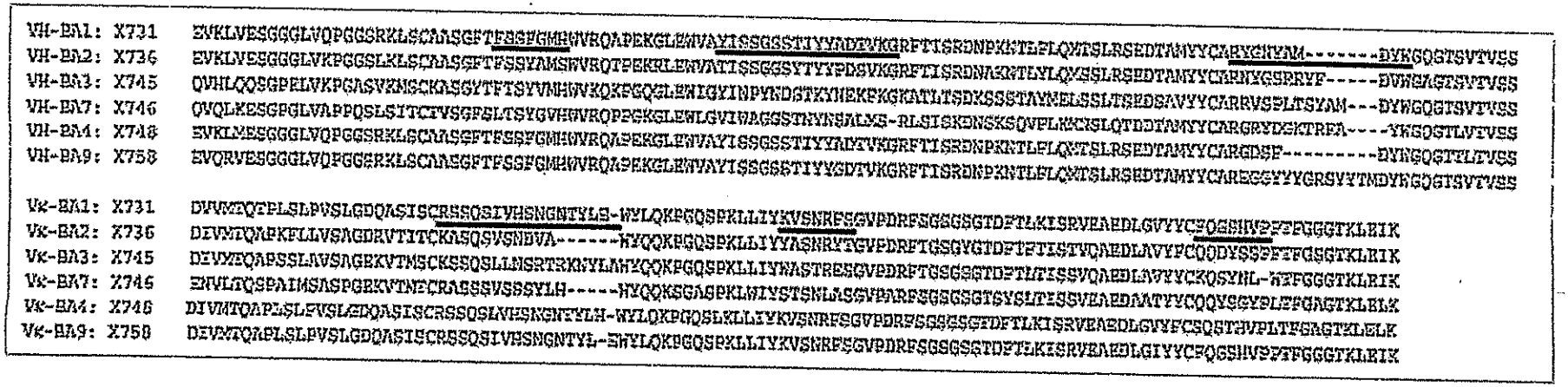
Table 1.

Amino acid sequence of variable regions of the heavy chain (VH) and light chain (VL/Vκ) from six different monoclonal antibodies specific for human wild-type Aβ protofibrils.



*Position of the various CDR regions (1-3) are underlined in VL and VH. The boundaries of the CDR regions (1-3) are shown in Table 3 and Table 4. Antibody BA9, also named 158 in the patent application., is an example of a high affinity protofibril specific antibody according to the invention.

Table 4.

Amino acid sequence of mouse framework regions of the mouse and human variable light chain (VL) region from protofibril specific antibodies

Mouse framework* VL regions	
Divmtqaplslpvslgdqasiscwylqkpgqspklliygvpdrfsgsgsgtdftlkisrveaedlgiyyc	antibody 158
.....	BA9_VL_fr123
.v....t.....v...	BA1_VL_fr123
........kf.l..a..rvt.t...q.....t...y.....ft..t.q....av.f.	BA2_VL_fr123
Human framework VL regions	
......t......tp.ep.....q.....v.v...	VKII-3-1-(1)-O11
......s......tp.ep.....q.....v.v...	VKII-4-1-(1)-A19
......t....s.tp.qp.....q.....v.v...	VKII-4-1-(1)-A18
......t....s.tp.qp.....p.q.....v.v...	VKII-4-1-(1)-A2
.v....s......t..qp......fq.r.....rr.....v.v...	VKII-4-1-(1)-A17

* Framework region is the region outside the CDR regions. The CDR regions has been deleted for clarity.

Table 5.

Amino acid sequence of mouse and human framework regions of the mouse and human variable light heavy (VH) region from protofibril specific antibodies

Mouse framework* VH regions	
Evklmesggglvqpggsrklscaaswvrqapekglewvarftisrdnpkntlflqmtslrsedtamyycar	antibody 158
.....	BA9_VH_fr123
....v.....	BA1_VH_fr123
....v.......k....l..........t...r.............a....y...s..............	BA2_VH_fr123
Human framework VH regions	
..q.v.............lr.............g................a..s.y...n...a....v.....	VH3-7_fr123
..q.v......i.....lr.............g......s........s....y...n...a....v.....	VH3-53_fr123
..q.l.............lr.............g......s........s....y...n...a....v....k	VH3-23_fr123
..q.v.............lr.............g......s........a..s.y...n...d....v.....	VH3-48_fr123
..q.v.............lr.............g...v..s........a....y...n...a....v.....	VH3-74_fr123

* Framework region is the region outside the CDR regions. The CDR regions has been deleted for clarity.

