI	AGIKLMQRV	
		D	S	ADEGHIKLNPSTV	DSA	ADEGHIKLNPSTV	
	31	T	N	DEGNSP	DN	DEGN	SPND
		Y	Y	ILM	L	ILM	IL
	33	L	L	AILMV		AILMV	V
		H	A	FHYS	H	FHYS	
CDR-L2	49	K	Y	KN	KN		
		Y	A	Y	Y		
	51	A	A				
		S	S				
	53	Q	S	QS	QS		
		S	L	SLR	SL		R
	55	I	E	EIKTV	IEKV		T
		S	S				
CDR-L3	89	Q	Q				
		Q	Q				
	91	G	Y	G	G		
		N	N				
	93	S	S				
		L	L				
	95	P	P				
		N	W	AFHILMNRSTVWY	NWYRS	AFHILMNRSTVWY	
	97	T	T				

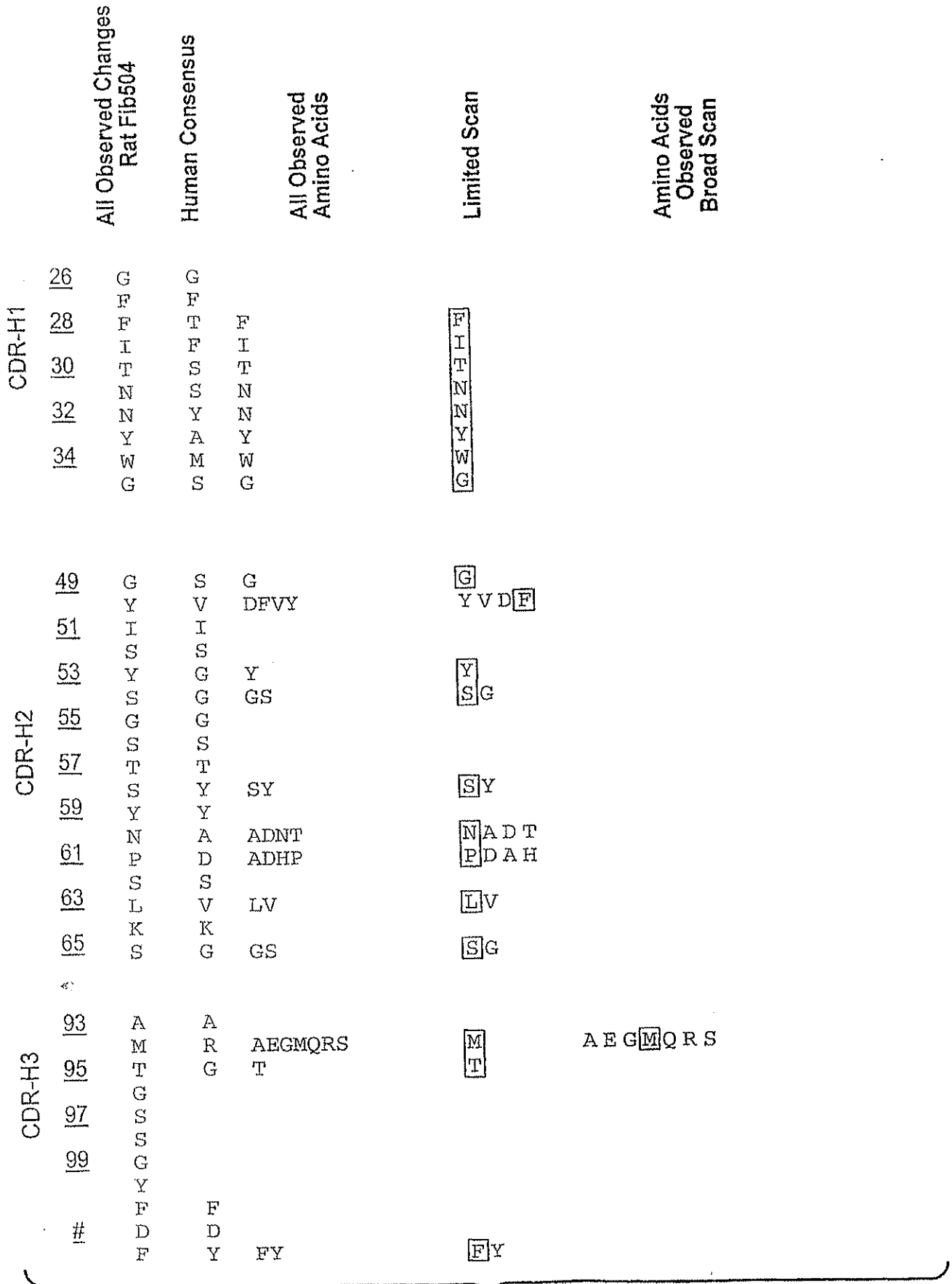

All Observed Changes Rat Fib504
Human Consensus
All Observed Amino Acids
Limited Scan
Amino Acids Observed Broad Scan
CDR-H1
CDR-H2
CDR-H3
26
28
30
32
34
49
51
53
55
57
59
61
63
65
93
95
97
99
#

