Figure 1

Study Design

Groups (n=6)

G1: Vehicle (A5Su buffer)

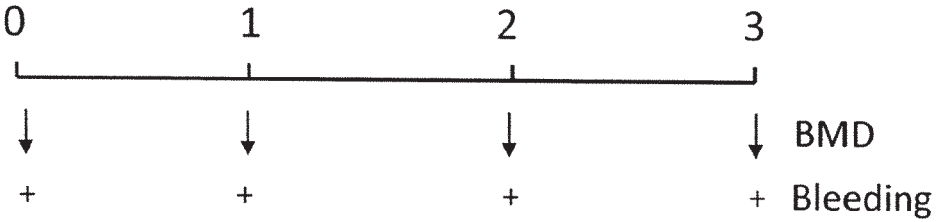
G2: huDVD Ig

G3: Ab5 (sclerostin antibody)

G4: Hetero Ig –1 (Ab23-6.147)

G5: Hetero Ig –2 (Ab5-6.37.5)

G6: Hetero Ig –3 (7Ab5-6.147)



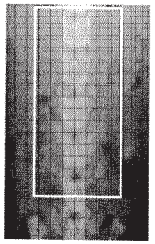
- S.C. injection twice per week
- Dose: 12.5 mg/kg, 2x a week

- 10 week old male B6D2F1 mice
- Primary endpoints: in vivo DXA scan at BL, then weekly

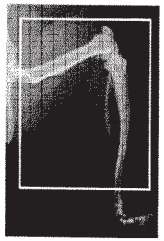
Figure 2

Hetero-Ig Increased bone mass in Lumbar Vertebrae and Leg (at week 3)