Table 11. DNA sequence of 158 VK, primer MKV1 and the VK sequence derived using primers located within the V region

```
  1 ATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGGATTCCTGCTTCCAGCAGTGATGTTTTGATGACCCAAACTCCACTCTCCCTG 158 VK
  1 .........VV.....................                                                             MKV1
  1 ------------------------------------------------------...A..G..........GG..............  *** VK

 91 CCTGTCAGTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCTAGTCAGAGCATTGTACATAGTAATGGAAACACCTATTTAGAATGGTAC 158 VK
 34 ..........................................................................................  *** VK

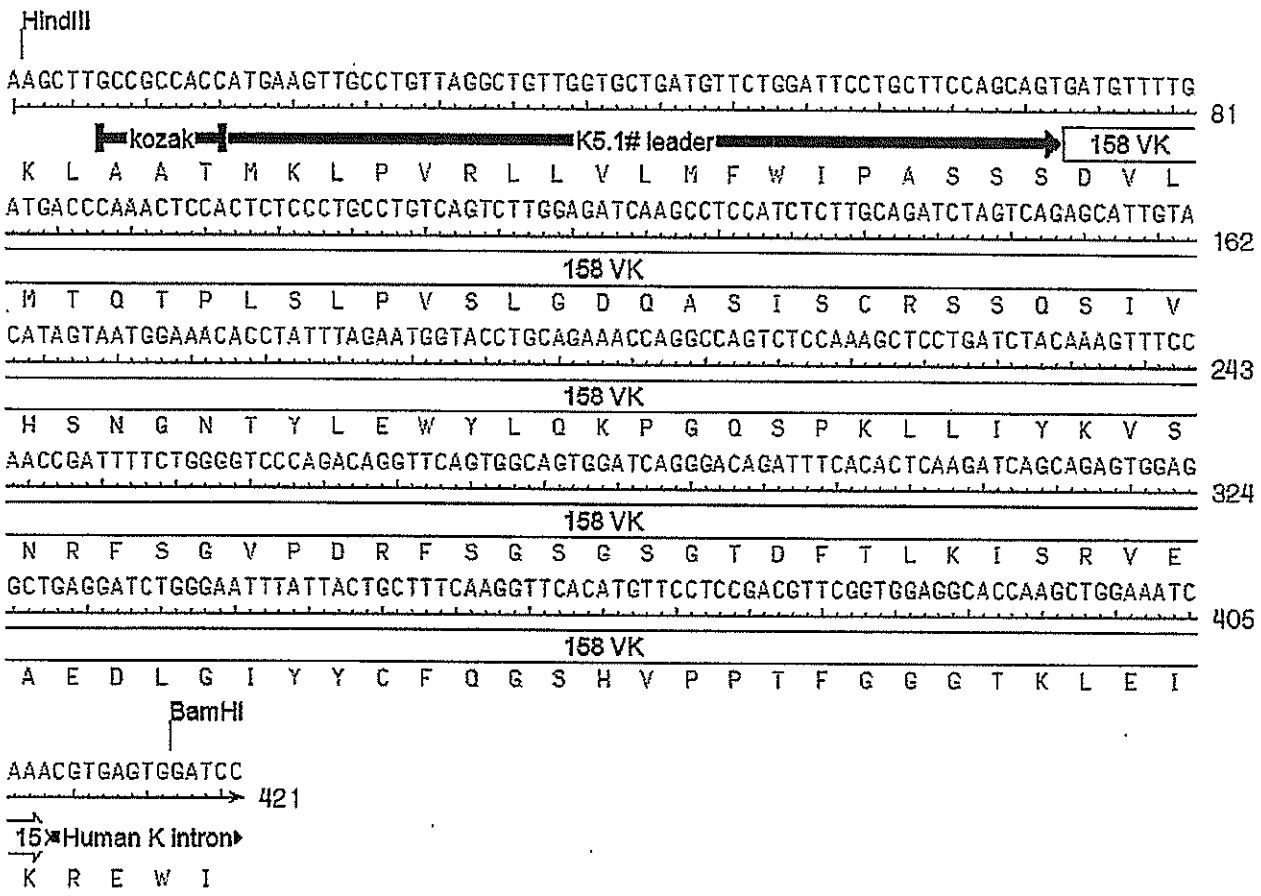
181 CTGCAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGA 158 VK
124 ..........................................................................................  *** VK

271 TCAGGGACAGATTTCACACTCAAGATCAGCAGAGTGGAGGCTGAGGATCTGGGAATTTATTACTGCTTTCAAGGTTCACATGTTCCTCCG 158 VK
214 ..........................................................................................  *** VK

361 ACGTTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGCTG                                                   158 VK
304 ................................                                                            *** VK
```

Legend: Residues identical to 158 VK are indicated by a dot. ***Sequencing using primers located within the V region.

Table 14. Protein and DNA sequence of chimeric 158 VK construct



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Table 15. DNA sequence of 158 VH, primer MHV5 and the sequence derived using primers located within the V region

```
  1 ATGGACTCCAGGCTCAATTTAGTTTTCCTTGTCCTTATTTTAAAAGGTGTCCAGTGTGATGTGCAGCTGGTGGAGTCTGGGGGAGGCTTA 158 VH
  1 ----------------------------------------------------------..G...A.....A....A.............. *** VH
  1 ............................                                                                  MHV5

 91 GTGCAGCCTGGAGGGTCCCGGAAACTCTCCTGTGCAGCCTCTGGATTCACTTTCAGTAGCTTTGGAATGCACTGGGTTCGTCAGGCTCCA 158 VH
 34 ..................................................................................................... *** VH

181 GAGAAGGGGCTGGAGTGGGTCGCATACATTAGTAGTGGCAGTAGTACCATCTACTATGGAGACACAGTGAAGGGCCGATTCACCATCTCC 158 VH
124 ..................................................................................................... *** VH

271 AGAGACAATCCCAAGAACACCCTGTTCCTGCAAATGACCAGTCTAAGGTCTGAGGACACGGCCATGTATTACTGTGCAAGAGAGGGGGGA 158 VH
214 ..................................................................................................... *** VH

361 TATTACTACGGTAGGAGTTACTATACTATGGACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCCTCAGCCAAAACAACAGCCCCA    158 VH
304 ..........................................................................                    *** VH
```

Legend: Residues identical to 158 VH are indicated by a dot . ***Sequencing using primers located within the V region.

Table 16. Chimeric VH leader selection - NL-1 VH leader sequence

158 VH leader	MDSRLNLVFLVLILKGVQC
NL-1 protein	MDSRLNLVFLVLILKGVQC
NL-1 DNA	ATGGACTCCAGGCTCAATTTAGTTTTCCTTGTCCTTATTTTAAAAGGTGTCCAGTGT

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Table 18 - Protein and DNA sequence of chimeric 158 VH