FIG. 13B

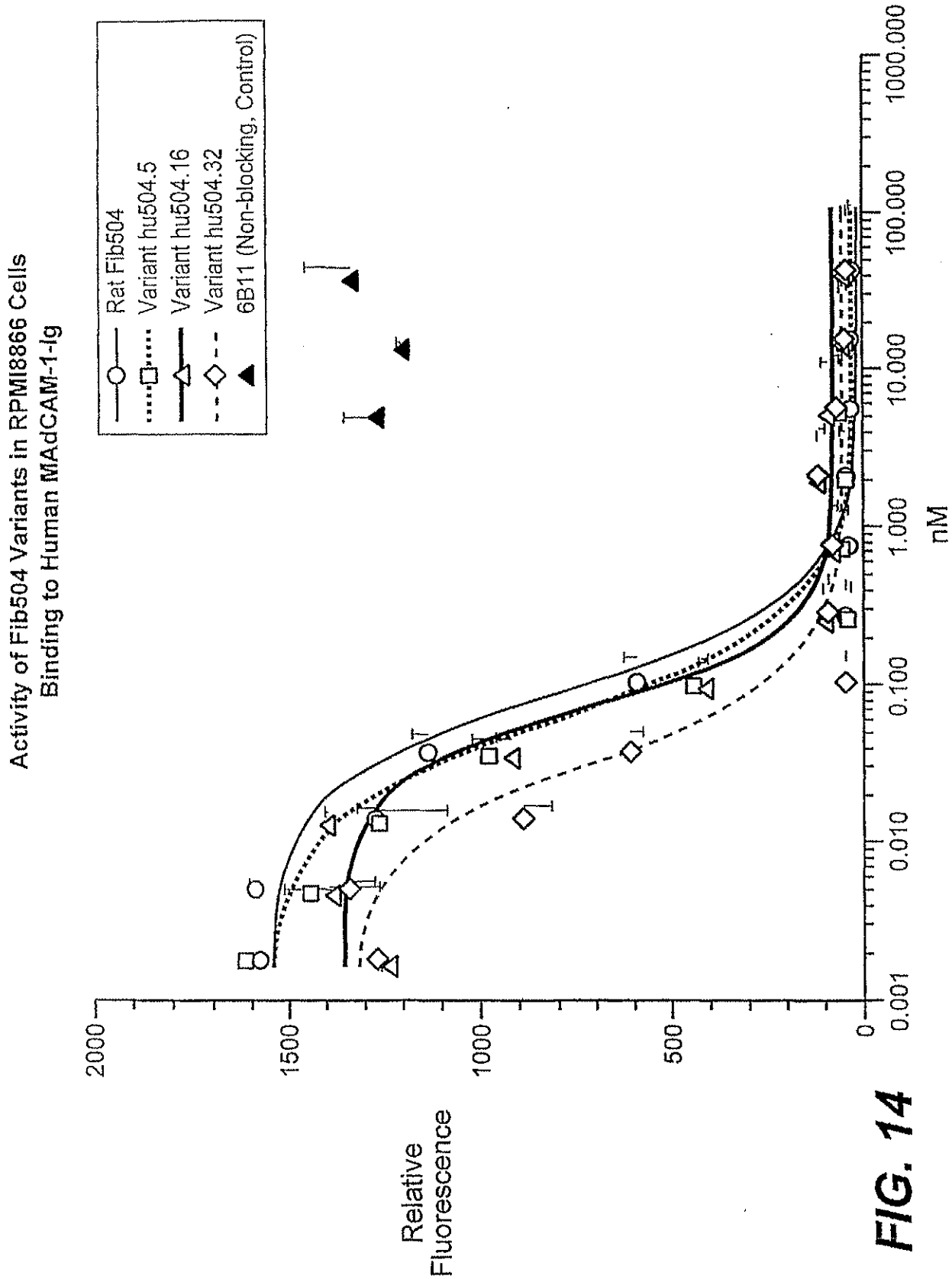

Activity of Fib504 Variants in RPMI8866 Cells
Binding to Human MAdCAM-1-Ig
Rat Fib504
Variant hu504.5
Variant hu504.16
Variant hu504.32
6B11 (Non-blocking, Control)
Relative Fluorescence
2000
1500
1000
500
0
0.001
0.010
0.100
1.000
10.000
100.000
1000.000
nM

FIG. 14

FIG. 15

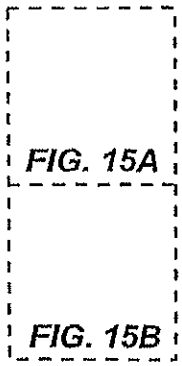


FIG. 15A

	Position		504.32R	Amino Acid Substitutions
	Kabat #	Relative #	Amino Acid	
HVR-L1	24	A1	R	
	25	A2	A	G S T V
	26	A3	S	G I K N P Q R T
	27	A4	E	V Q A D G H I K L N R
	28	A5	S	Y A D G H I K N P R T V
	29	A6	V	R I A G K L M Q
	30	A7	D	V S A E G H I K L N P S T
	31	A8	D	G N E T P S
	32	A9	L	Y I M
	33	A10	L	A I M V
	34	A11	H	Y F S
HVR-L2	49	B1	K	Y N
	50	B2	Y	