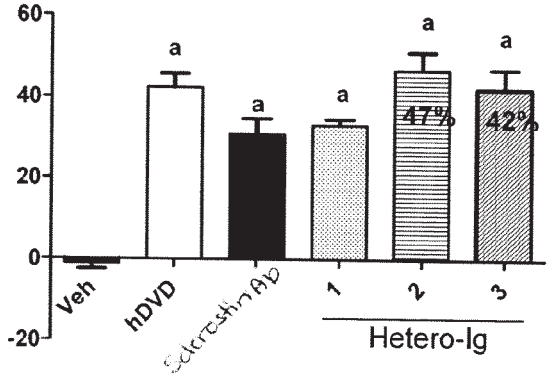
In vivo DXA

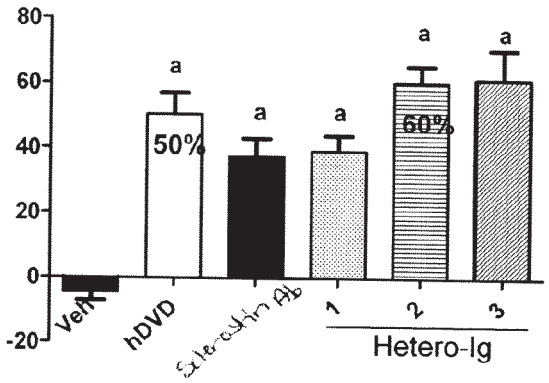


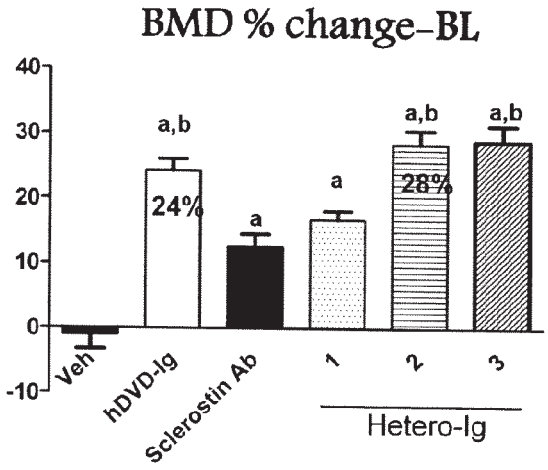
LV1-5

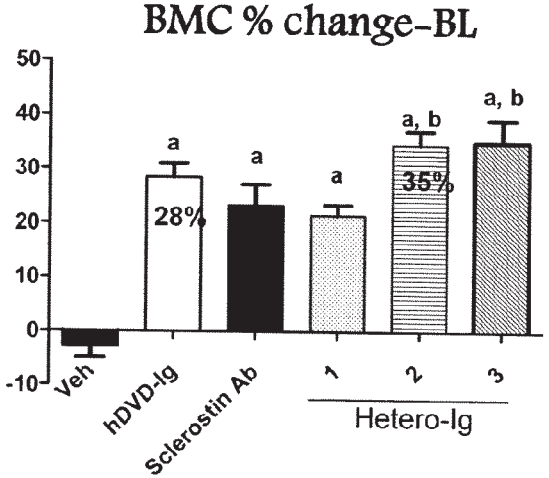


Femur-Tibia









[a] p<0.05 vs. Vehicle
[b] p<0.05 vs Sclerostin ab

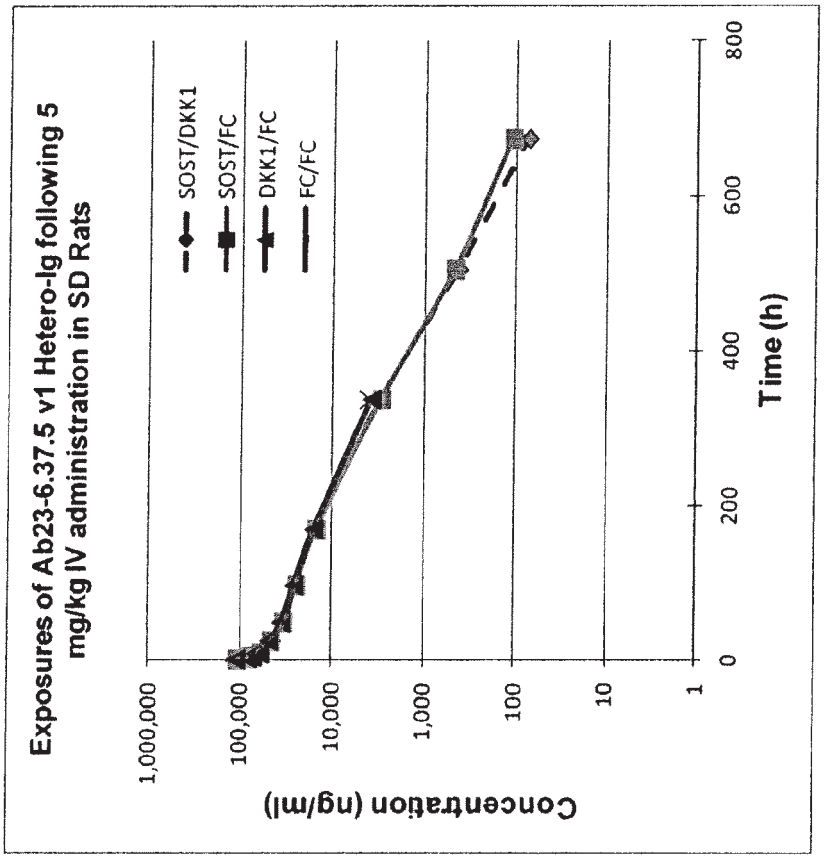


Figure 3A

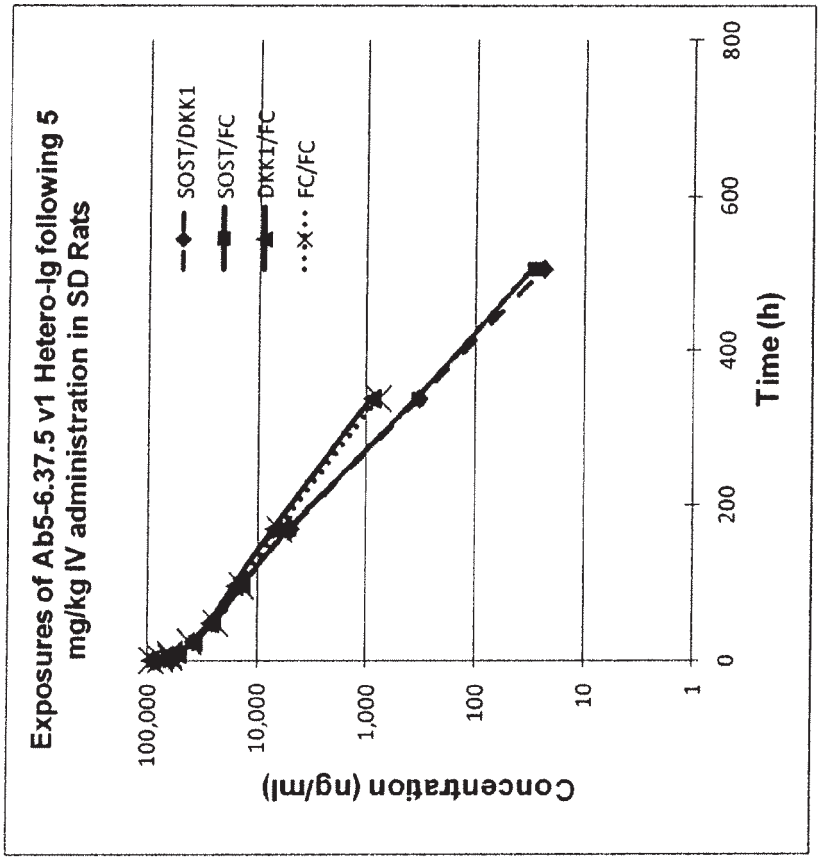


Figure 3B

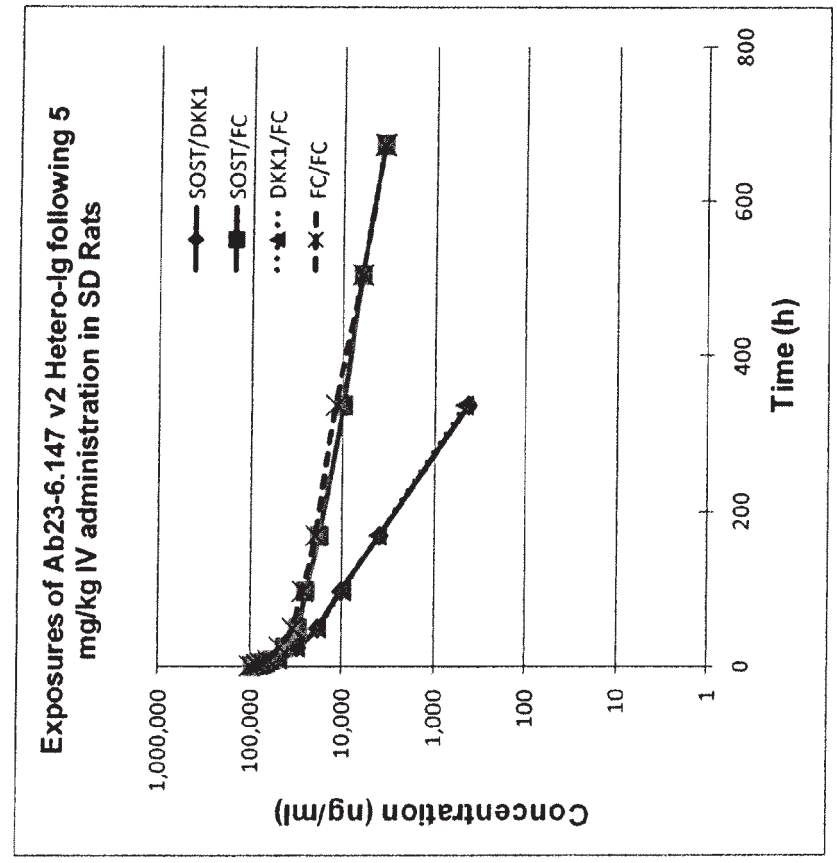


Figure 3D

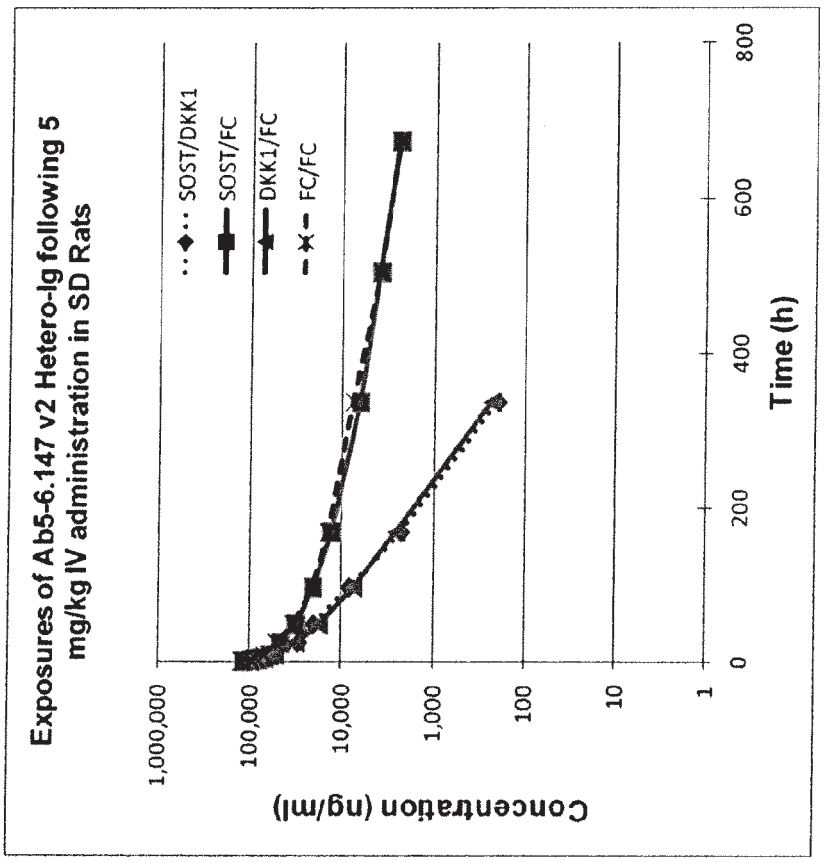


Figure 3C

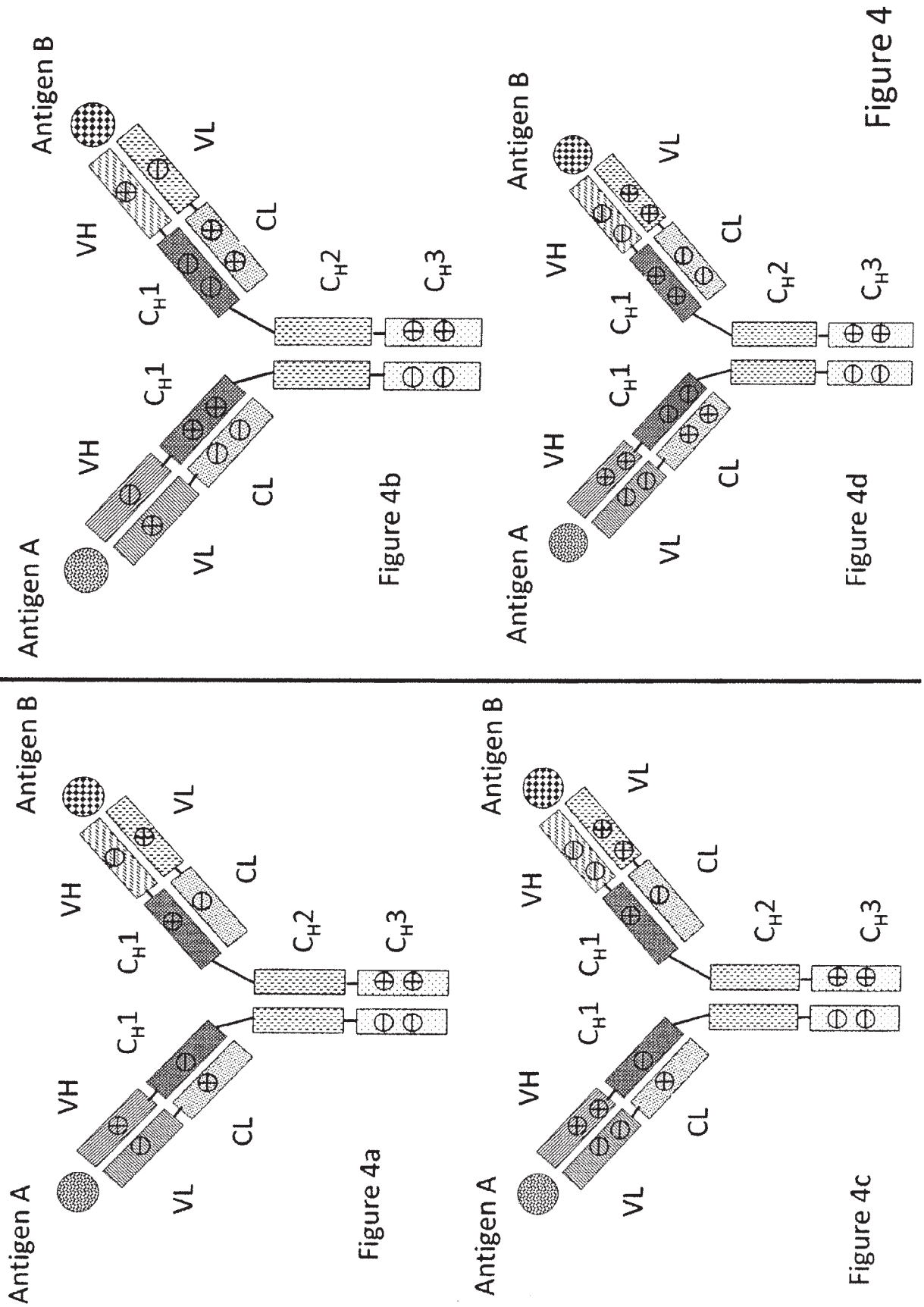


Figure 4a

Figure 4b

Figure 4c

Figure 4d

Figure 4

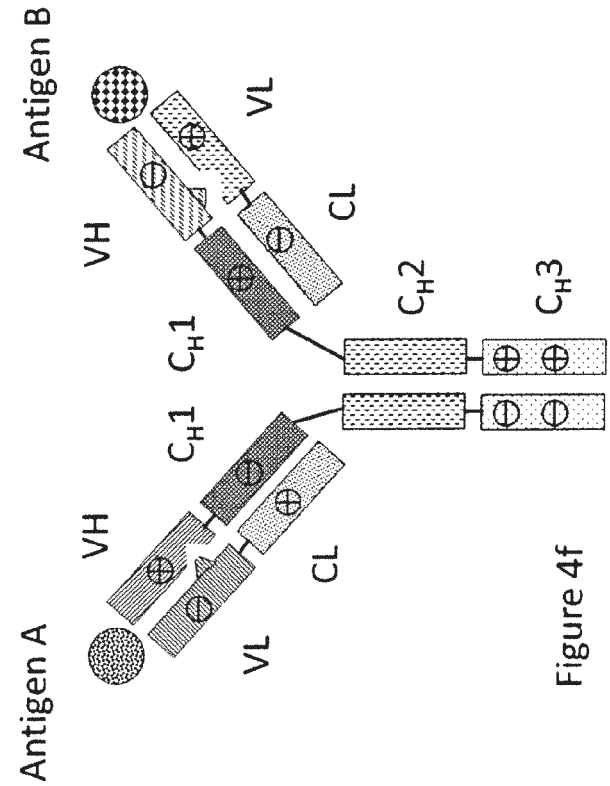


Figure 4f

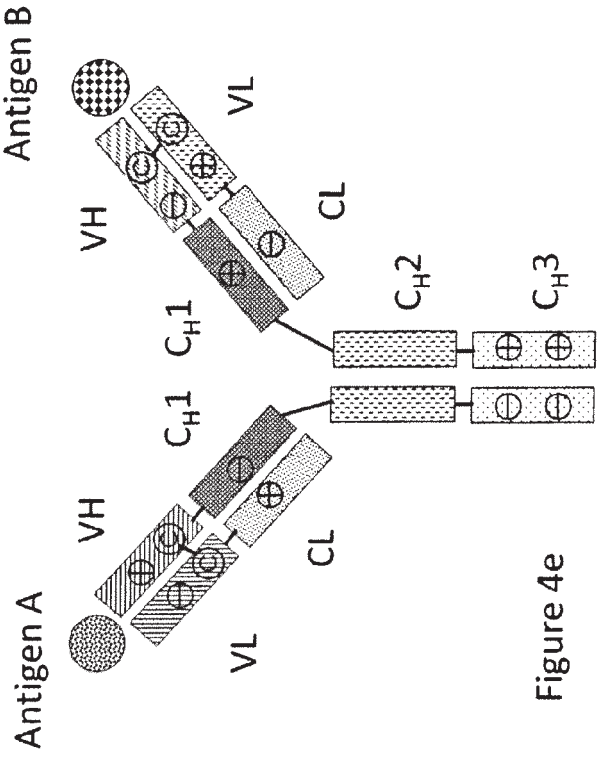
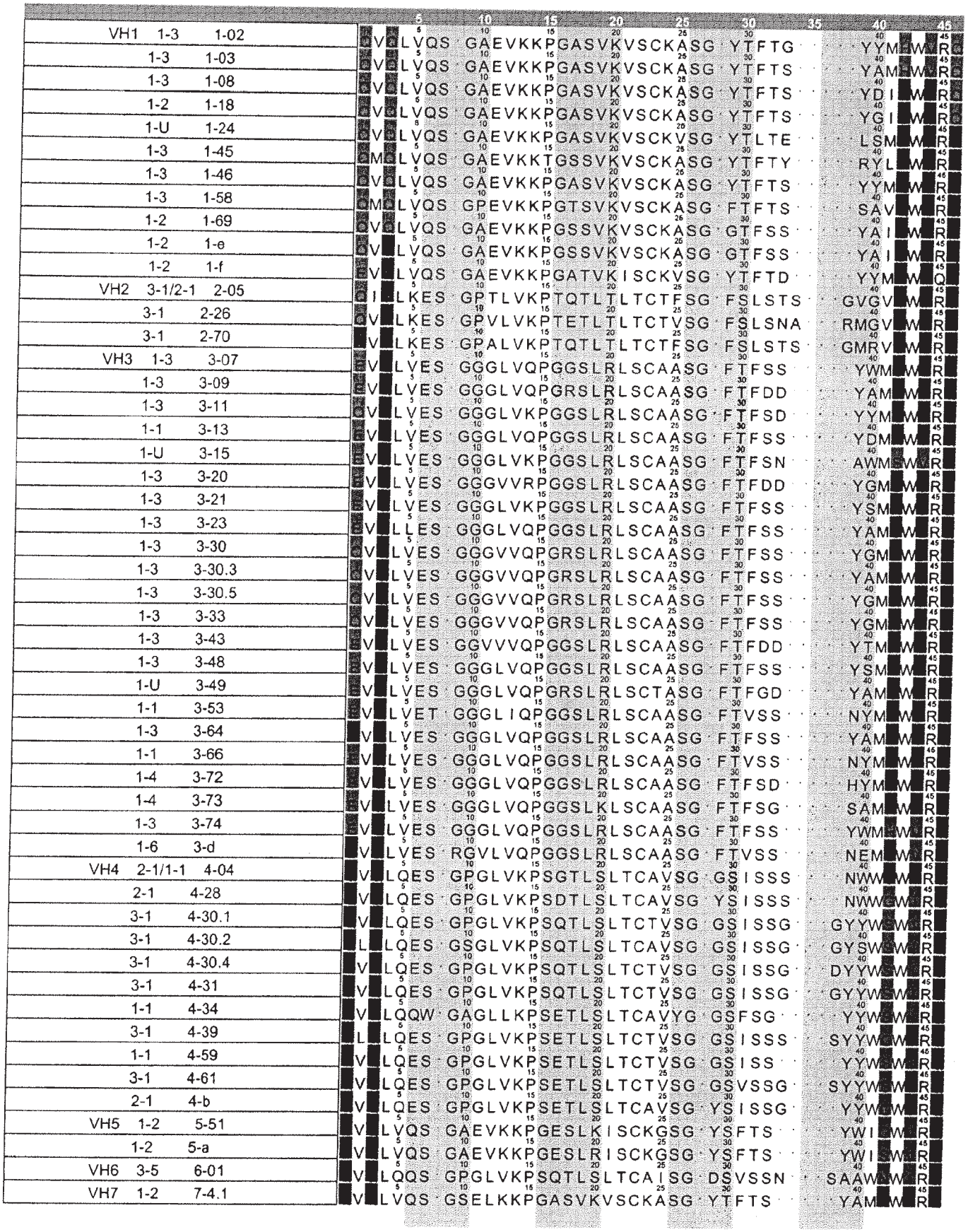
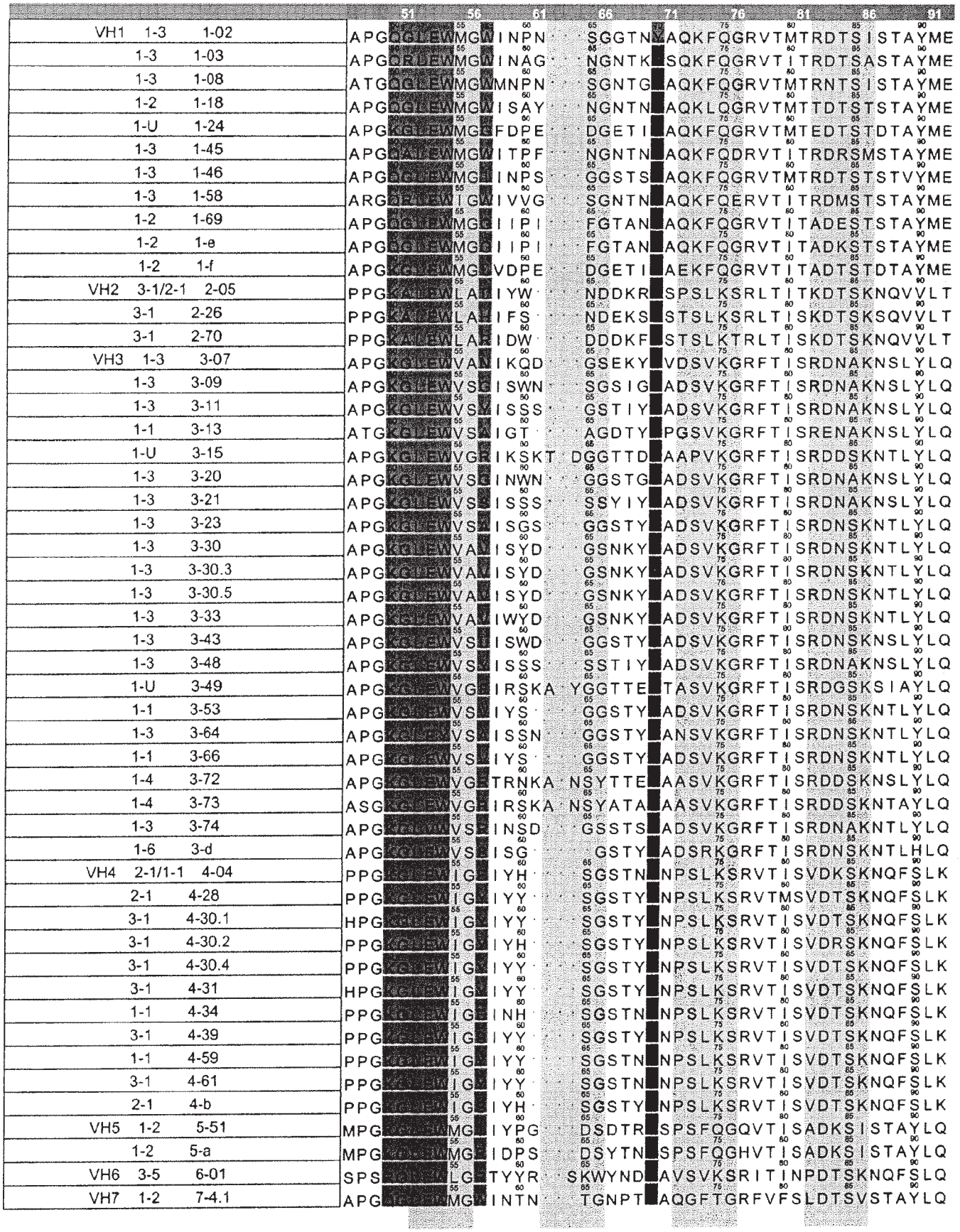


Figure 4e

Figure 4

FIGURE 5A


VH1 1-3 1-02
1-3 1-03
1-3 1-08
1-2 1-18
1-U 1-24
1-3 1-45
1-3 1-46
1-3 1-58
1-2 1-69
1-2 1-e
1-2 1-f