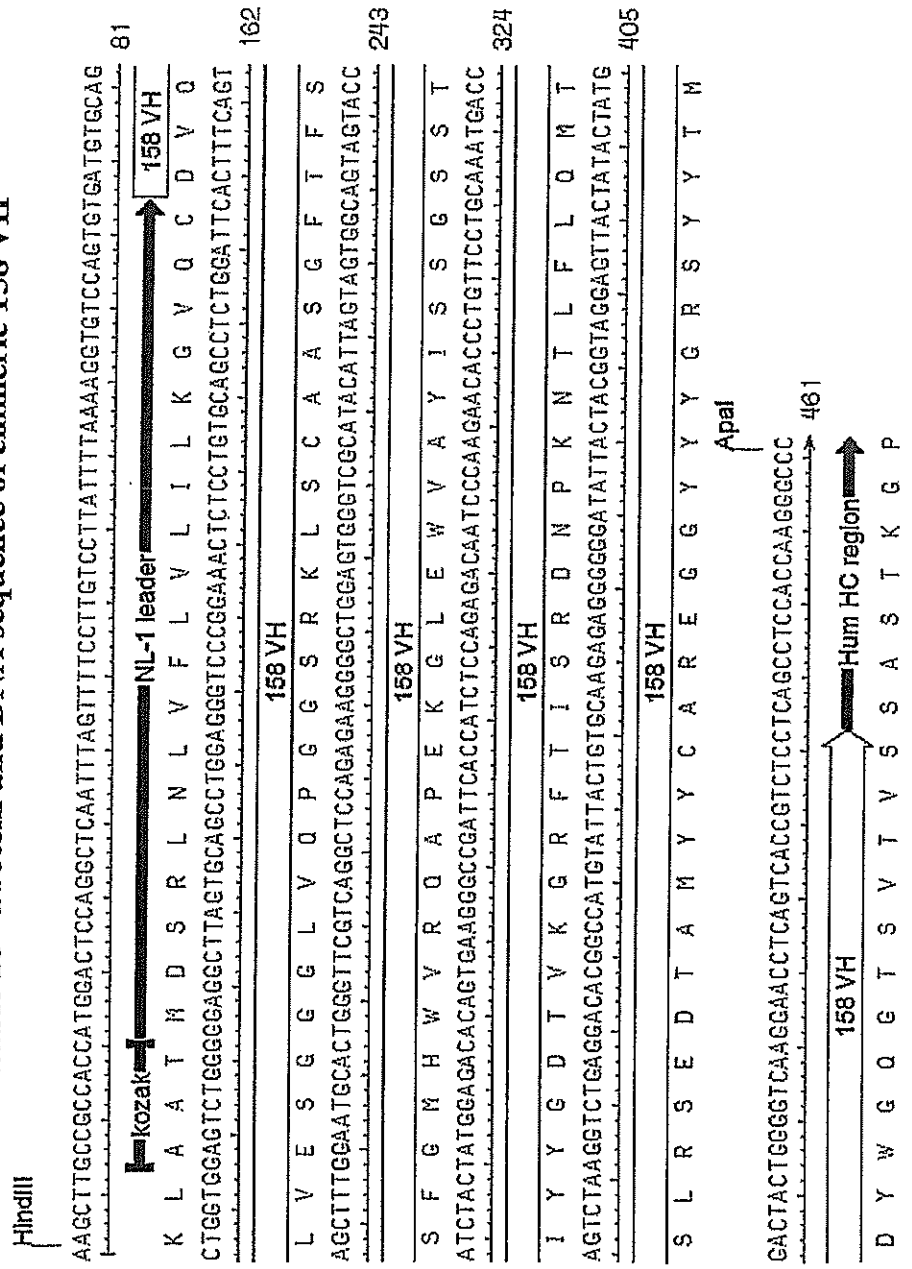


Table 19 - Expression of chimeric 158 antibody in COS cells

Number of Co-transfections	Expression Vector Constructs Co-Transfected	Antibody Concentration (ng/ml)
2 pooled	pG1D200158 and pKN100158	300
2 pooled	pG1D200158 and pKN100158	3700

Legend: Antibody concentration was measured by ELISA in 3-day cultures of transfected COS 7 cells. COS cells were co-transformed with 10μg each of the heavy and light chain chimeric expression vectors pG1D200158 and pKN100158.

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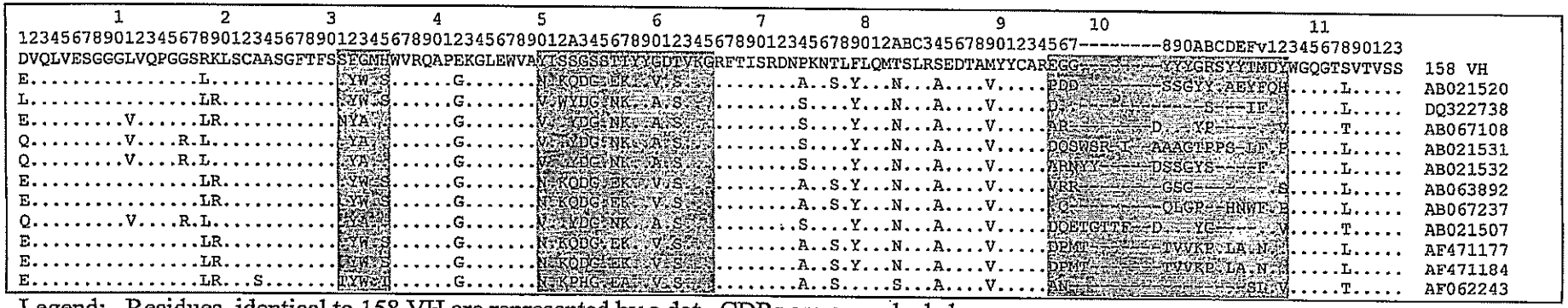
Table 20. Amino acid sequence of 158 VH and 158 VK

VH	DVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMHWVRQAPEKGLEWVAYISSGSSTIYYGDTVKGRFTISRDNPKNTLFLQMTSLRSEDTAMYYCAREGGYYYGRSYYTMDYWGQGTSVTVSS
VK	DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHVPPTFGGGTKLEIK

Table 22. Sequences of best VCI-scoring human VH, compared with 158 VH

Kabat Number[6]	1 2 3 4 5 6 7 8 9 10 11 -12345678901234567890123456789012345AB67890123456789012ABC345678901234567890123456789012ABC3456789012345678 90ABCDEFGHIJKlmnopqrstuvl234567890123
Canonical	1 11 1 1 2 22 2 1
Vernier	* **** *** * * * * * ** *
Interface	I I I I I I I I I I
Kabat CDR	******* ********** **********
158 VH	-DVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMH--WVRQAPEKGLEWVAYISS--GSSTIYYGDTVKGRFTISRDNPKNTLFLQMTSLRSEDTAMYYCAREGGYYYGRSYYT----------MDYWGQGTSVTVSS
AB021520	-EVQLVESGGGLVQPGGSLKLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKQ--DGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARPDDSSGYYSAEY----------FQHWGQGTLVTVSS
AJ556669	-EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKE--DGGEKFYVDSVKGRFTISRDNPKNSLFLQMNSLRAEDTAVYYCARERGHDFWSIYYTH----------FDYWGQGALVTVSS
DQ322738	PLVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVAVIWY--DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDGGSI----------FDYWGQGTLVTVSS
AB067108	-EVQLVESGGGVVQPGGSLRLSCAASGFTFSNYAMH--WVRQAPGKGLEWVAVISY--DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARARDYYYYP----------MDVWGQGTTVTVSS
AB021531	-QVQLVESGGGVVQPGRSLKLSCAASGFTFSSYAMH--WVRQAPGKGLEWVAVISY--DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDQSWSRIAAAGTPPSL----------FDPWGQGTLVTVSS
AB021532	-QVQLVESGGGVVQPGRSLKLSCAASGFTFSSYAMH--WVRQAPGKGLEWVAVISY--DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARARNYYDSSGYS----------FDYWGQGTLVTVSS
AB063892	-EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKQ--DGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARVRRGS----------GDSWGQGTLVTVSS
AB067237	-EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKQ--DGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREQQLGPHNW----------FDPWGQGTLVTVSS
AB021507	-QVQLVESGGGVVQPGRSLKLSCAASGFTFSSYAMH--WVRQAPGKGLEWVAVISY--DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDQETGTTFDYYYYG----------MDVWGQGTTVTVSS
AF471177	-EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKQ--DGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDPMTTVVKPSLAT----------NDYWGQGTLVTVSS
AF471184	-EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKQ--DGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDCVGALGA----------FDIWGQGTMVTVSS
AF062243	CEVQLVESGGGLVQPGGSLRLSCSASGFTFSTYWMT--WVRQAPGKGLEWVANIKP--HGSEAYYVDSVKGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCARANS----------LDVWGQGTTVTVSS
AF174030	CEVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMS--WVRQAPGKGLEWVANIKQ--DGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDGDIGDWW----------FDPWGQGTLVTVSS
AF466141	-QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH--WVRQAPGKGLEWVAVIWY--DGSNKYYADSAKGRFTISRDNSKNTLFLQMNSLRAEDTAVYYCARDKGYYDYVWGSYRSNPKNDA--------FDIWGQGTMVTVSS
AF466142	-QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH--WVRQAPGKGLEWVAVIWY--DGSNKYYADSAKGRFTISRDNSKNTLFLQMNSLRAEDTAVYYCARDKGYYDYVWGSYRSNPKNDA--------FDIWGQGTMVTVSS
AJ245279	-QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH--WVRQAPGKGLEWVAVIWY--DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDRFF----------FDNWGQGTLVTVSS