	51	B3	A	
	52	B4	S	D
	53	B5	Q	S
	54	B6	S	D L R
	55	B7	I	V E K T
	56	B8	S	
HVR-L3	89	C1	Q	
	90	C2	Q	
	91	C3	G	
	92	C4	N	
	93	C5	S	
	94	C6	L	
	95	C7	P	
	96	C8	N	V W Y R S T A F H I L M
	97	C9	T	

	Position		504.32R	Amino Acid Substitutions
	Kabat #	Relative #	Amino Acid	
HVR-H1	26	D1	G	
	27	D2	F	
	28	D3	F	
	29	D4	I	
	30	D5	T	
	31	D6	N	
	32	D7	N	
	33	D8	Y	
	34	D9	W	
	35	D10	G	
HVR-H2	49	E1	G	
	50	E2	Y	FVD
	51	E3	I	
	52	E4	S	
	53	E5	Y	
	54	E6	S	G
	55	E7	G	
	56	E8	S	
	57	E9	T	
	58	E10	S	Y
	59	E11	Y	
	60	E12	N	TAD
	61	E13	P	HDA
	62	E14	S	
	63	E15	L	V
	64	E16	K	
	65	E17	S	G
HVR-H3	93	F1	A	
	94	F2	R	MAEGQS
	95	F3	T	
	96	F4	G	
	97	F5	S	
	98	F6	S	
	99	F7	G	
	100	F8	Y	
	k	F9	F	
	101	F10	D	
	102	F11	F	Y
Heavy Chain FR3	71		R	AT
	73		T	N
	78		F	AFL