VH2 3-1/2-1 2-05
3-1 2-26
3-1 2-70
VH3 1-3 3-07
1-3 3-09
1-3 3-11
1-1 3-13
1-U 3-15
1-3 3-20
1-3 3-21
1-3 3-23
1-3 3-30
1-3 3-30.3
1-3 3-30.5
1-3 3-33
1-3 3-43
1-3 3-48
1-U 3-49
1-1 3-53
1-3 3-64
1-1 3-66
1-4 3-72
1-4 3-73
1-3 3-74
1-6 3-d
VH4 2-1/1-1 4-04
2-1 4-28
3-1 4-30.1
3-1 4-30.2
3-1 4-30.4
3-1 4-31
1-1 4-34
3-1 4-39
1-1 4-59
3-1 4-61
2-1 4-b
VH5 1-2 5-51
1-2 5-a
VH6 3-5 6-01
VH7 1-2 7-4.1


VH1 1-3 1-02
1-3 1-03
1-3 1-08
1-2 1-18
1-U 1-24
1-3 1-45
1-3 1-46
1-3 1-58
1-2 1-69
1-2 1-e
1-2 1-f
VH2 3-1/2-1 2-05
3-1 2-26
3-1 2-70
VH3 1-3 3-07
1-3 3-09
1-3 3-11
1-1 3-13
1-U 3-15
1-3 3-20
1-3 3-21
1-3 3-23
1-3 3-30
1-3 3-30.3
1-3 3-30.5
1-3 3-33
1-3 3-43
1-3 3-48
1-U 3-49
1-1 3-53
1-3 3-64
1-1 3-66
1-4 3-72
1-4 3-73
1-3 3-74
1-6 3-d
VH4 2-1/1-1 4-04
2-1 4-28
3-1 4-30.1
3-1 4-30.2
3-1 4-30.4
3-1 4-31
1-1 4-34
3-1 4-39
1-1 4-59
3-1 4-61
2-1 4-b
VH5 1-2 5-51
1-2 5-a
VH6 3-5 6-01
VH7 1-2 7-4.1