Table 23. Alignment of 158 VH with the best VCI-scoring human VH



Legend: Residues identical to 158 VH are represented by a dot. CDRs are grey-shaded

Table 24. VH signal peptide selection - 5.5.1 V-gene alignment of 158 VH, human AF062243 and human germline M99649 (VH3-07)

```
DVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMHWVRQAPEKGLEWVAYIS 158 VH
E.....LR...S.....TYW.T.....G.....N.K AF062243
E.....LR.....YW.S.....G.....N.K M99649

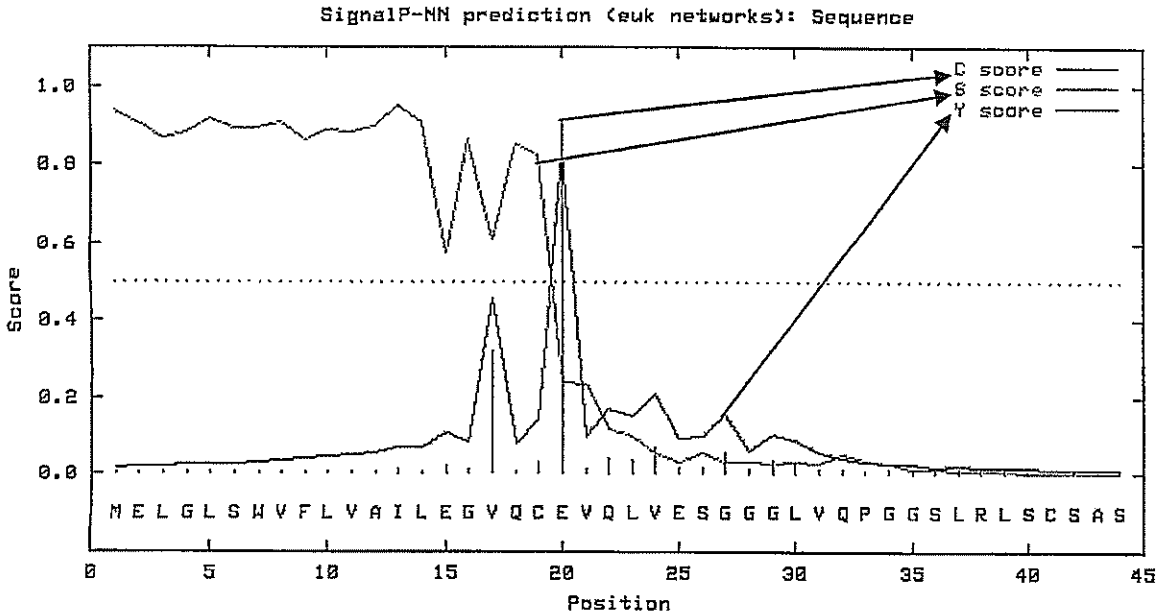
SGSSTIYYGDTVKGRFTISRDNPKNTLFLQMTSLRSEDTAMYYCAR       158 VH
PHG.EA..V.S.....A..S.....S...A....V.....              AF062243
QDG.EK..V.S.....A..S.Y...N...A....V.....              M99649
```

Legend: V-gene residues identical to 158 VH are represented by a dot.

Table 25. Signal peptide of M99649 human germline VH gene

DNA	ATGGAATTGGGGCTGAGCTGGGTTTTCCTTGTTGCTATTTTAGAAGGTGTCCAGTGT
protein	MELGLSWVFLVAILEGVQC

Table 26. M99649 signal peptide cutting prediction



# Measure	Position	Value	Cutoff	signal peptide?
max. C	20	0.909	0.32	YES
max. Y	20	0.836	0.33	YES
max. S	13	0.953	0.87	YES
mean S	1-19	0.859	0.48	YES
D	1-19	0.848	0.43	YES

Highest probability for cleavage is between amino acid residue 19-20: VQC-DV.

Legend: The signal P algorithm[10] generates the combination score Y ,from the cleavage site score C, and the signal peptide score S