FIG. 15B

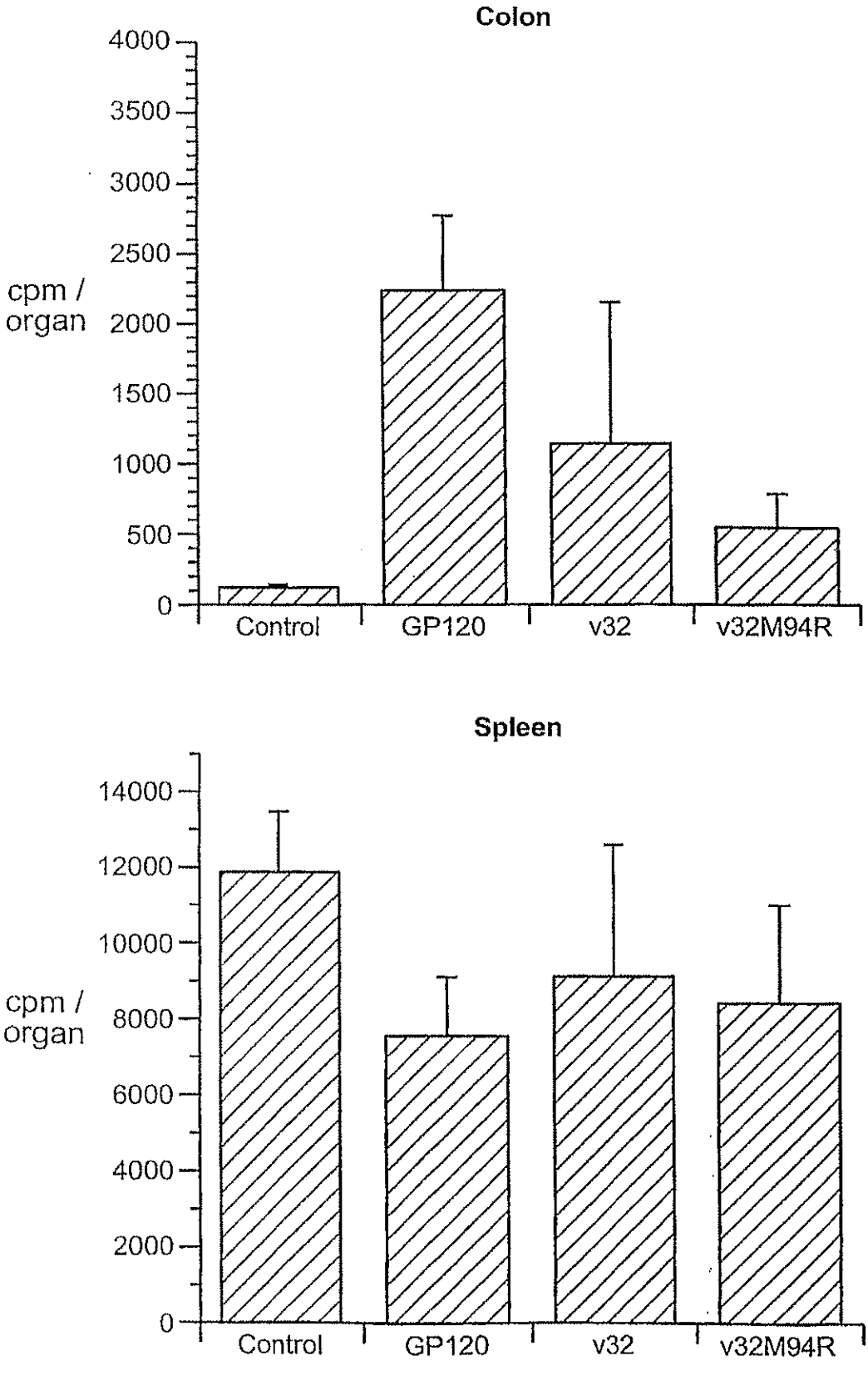

Colon
4000
3500
3000
2500
2000
1500
1000
500
0
cpm / organ
Control
GP120
v32
v32M94R
Spleen
14000
12000
10000
8000
6000
4000
2000
0
cpm / organ
Control
GP120
v32
v32M94R

FIG. 16