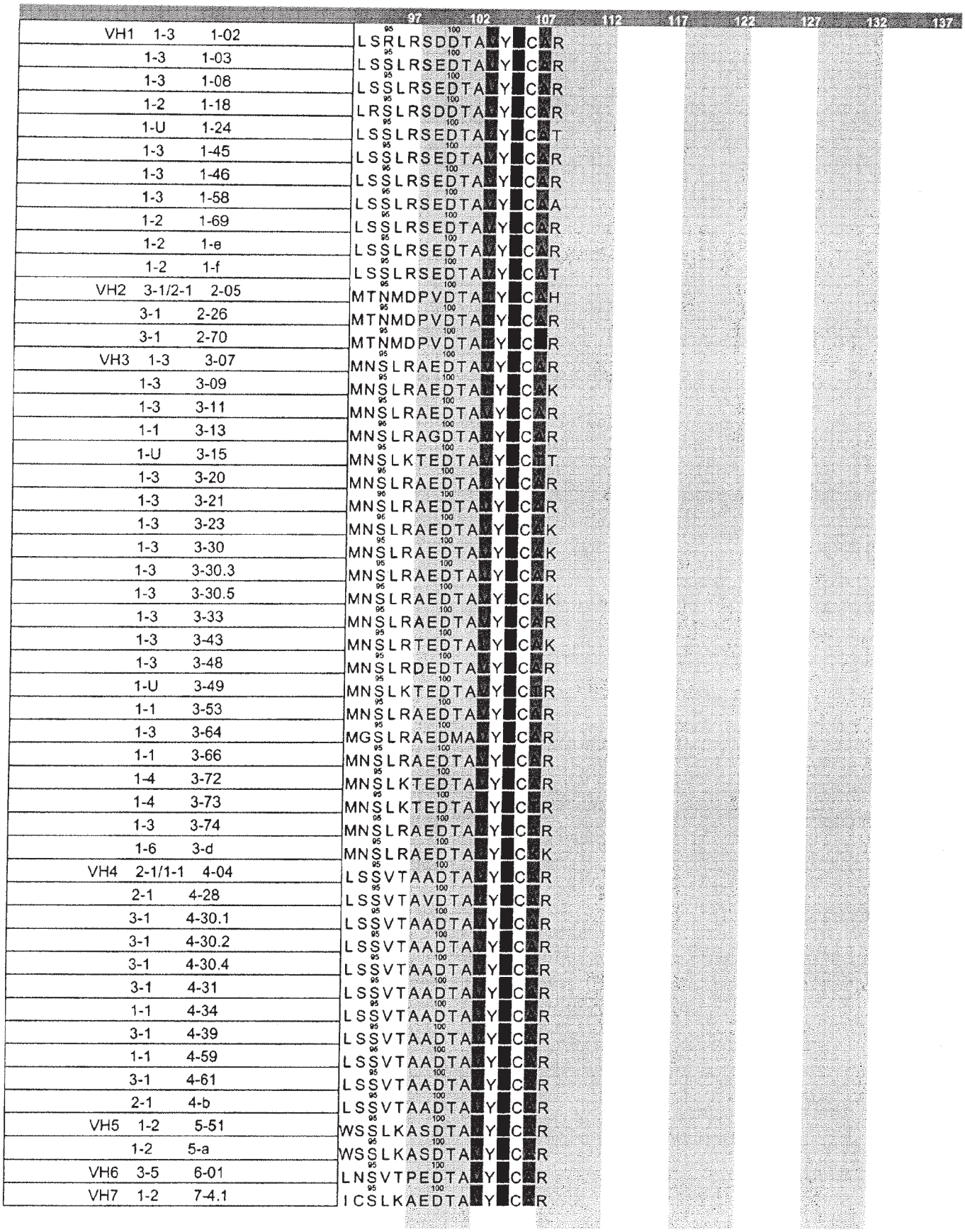

97 102 107 112 117 122 127 132 137
VH1 1-3 1-02
1-3 1-03
1-3 1-08
1-2 1-18
1-U 1-24
1-3 1-45
1-3 1-46
1-3 1-58
1-2 1-69
1-2 1-e
1-2 1-f
VH2 3-1/2-1 2-05
3-1 2-26
3-1 2-70
VH3 1-3 3-07
1-3 3-09
1-3 3-11
1-1 3-13
1-U 3-15
1-3 3-20
1-3 3-21
1-3 3-23
1-3 3-30
1-3 3-30.3
1-3 3-30.5
1-3 3-33
1-3 3-43
1-3 3-48
1-U 3-49
1-1 3-53
1-3 3-64
1-1 3-66
1-4 3-72
1-4 3-73
1-3 3-74
1-6 3-d
VH4 2-1/1-1 4-04
2-1 4-28
3-1 4-30.1
3-1 4-30.2
3-1 4-30.4
3-1 4-31
1-1 4-34
3-1 4-39
1-1 4-59
3-1 4-61
2-1 4-b
VH5 1-2 5-51
1-2 5-a
VH6 3-5 6-01
VH7 1-2 7-4.1

FIGURE 5B

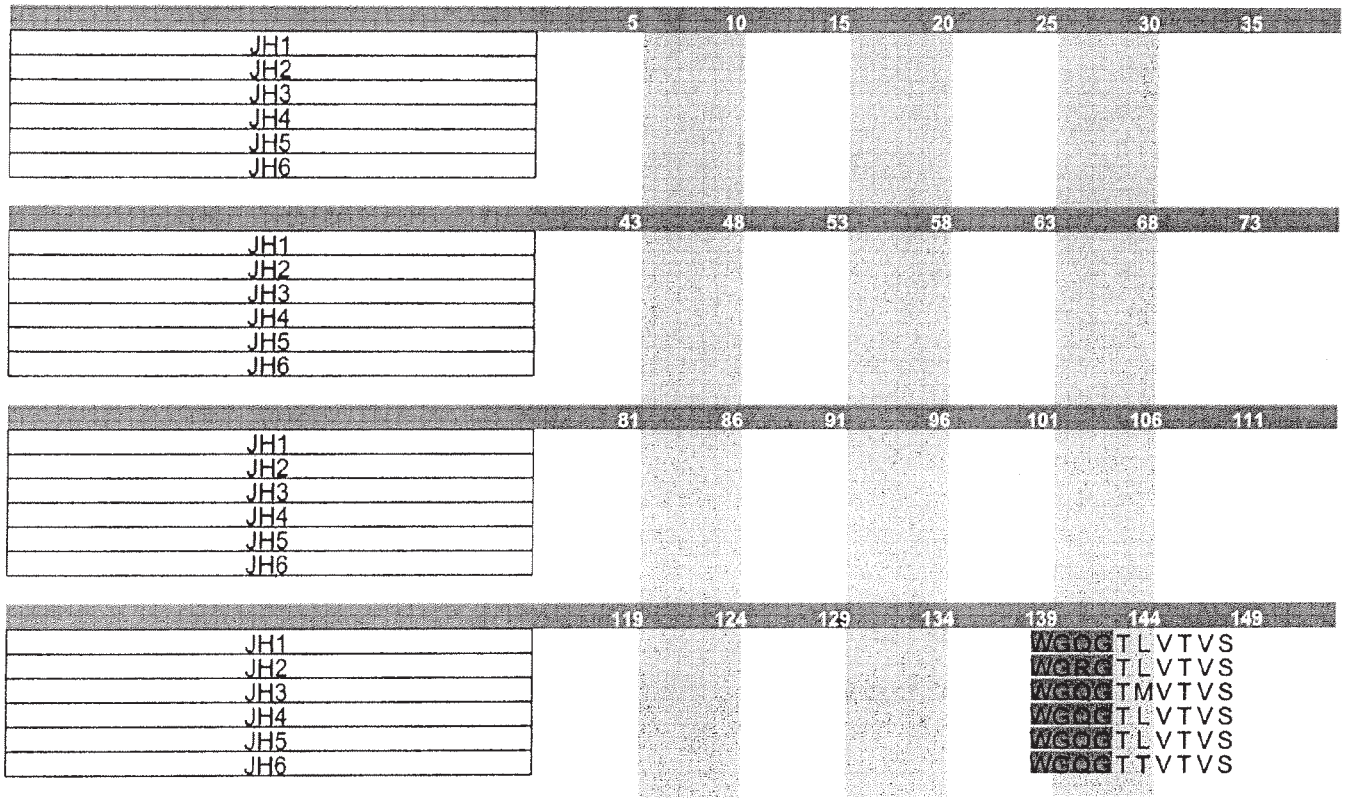
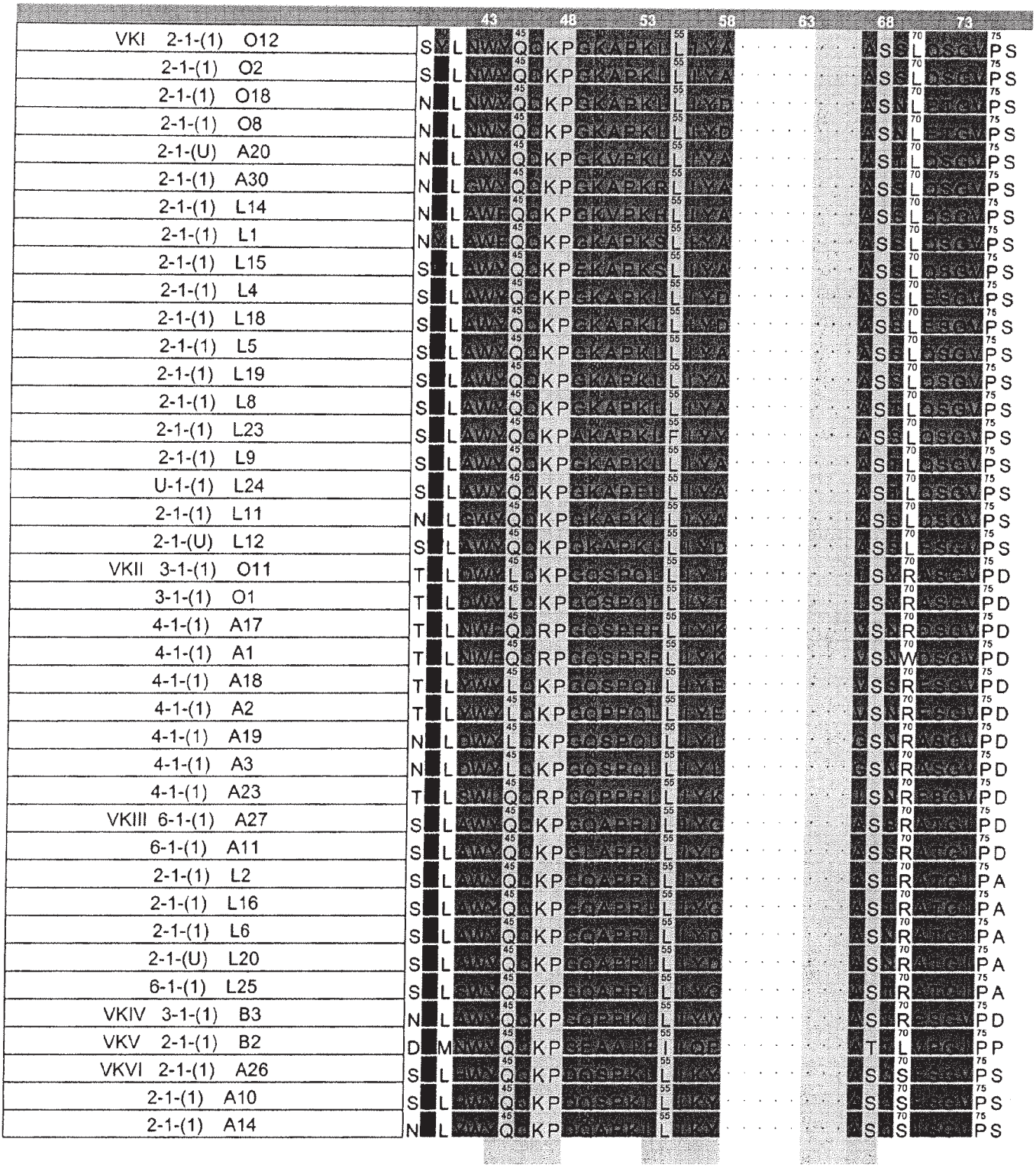

5 10 15 20 25 30 35
JH1
JH2
JH3
JH4
JH5
JH6
43 48 53 58 63 68 73
JH1
JH2
JH3
JH4
JH5
JH6
81 86 91 96 101 106 111
JH1
JH2
JH3
JH4
JH5
JH6
119 124 129 134 138 144 149
JH1 WGQGTLVTVS
JH2 WGRGTLVTVS
JH3 WGQGTMVTVS
JH4 WGQGTLVTVS
JH5 WGQGTLVTVS
JH6 WGQGTTVTVS