Table 27. Generation of 158RHA protein sequence

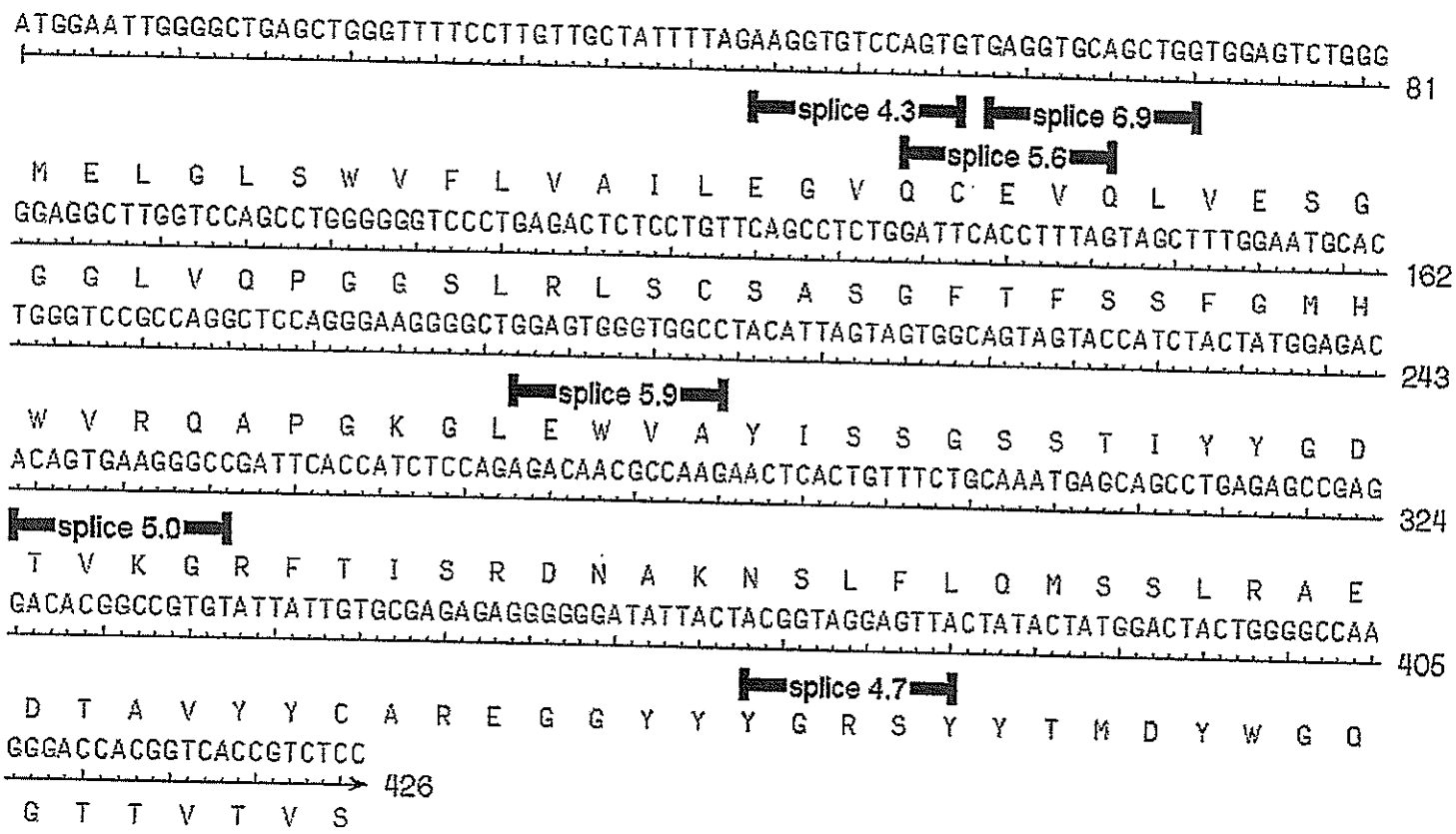
Kabat Number[6]	1 2 3 4 5 6 7 8 9 10 11 01234567890123456789012345678901234567AB8901234567890123456789012ABC3456789012345678901234567890123456789012ABC34567890123456789ABCDEFGHIJK1234567890123
CDR	===H1== =====H2========== =========H3=========
158VH	EVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMH--WVRQAPEKGLEWVAYISS--GSSTIYYGDTVKGRFTISRDNPKNTLFLQMTSLRSEDTAMYYCAREGGYYYGRSYYT----MDYWGQGTSVTVSS
158CDR	SFGMH YISS GSSTIYYGDTVKG EGGYYYGRSYYT MDY
158RHA	-EVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMH--WVRQAPGKGLEWVAYISS--GSSTIYYGDTVKGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCAREGGYYYGRSYYT----MDYWGQGTTVTVS
AF062243 FW	-EVQLVESGGGLVQPGGSLRLSCSASGFTFS WVRQAPGKGLEWVA RFTISRDNAKNSLFLQMSSLRAEDTAVYYCAR WGQGTTVTVS
AF062243	CEVQLVESGGGLVQPGGSLRLSCSASGFTFSTYWMT--WVRQAPGKGLEWVANIKP--HGSEAYYVDSVKGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCARANS----------LDVWGQGTTVTVSS

Table 28. Generation of 158RHA DNA sequence - Generation of 158RHAss DNA sequence

Region	DNA	Protein
VH3-07 leader	ATGGAATTGGGGCTGAGCTGGGTTTTCCTTGTTGCTATTTTAGAAGGTGTCCAGTGT	MELGLSWVFLVAILEGVQC
AF062243 FW1	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTTCAGCCTCTGGATTCACCTTTAGT	EVQLVESGGGLVQPGGSLRLS CSASGFTFS
158CDR1	AGCTTTGGAATGCAC	SFGMH
AF062243 FW2	TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCC	WVRQAPGKGLEWVA
158CDR2	TACATTAGTAGTGGCAGTAGTACCATCTACTATGCAGACACAGTGAAGGGC	YISSGSSTIYYGDTVKG
AF062243 FW3	CGATTCACCATCTCCAGAGACAACGCCAAGAACTCACTGTTTCTGCAAATGAGCAGCCTGAGAGCCGAGGACACGGCCGT GTATTATTGTGCGAGA	RFTISRDNAKNSLFLQMSSLR AEDTAVYYCAR
158CDR3	GAGGGGGGATATTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAG	EGGYYYGRSYYTMDY
AF062243 FW4	TGGGGCCAAGGGACCACGGTCACCGTCTCC	WGQGTTVTVS

Legend: Human VH3-07 leader and AF062243VH FWs intercalated with 158 VH CDRs (grey-shaded) to generate 158RHAss. (relate to Tables 27 and 28)