FIGURE 6A

VKI 2-1-(1) O12	DIQMTQSPSSLSASVGDRVTITCRAS QSIS
2-1-(1) O2	DIQMTQSPSSLSASVGDRVTITCRAS QSIS
2-1-(1) O18	DIQMTQSPSSLSASVGDRVTITCQAS QDIS
2-1-(1) O8	DIQMTQSPSSLSASVGDRVTITCQAS QDIS
2-1-(U) A20	DIQMTQSPSSLSASVGDRVTITCRAS QGIS
2-1-(1) A30	DIQMTQSPSSLSASVGDRVTITCRAS QGIR
2-1-(1) L14	NIQMTQSPSAMSASVGDRVTITCRAR QGIS
2-1-(1) L1	DIQMTQSPSSLSASVGDRVTITCRAS QGIS
2-1-(1) L15	DIQMTQSPSSLSASVGDRVTITCRAS QGIS
2-1-(1) L4	AIQLTQSPSSLSASVGDRVTITCRAS QGIS
2-1-(1) L18	AIQLTQSPSSLSASVGDRVTITCRAS QGIS
2-1-(1) L5	DIQMTQSPSSVSASVGDRVTITCRAS QGIS
2-1-(1) L19	DIQMTQSPSSVSASVGDRVTITCRAS QGIS
2-1-(1) L8	DIQLTQSPSFLSASVGDRVTITCRAS QGIS
2-1-(1) L23	AIRMTQSPFSLSASVGDRVTITCWAS QGIS
2-1-(1) L9	AIRMTQSPSSFSASTGDRVTITCRAS QGIS
U-1-(1) L24	VIWMTQSPSLLSASTGDRVTISCRMS QGIS
2-1-(1) L11	AIQMTQSPSSLSASVGDRVTITCRAS QGIR
2-1-(U) L12	DIQMTQSPSTLSASVGDRVTITCRAS QSIS
VKII 3-1-(1) O11	DIVMTQTPLSLPVTPGEPASISCRSS QSLLDSDDGN
3-1-(1) O1	DIVMTQTPLSLPVTPGEPASISCRSS QSLLDSDDGN
4-1-(1) A17	DVVMTQSPLSLPVTLGQPASISCRSS QSLVYSDGN
4-1-(1) A1	DVVMTQSPLSLPVTLGQPASISCRSS QSLVYSDGN
4-1-(1) A18	DIVMTQTPLSLSVTPGQPASISCKSS QSLLHSDGK
4-1-(1) A2	DIVMTQTPLSLSVTPGQPASISCKSS QSLLHSDGK
4-1-(1) A19	DIVMTQSPLSLPVTPGEPASISCRSS QSLLHSNGY
4-1-(1) A3	DIVMTQSPLSLPVTPGEPASISCRSS QSLLHSNGY
4-1-(1) A23	DIVMTQTPLSSPVTLGQPASISCRSS QSLVHSDGN
VKIII 6-1-(1) A27	EIVLTQSPGTLSLSPGERATLSCRAS QSVSS
6-1-(1) A11	EIVLTQSPATLSLSPGERATLSCGAS QSVSS
2-1-(1) L2	EIVMTQSPATLSVSPGERATLSCRAS QSVS
2-1-(1) L16	EIVMTQSPATLSVSPGERATLSCRAS QSVS
2-1-(1) L6	EIVLTQSPATLSLSPGERATLSCRAS QSVS
2-1-(U) L20	EIVLTQSPATLSLSPGERATLSCRAS QGVS
6-1-(1) L25	EIVMTQSPATLSLSPGERATLSCRAS QSVSS
VKIV 3-1-(1) B3	DIVMTQSPDSLAVSLGERATINCKSS QSVLYSSNNK
VKV 2-1-(1) B2	ETTLTQSPAFMSATPGDKVNISCKAS QDID
VKVI 2-1-(1) A26	EIVLTQSPDFQSVTPKEKVTITCRAS QSIG
2-1-(1) A10	EIVLTQSPDFQSVTPKEKVTITCRAS QSIG
2-1-(1) A14	DVVMTQSPAFLSVTPGEKVTITCQAS EGIG


VKI 2-1-(1) O12
2-1-(1) O2
2-1-(1) O18
2-1-(1) O8
2-1-(U) A20
2-1-(1) A30
2-1-(1) L14
2-1-(1) L1
2-1-(1) L15
2-1-(1) L4
2-1-(1) L18
2-1-(1) L5
2-1-(1) L19
2-1-(1) L8
2-1-(1) L23
2-1-(1) L9
U-1-(1) L24
2-1-(1) L11
2-1-(U) L12
VKII 3-1-(1) O11
3-1-(1) O1
4-1-(1) A17
4-1-(1) A1
4-1-(1) A18
4-1-(1) A2
4-1-(1) A19
4-1-(1) A3
4-1-(1) A23
VKIII 6-1-(1) A27
6-1-(1) A11
2-1-(1) L2
2-1-(1) L16
2-1-(1) L6
2-1-(U) L20
6-1-(1) L25
VKIV 3-1-(1) B3
VKV 2-1-(1) B2
VKVI 2-1-(1) A26
2-1-(1) A10
2-1-(1) A14
43
48
53
58
63
68
73

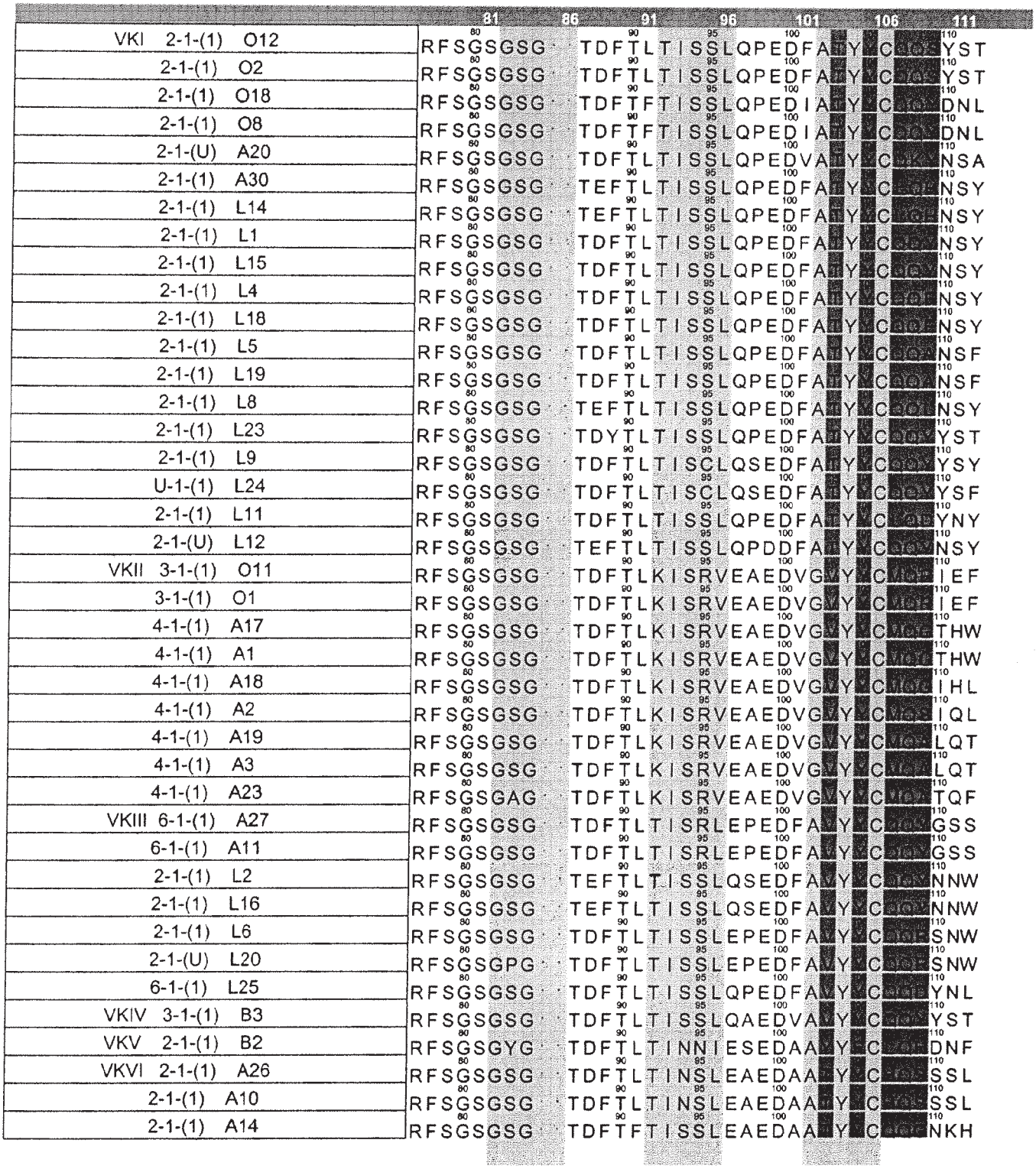

VKI 2-1-(1) O12
2-1-(1) O2
2-1-(1) O18
2-1-(1) O8
2-1-(U) A20
2-1-(1) A30
2-1-(1) L14
2-1-(1) L1
2-1-(1) L15
2-1-(1) L4
2-1-(1) L18
2-1-(1) L5
2-1-(1) L19
2-1-(1) L8
2-1-(1) L23
2-1-(1) L9
U-1-(1) L24
2-1-(1) L11
2-1-(U) L12
VKII 3-1-(1) O11
3-1-(1) O1
4-1-(1) A17
4-1-(1) A1
4-1-(1) A18
4-1-(1) A2
4-1-(1) A19
4-1-(1) A3
4-1-(1) A23
VKIII 6-1-(1) A27
6-1-(1) A11
2-1-(1) L2
2-1-(1) L16
2-1-(1) L6
2-1-(U) L20
6-1-(1) L25
VKIV 3-1-(1) B3
VKV 2-1-(1) B2
VKVI 2-1-(1) A26
2-1-(1) A10
2-1-(1) A14