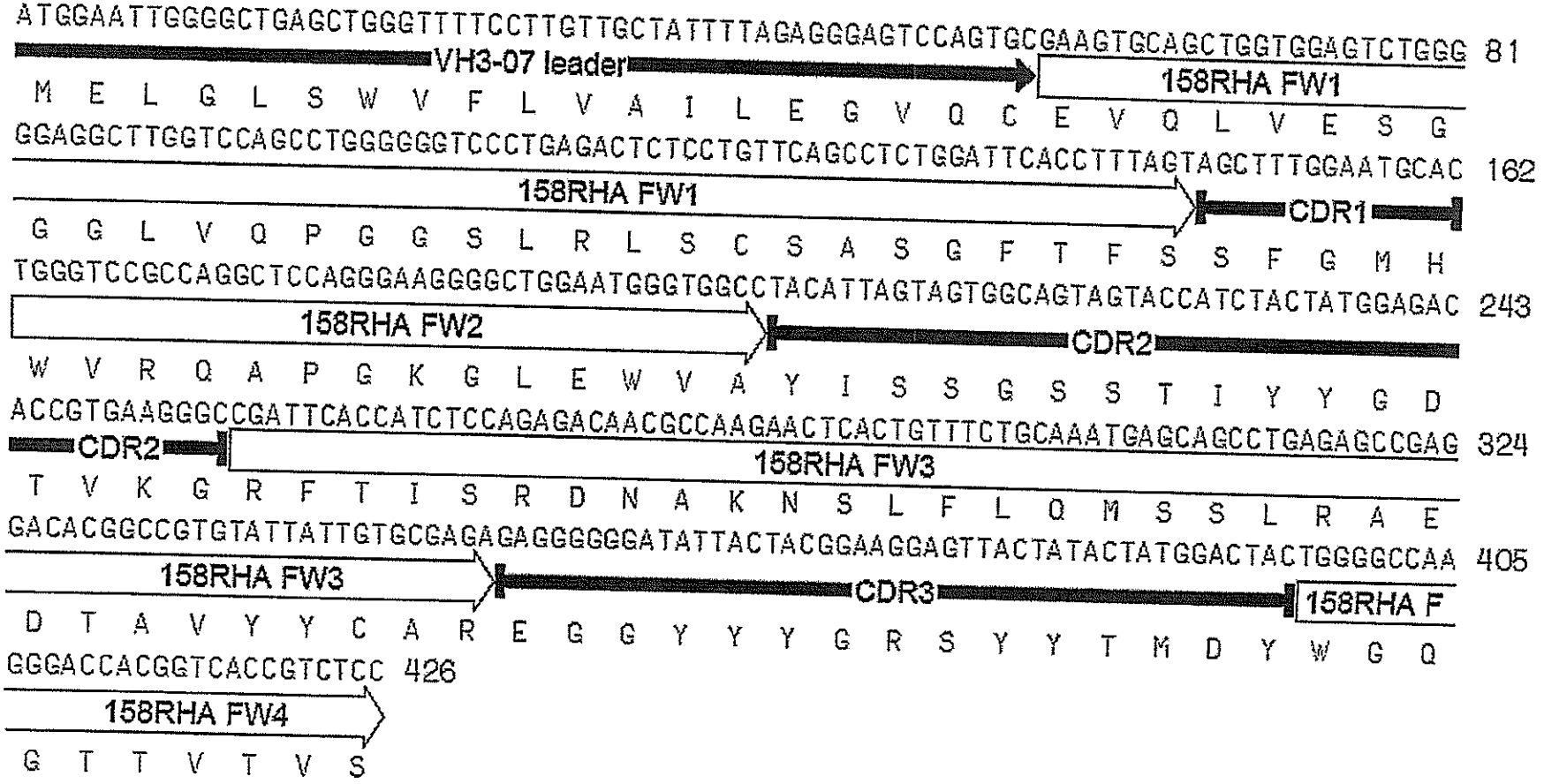
Table 29. DNA and protein sequence of 158RHAss



Legend:
Splice donor sites predicted by Lasergene 6.0 GeneQuest analysis, together with their score, using the human_ds_2 matrix with a threshold of 4.2.

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Table 31. DNA and protein sequence of 158RHA



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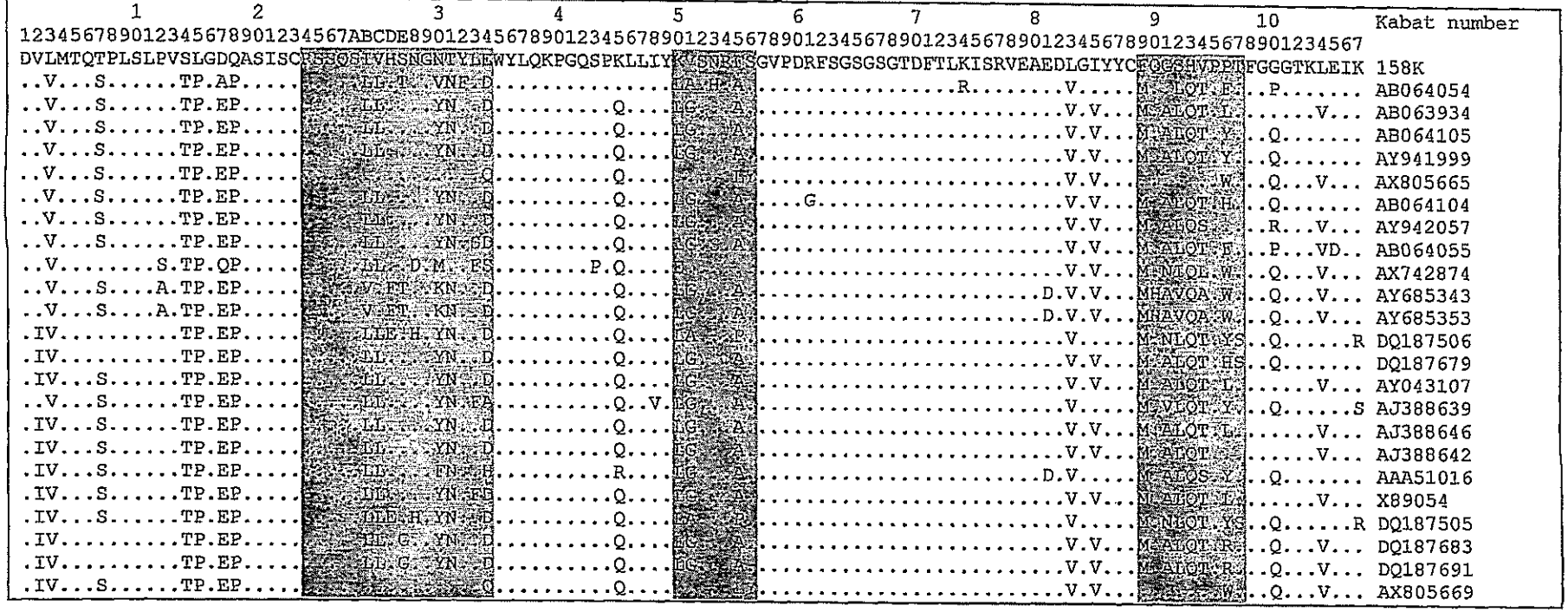
24/45

PCT/SE2007/000292

Table 33. Sequences of best VCI-scoring human VK, compared with 158 VK

Kabat number [5]	1 2 3 4 5 6 7 8 9 10 12345678901234567890123456789ABCDEF012345678901234567890123456789012345678901234567890123456789012345ABCDEF678901234567
Canonical [6]	1 1 1 1 1 2 2 1 3 3 3
Vernier [7]	* * ** **** * * ** * *
Interface [3]	F F F F F F F F F
VCI	1 * 1 1 1 1F*F F F **** * * ** * F F3F 33 * F3F
Kabat CDR	********** ******* **********
158 VK	DVLMTQTPLSLPVSLGDQASISCRSSQSIVHS-NGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHVP------PTFGGGTKLEIK
AB064054	DVVMTQSPLSLPVTPGAPASISCRSSQSLLHT-NGVNFLDWYLQKPGQSPKLLIYLASHRASGVPDRFSGSGSGTDFTLRISRVEAEDVGIYYCMQGLQTP------FTFGPGTKLEIK
AB063934	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------LTFGGGTKVEIK
AB064105 scFv	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------YTFGQGTKLEIK
AY941999 scFv	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------YTFGQGTKLEIK
AX805665 patent	DVVMTQSPLSLPVTPGEPASISCRSSQSIVHS-NGNTYLQWYLQKPGQSPQLLIYKVSNRLYGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP------WTFGQGTKVEIK
AB064104	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDGFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------HTFGQGTKLEIK
AY942057 scFv	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQSP------PTFGRGTKVEIK
AB064055	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYSDWYLQKPGQSPQLLIYLGSSRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------FTFGPGTKVDIK
AX742874	DVVMTQTPLSLSVTPGQPASISCRSSQSLLHS-DGMTYFSWYLQKPGQPPQLLIYEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQNIQLP------WTFGQGTKVEIK
AY685343	DVVMTQSPLSLAVTPGEPASISCRSSQSVVFT-NGKNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEADDVGVYYCMHAVQAP------WTFGQGTKVEIK
AY685353	DVVMTQSPLSLAVTPGEPASISCRSSQSVVFT-NGKNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEADDVGVYYCMHAVQAP------WTFGQGTKVEIK
DQ187506	DIVMTQTPLSLPVTPGEPASISCRSSQSLLES-HGYNYLDWYLQKPGQSPQLLIYLASNRPSGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQNLQTP------YSFGQGTKLEIR
DQ187679	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------HSFGQGTKLEIK
AY043107	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------LTFGGGTKVEIK
AJ388639	DVVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYFAWYLQKPGQSPQLLVYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQVLQTP------YTFGQGTKLEIS
AJ388646	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------LTFGGGTKVEIK
AJ388642	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------PTFGGGTKVEIK
M74470	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGFNYLHWYLQKPGQSPRLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEADDVGIYYCMQALQSP------YTFGQGTKLEIK
X72466	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHN-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQVLQIP------LTFGGGTKVEIK
U95244	DIVMTQSPLSLPVTPGEPASISCRSSQSLLYS-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGDYYCMQALQSP------LTFGGGTKVEIK
AAA51016	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGFNYLHWYLQKPGQSPRLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEADDVGIYYCMQALQSP------YTFGQGTKLEIK
X89054	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHS-NGYNYFDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------LTFGGGTKVEIK
DQ187505	DIVMTQSPLSLPVTPGEPASISCRSSQSLLES-HGYNYLDWYLQKPGQSPQLLIYLASNRPSGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQNLQTP------YSFGQGTKLEIR
DQ187683	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHG-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------RTFGQGTKVEIK
DQ187691	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHG-NGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP------RTFGQGTKVEIK
AX805669	DIVMTQSPLSLPVTPGEPASISCRSSQSIVHS-NGNTYLQWYLQKPGQSPQLLIYKVSNRLYGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP------WTFGQGTKVEIK

Table 34. Alignment of 158 VK with the best VCI-scoring human VK



1 2 3 4 5 6 7 8 9 10	Kabat number
12345678901234567890123456789ABCDE8901234567890123456789012345678901234567890123456789012345678901234567	
DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHVPPTFGGGTKLEIK	158K
..V...S......TP.AP.....S.....LL.T..VNF.D.....MA.H.A.....R.....V.....M.LQT.F..P.....	AB064054
..V...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQT.I.....V...	AB063934
..V...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQT.Y..Q.....	AB064105
..V...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQT.Y..Q.....	AY941999
..V...S......TP.EP.....S.....L.....Q.....Q....LG...F.....V.V.....W..Q...V...	AX805665
..V...S......TP.EP.....S.....LL...YN..D.....Q....LG...A....G.....V.V...M.ALQT.H..Q.....	AB064104
..V...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQS...R...V...	AY942057
..V...S......TP.EP.....S.....LL...YN.SD.....Q....LG...A.....V.V...M.ALQT.F..P...VD..	AB064055
..V.....S.TP.QP.....S.....LL..D.M..ES.....P.Q....LG.....V.V...M.NLQL.W..Q...V...	AX742874
..V...S....A.TP.EP.....S.....V..ET..KN..D.....Q....LG...A.....D.V.V...MHAVQA.W..Q...V...	AY685343
..V...S....A.TP.EP.....S.....V..ET..KN..D.....Q....LG...A.....D.V.V...MHAVQA.W..Q...V...	AY685353
.IV.....TP.EP.....S.....LLE.H.YN..D.....Q....LA...P.....V.....M.NLQT.YS..Q.....R	DQ187506
.IV.....TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQT.HS..Q.....	DQ187679
.IV...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.AIQT.L.....V...	AY043107
..V...S......TP.EP.....S.....LL...YN.FA.....Q..V.LG...A.....V.....M.VLQT.Y..Q.....S	AJ388639
.IV...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQT.L.....V...	AJ388646
.IV...S......TP.EP.....S.....LL...YN..D.....Q....LG...A.....V.V...M.ALQT.....V...	AJ388642
.IV...S......TP.EP.....S.....LL...TN..H.....R....LG...A.....D.V.....M.ALQS.Y..Q.....	AAA51016
.IV...S......TP.EP.....S.....LL...YN.FG.....Q....LG...A.....V.V...M.AIQT.I.....V...	X89054
.IV...S......TP.EP.....S.....LLE.H.YN..D.....Q....LA...R.....V.....M.NLQT.YS..Q.....R	DQ187505
.IV.....TP.EP.....S.....LL.G..YN..D.....Q....LG...A.....V.V...M.ALQT.R..Q...V...	DQ187683
.IV.....TP.EP.....S.....LL.G..YN..D.....Q....LG...A.....V.V...M.ALQT.R..Q...V...	DQ187691
.IV...S......TP.EP.....S.....L.....Q.....Q....LG...F.....V.V.....W..Q...V...	AX805669

Legend: CDR 1, 2 and 3 are grey-shaded.