FIGURE 6B

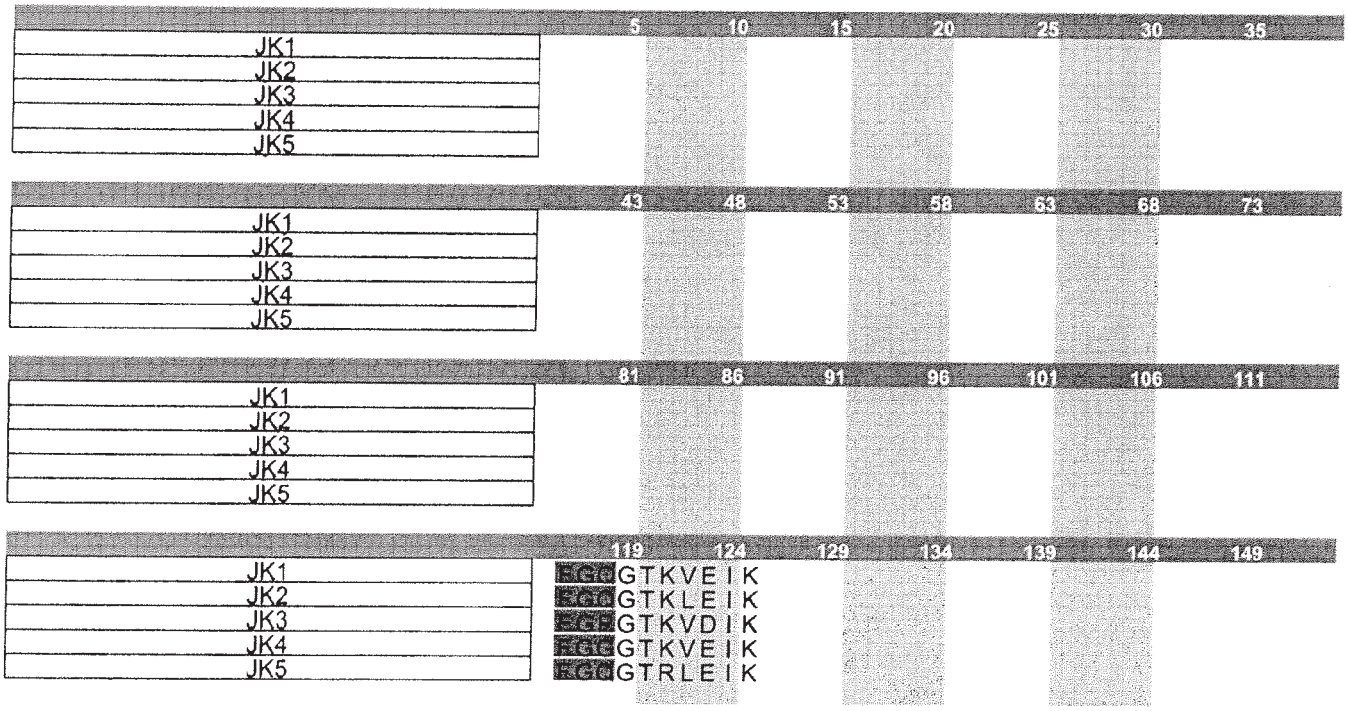
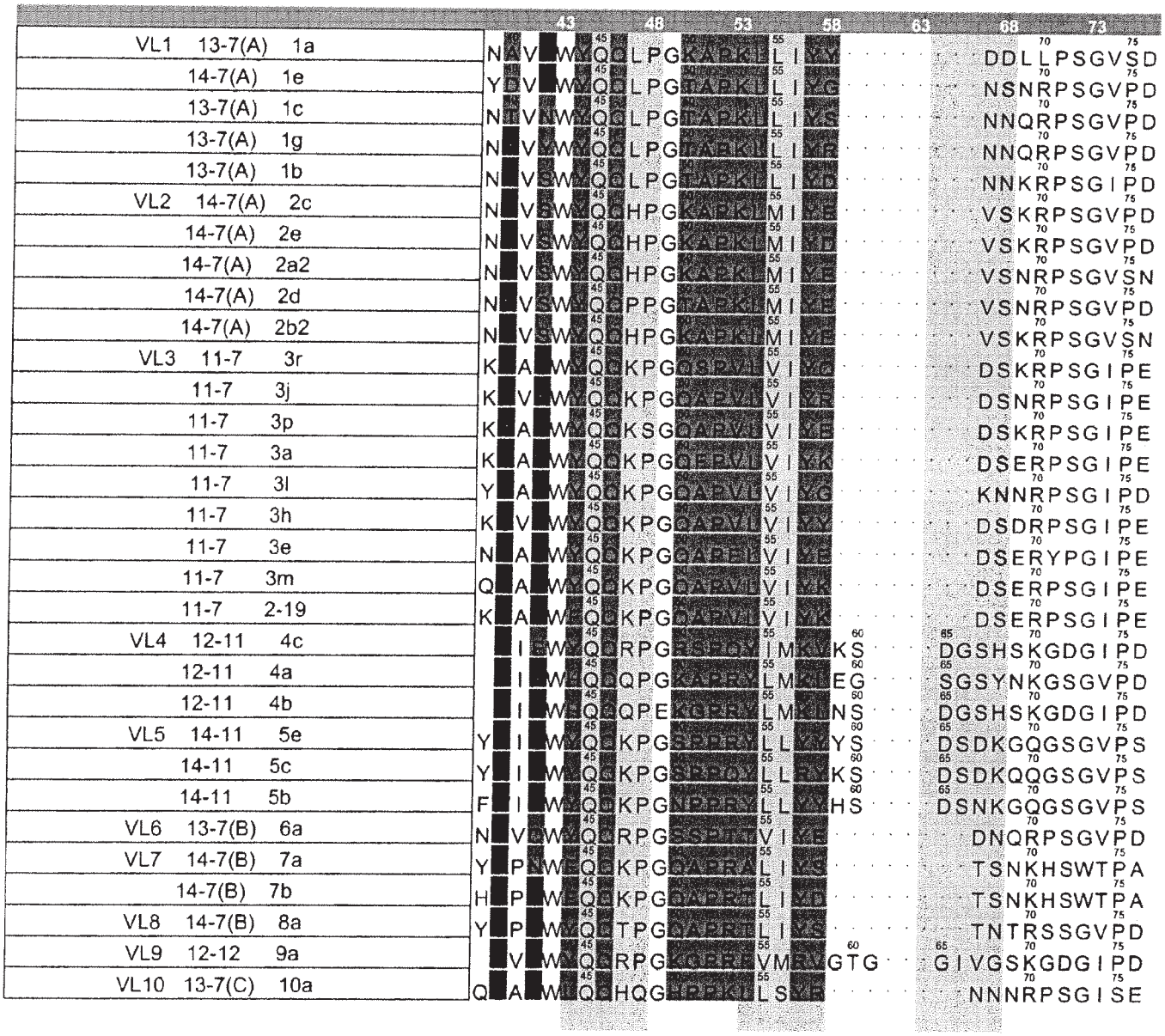
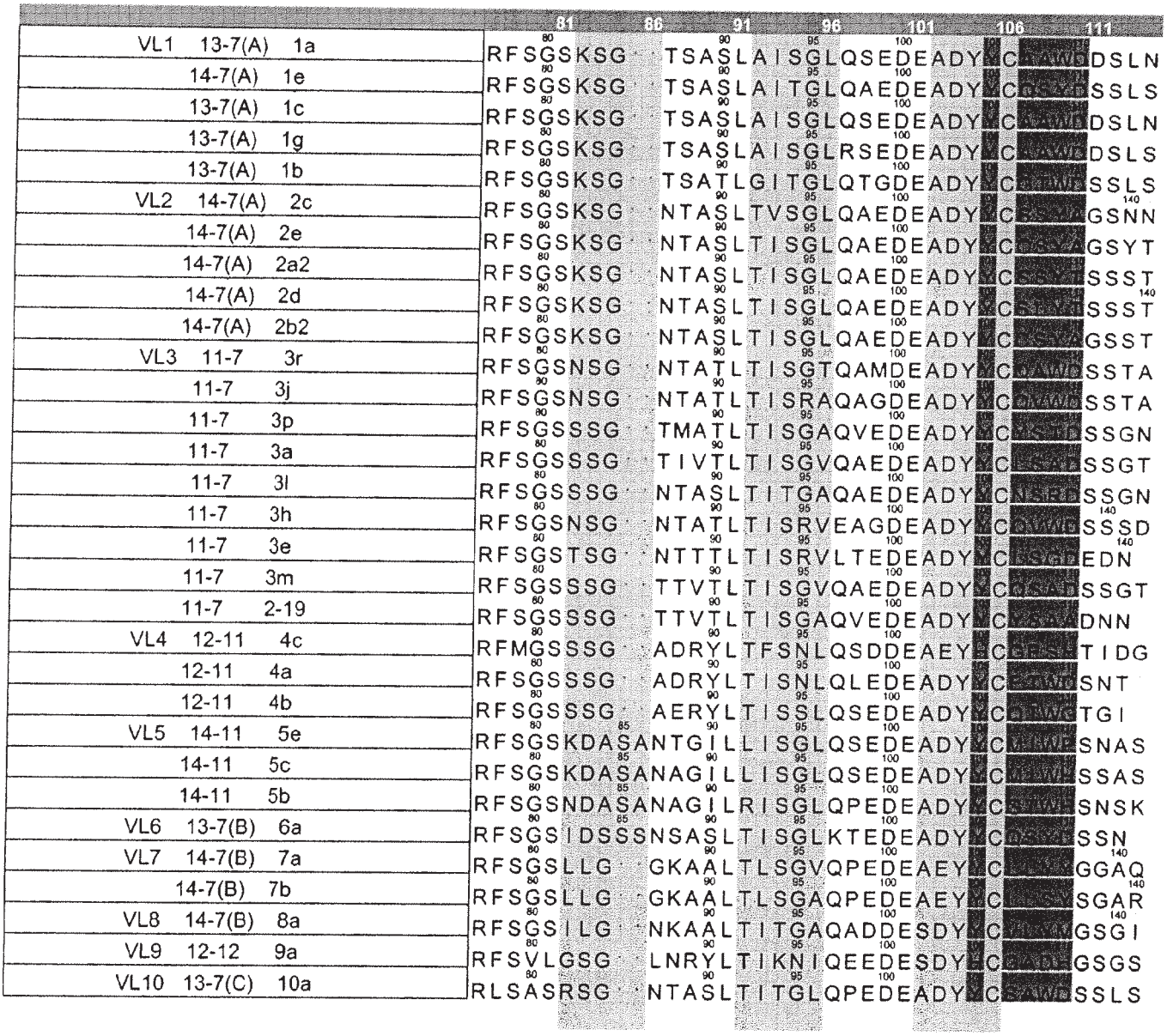

5 10 15 20 25 30 35
JK1
JK2
JK3
JK4
JK5
43 48 53 58 63 68 73
JK1
JK2
JK3
JK4
JK5
81 86 91 96 101 106 111
JK1
JK2
JK3
JK4
JK5
119 124 129 134 139 144 149
JK1 FGGGTKVEIK
JK2 FGGGTKLEIK
JK3 FGGGTKVDIK
JK4 FGGGTKVEIK
JK5 FGGGTRLEIK

FIGURE 7A

			5 10 15 20 25 30 35
VL1	13-7(A)	1a	QSVLTQP PSVSEAPRQRVTISCSGSS SNIGN
	14-7(A)	1e	QSVLTQP PSVSGAPGQRVTISCTGSS SNIGAG
	13-7(A)	1c	QSVLTQP PSASGTPGQRVTISCSGSS SNIGS
	13-7(A)	1g	QSVLTQP PSASGTPGQRVTISCSGSS SNIGS
	13-7(A)	1b	QSVLTQP PSVSAAPGQKVTISCSGSS SNIGN
VL2	14-7(A)	2c	QSALTQP PSASGSPGQSVTISCTGTS SDVGGY
	14-7(A)	2e	QSALTQP RSVSGSPGQSVTISCTGTS SDVGGY
	14-7(A)	2a2	QSALTQP ASVSGSPGQSITISCTGTS SDVGGY
	14-7(A)	2d	QSALTQP PSVSGSPGQSVTISCTGTS SDVGSY
	14-7(A)	2b2	QSALTQP ASVSGSPGQSITISCTGTS SDVGSY
VL3	11-7	3r	SYELTQP PSVSVSPGQTASITCSGD KLGD
	11-7	3j	SYELTQP LSVSVALGQTARITCGGN NIGS
	11-7	3p	SYELTQP PSVSVSPGQTARITCSGD ALPK
	11-7	3a	SYELTQP PSVSVSLGQMARITCSGE ALPK
	11-7	3l	SSELTQD PAVSVALGQTVRITCQGD SLRS
	11-7	3h	SYVLTQP PSVSVAPGKTARITCGGN NIGS
	11-7	3e	SYELTQL PSVSVSPGQTARITCSGD VLGE
	11-7	3m	SYELMQP PSVSVSPGQTARITCSGD ALPK
	11-7	2-19	SYELTQP SSVSVSPGQTARITCSGD VLAK
VL4	12-11	4c	LPVLTQP PSASALLGASIKLTCTLSS EHSTY
	12-11	4a	QPVLTQS SSASASLGSSVKLTCTLSS GHSSY
	12-11	4b	QLVLTQS PSASASLGASVKLTCTLSS GHSSY
VL5	14-11	5e	QPVLTQP PSSSASPGESARLTCTLPS DINVGS
	14-11	5c	QAVLTQP ASLSASPGASASLTCTLRS GINVGT
	14-11	5b	QPVLTQP SSHSASSGASVRLTCMLSS GFSVGD
VL6	13-7(B)	6a	NFMLTQP HSVSESPGKTVTISCTRSS GSIAS
VL7	14-7(B)	7a	QTVVTQE PSLTVSPGGTVTLTCASST GAVTSG
	14-7(B)	7b	QAVVTQE PSLTVSPGGTVTLTCGSST GAVTSG
VL8	14-7(B)	8a	QTVVTQE PSFSVSPGGTVTLTCGLSS GSVSTS
VL9	12-12	9a	QPVLTQP PSASASLGASVTLTCTLSS GYSNY
VL10	13-7(C)	10a	QAGLTQP PSVSKGLRQTATLTCTGNS NNVGN


VL1 13-7(A) 1a
14-7(A) 1e
13-7(A) 1c
13-7(A) 1g
13-7(A) 1b
VL2 14-7(A) 2c
14-7(A) 2e
14-7(A) 2a2
14-7(A) 2d
14-7(A) 2b2
VL3 11-7 3r
11-7 3j
11-7 3p
11-7 3a
11-7 3l
11-7 3h
11-7 3e
11-7 3m
11-7 2-19
VL4 12-11 4c
12-11 4a
12-11 4b
VL5 14-11 5e
14-11 5c
14-11 5b
VL6 13-7(B) 6a
VL7 14-7(B) 7a
14-7(B) 7b
VL8 14-7(B) 8a
VL9 12-12 9a
VL10 13-7(C) 10a


VL1 13-7(A) 1a
14-7(A) 1e
13-7(A) 1c
13-7(A) 1g
13-7(A) 1b
VL2 14-7(A) 2c
14-7(A) 2e
14-7(A) 2a2
14-7(A) 2d
14-7(A) 2b2
VL3 11-7 3r
11-7 3j
11-7 3p
11-7 3a
11-7 3l
11-7 3h
11-7 3e
11-7 3m
11-7 2-19
VL4 12-11 4c
12-11 4a
12-11 4b
VL5 14-11 5e
14-11 5c
14-11 5b
VL6 13-7(B) 6a
VL7 14-7(B) 7a
14-7(B) 7b
VL8 14-7(B) 8a
VL9 12-12 9a
VL10 13-7(C) 10a
81
86
91
96
101
106
111

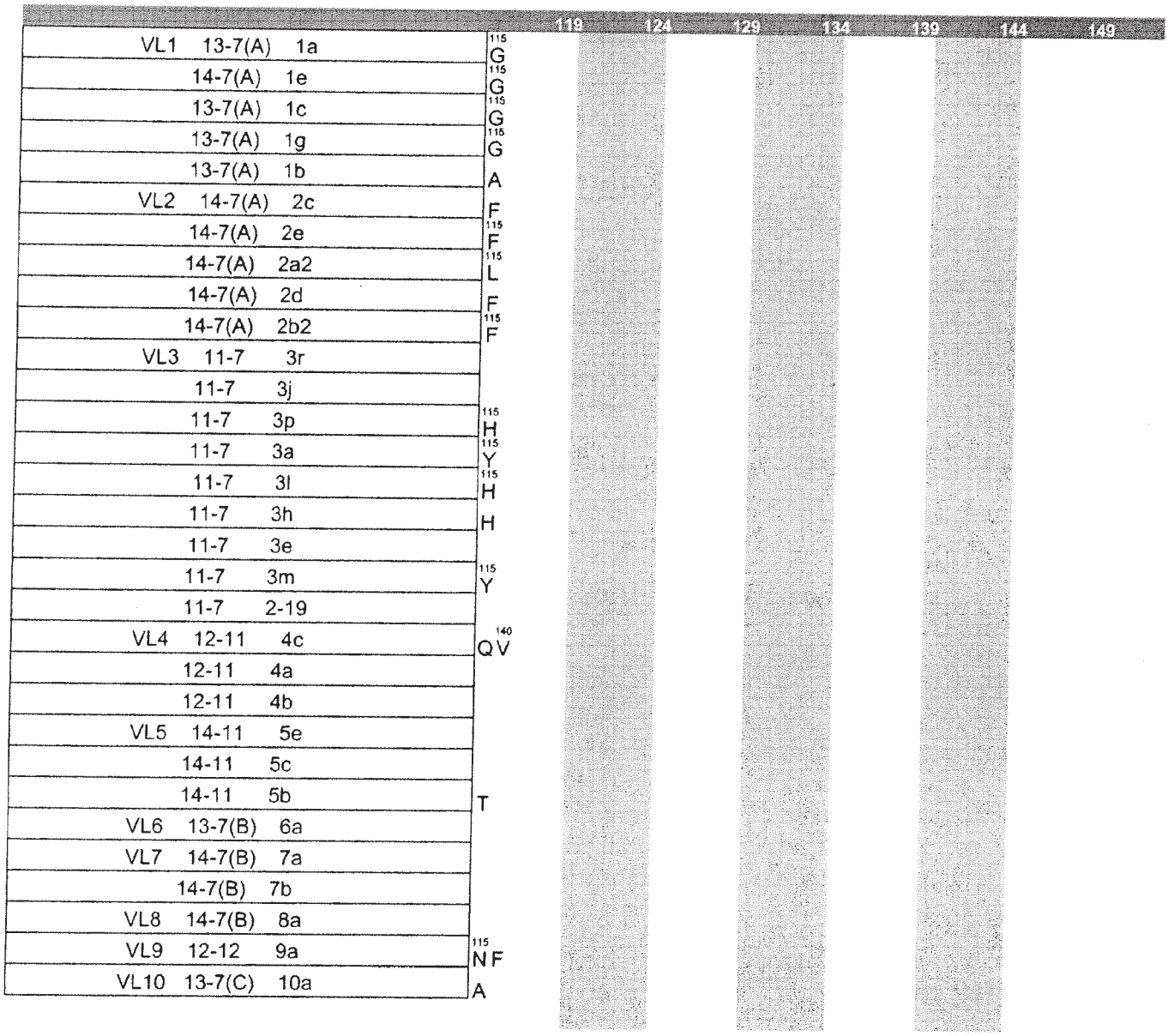
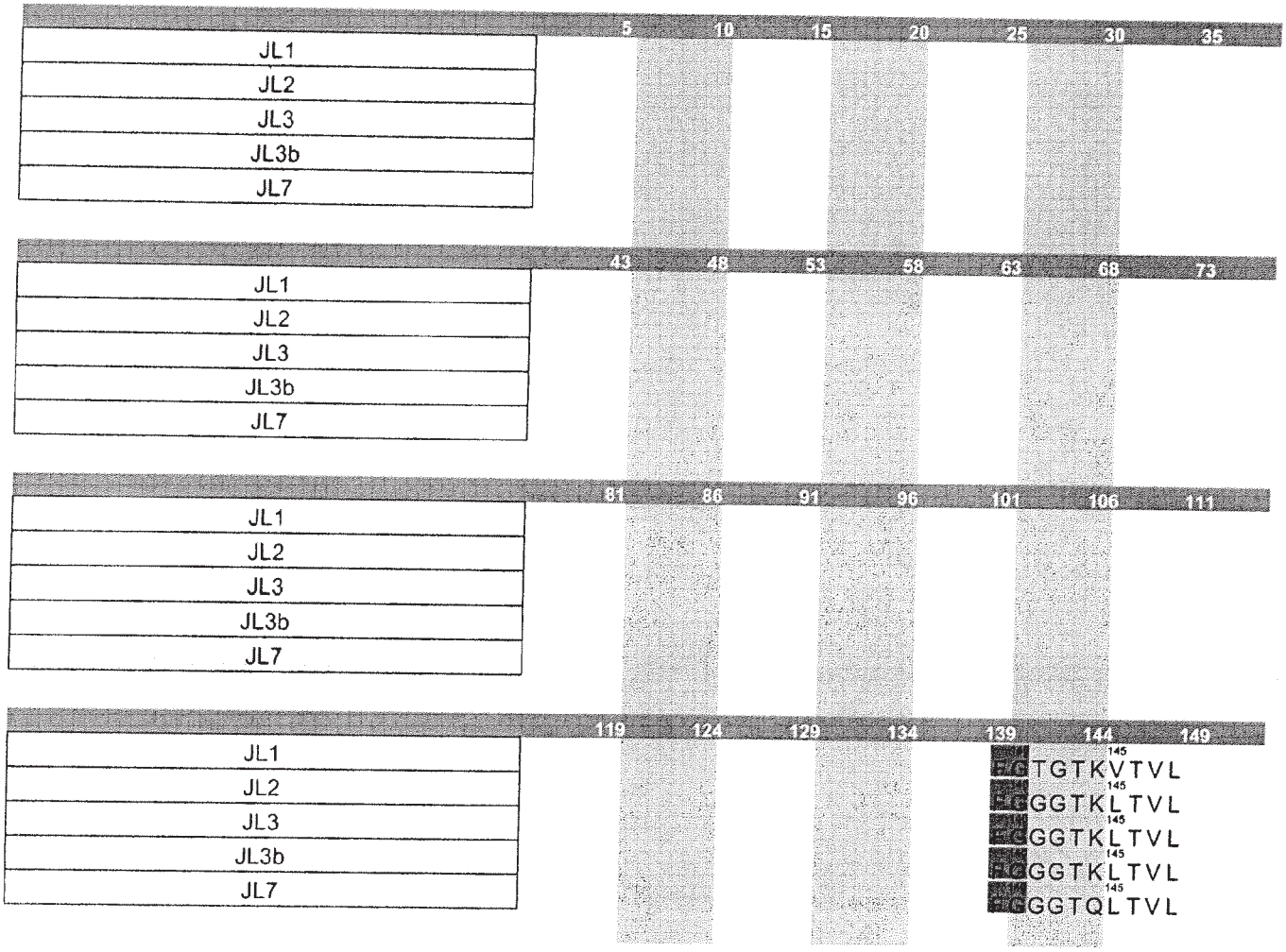

118
124
129
134
139
144
149
VL1 13-7(A) 1a
14-7(A) 1e
13-7(A) 1c
13-7(A) 1g
13-7(A) 1b
VL2 14-7(A) 2c
14-7(A) 2e
14-7(A) 2a2
14-7(A) 2d
14-7(A) 2b2
VL3 11-7 3r
11-7 3j
11-7 3p
11-7 3a
11-7 3l
11-7 3h
11-7 3e
11-7 3m
11-7 2-19
VL4 12-11 4c
12-11 4a
12-11 4b
VL5 14-11 5e
14-11 5c
14-11 5b
VL6 13-7(B) 6a
VL7 14-7(B) 7a
14-7(B) 7b
VL8 14-7(B) 8a
VL9 12-12 9a
VL10 13-7(C) 10a
115 G
115 G
115 G
115 G
A
F
115 F
115 L
F
115 F
115 H
115 Y
115 H
H
115 Y
140 Q V
T
115 N F
A

FIGURE 7B


JL1
JL2
JL3
JL3b
JL7
5 10 15 20 25 30 35
43 48 53 58 63 68 73
81 86 91 96 101 106 111
119 124 129 134 139 144 149
145
FGTGTKVTVL
FGGGTKLTVL
FGGGTKLTVL
FGGGTKLTVL
FGGGTQLTVL

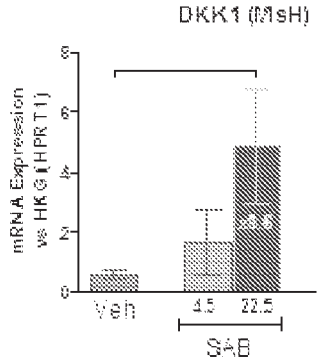


Figure 8

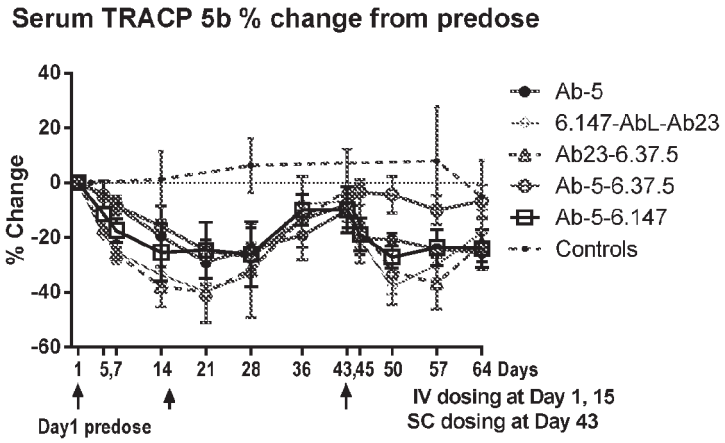


Figure 9

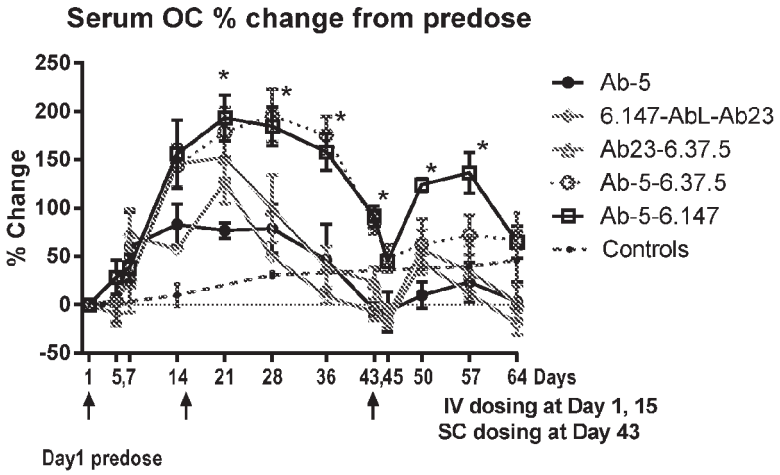


Figure 10

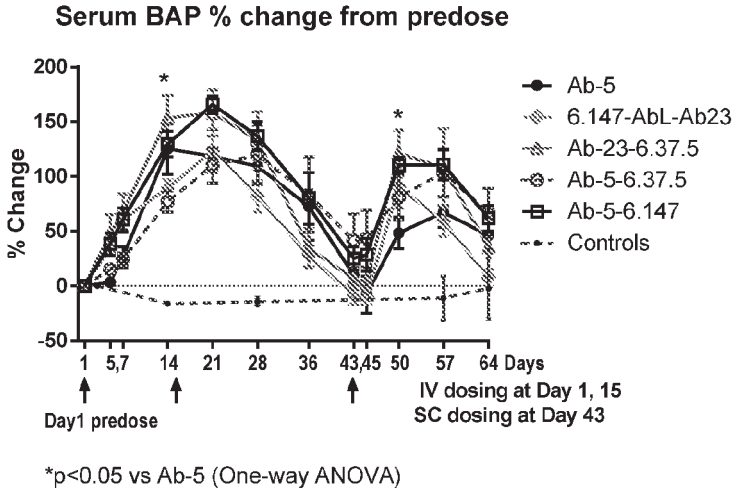


Figure 11

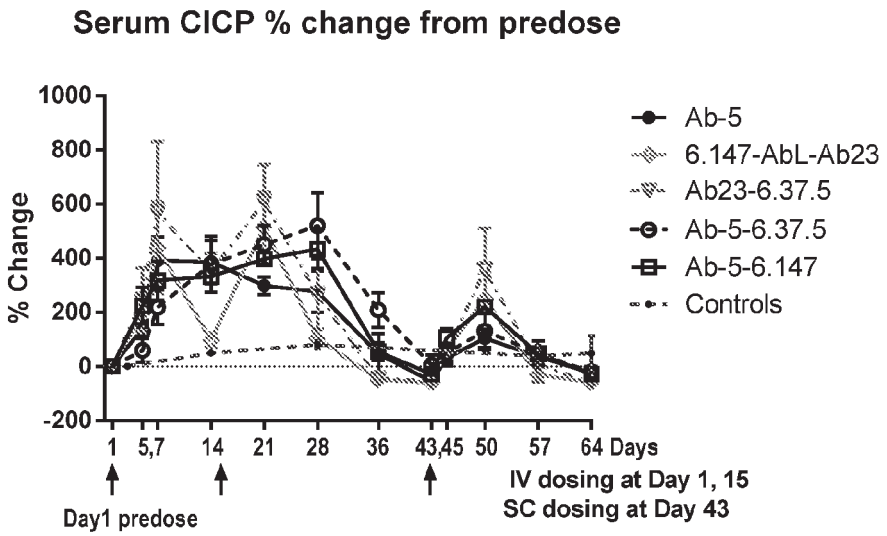


Figure 12

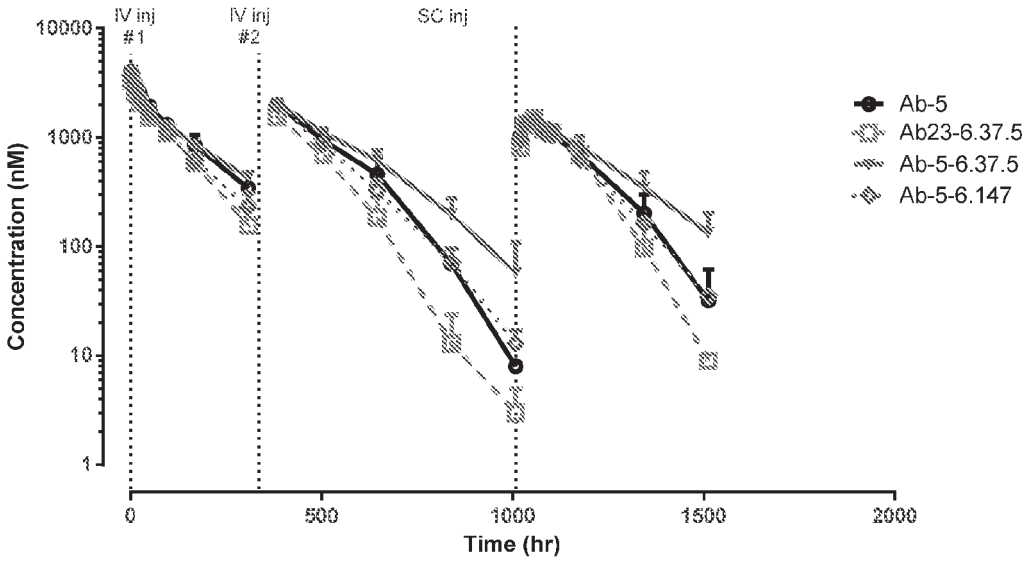


Figure 13

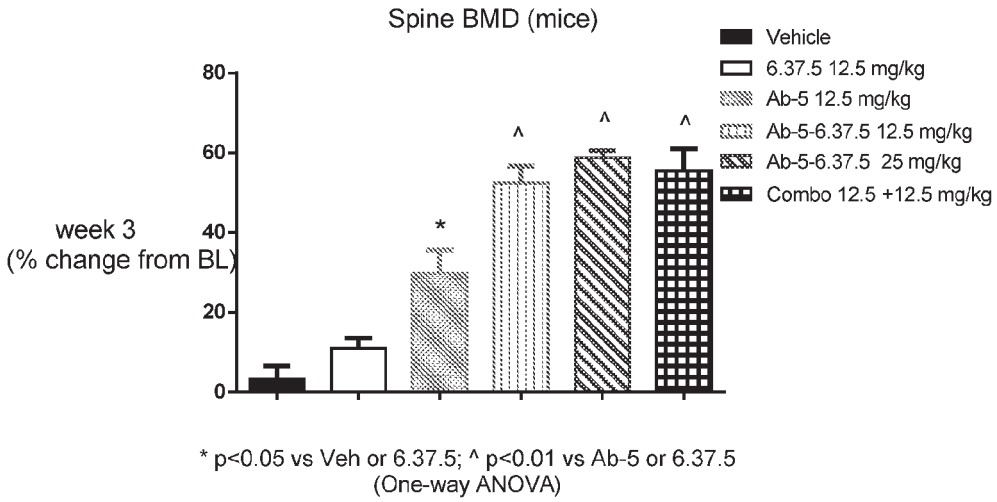

Spine BMD (mice)
week 3
(% change from BL)
80
60
40
20
0
*
^
^
^
Vehicle
6.37.5 12.5 mg/kg
Ab-5 12.5 mg/kg
Ab-5-6.37.5 12.5 mg/kg
Ab-5-6.37.5 25 mg/kg
Combo 12.5 +12.5 mg/kg
* p<0.05 vs Veh or 6.37.5; ^ p<0.01 vs Ab-5 or 6.37.5
(One-way ANOVA)

Figure 14