Table 38. Generation of 158RKA Protein Sequence

Kabat number [6]	1 2 3 4 5 6 7 8 9 10 1234567890123456789012345678ABCDEF8901234567890123456789012345678901234567890123456789012345ABCDEF67890123456
CDR	=======L1========== ==L2=== ======L3=======
158 VK	DVLMTQTPLSLPVSLGDQASISCRSSQSIVHS-NGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHVP-------PTFGGGTKLEIK
CDR	---------- RSSQSIVHS-NGNTYLE ---------- KVSNRFS ---------- FQGSHVP-------PT
158RKA	DVVMTQSPLSLPVTPGAPASISCRSSQSIVHS-NGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLRISRVEAEDVGIYYCFQGSHVP-------PTFGPGTKLEIK
FW	DVVMTQSPLSLPVTPGAPASISC WYLQKPGQSPKLLIY GVPDRFSGSGSGTDFTLRISRVEAEDVGIYYC FGPGTKLEIK
AB064054	DVVMTQSPLSLPVTPGAPASISCRSSQSLLHT-NGVNFLDWYLQKPGQSPKLLIYLASHRASGVPDRFSGSGSGTDFTLRISRVEAEDVGIYYCMQGLQTP------FTFGPGTKLEIK

Legend: 158 VK (grey-shaded) CDRs intercalated in human AB064054 FW to generate 158RKA

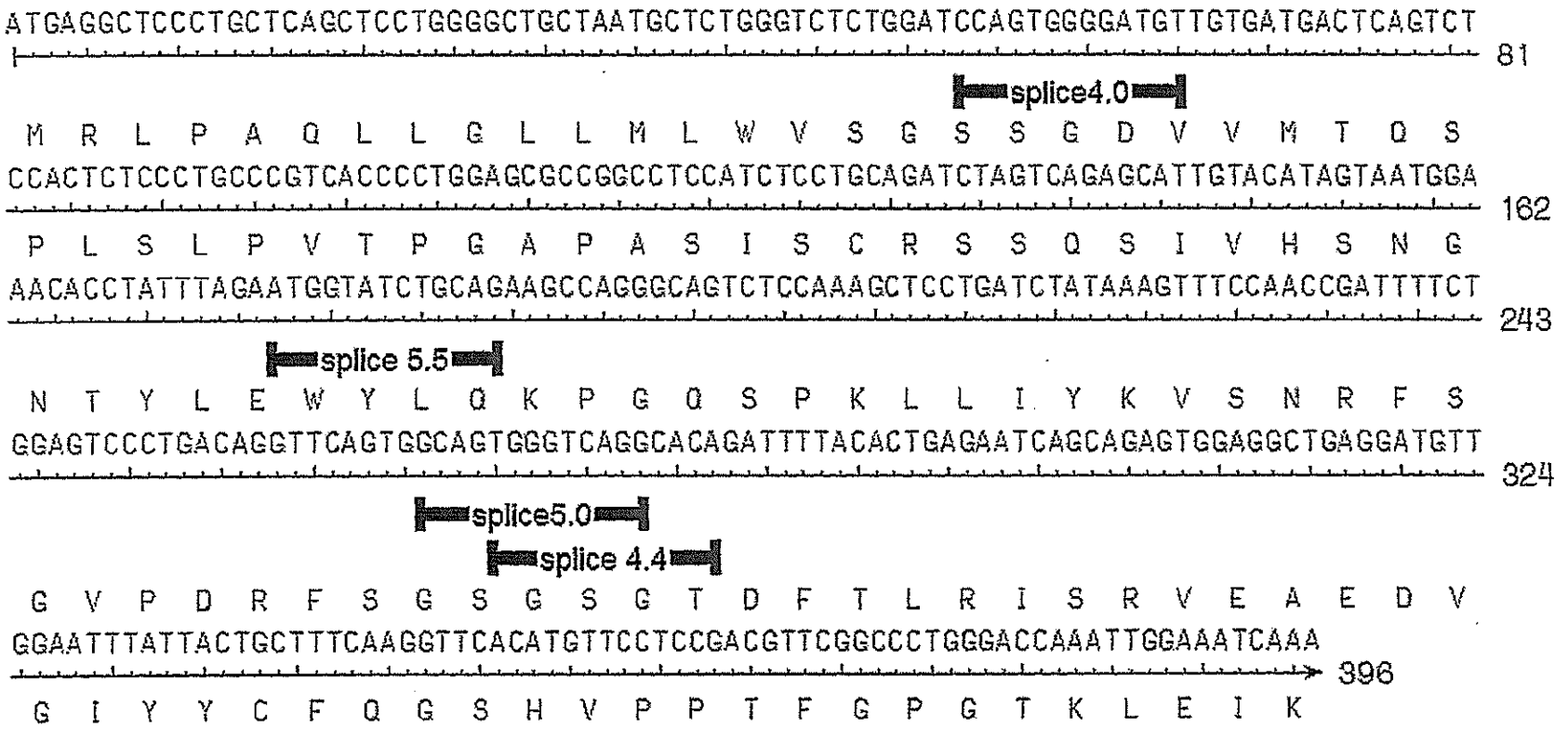
Table 39 - Generation of 158RKAss DNA Sequence - Intercalation of 158VK into AB064054 FW

Region	DNA	Protein
A19 leader	ATGAGGCTCCCTGCTCAGCTCCTGGGGCTGCTAATGCTCTGGGTCTCTGGATCCAGTGGG	MRLPAQLLGLLMLWVSGSSG
AB064054 FW1	GATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGCGCCGGCCTCCATCTCCTGC	DVVMTQSPLSLPVTPGAPASISC
158 CDR1	AGATCTAGTCAGAGCATTGTACATAGTAATGGAAACACCTATTTAGAA	RSSQSIVHSNGNTYLE
AB064054 FW2	TGGTATCTGCAGAAGCCAGGGCAGTCTCCAAAGCTCCTGATCTAT	WYLQKPGQSPKLLIY
158 CDR2	AAAGTTTCCAACCGATTTTCT	KVSNRFS
AB064054 FW3	GGAGTCCCTGACAGGTTCAGTGGCAGTGGGTCAGGCACAGATTTTACACTGAGAATCAGCAGAGTGGAGGC TGAGGATGTTGGAATTTATTACTGC	GVPDRFSGSGSGTDFTLRISRVEAEDVGIYYC
158 CDR3	TTTCAAGGTTCACATGTTCCGTACACG	FQGSHVPPT
AB064054 FW4	TTCGGCCCTGGGACCAAATTGGAAATCAAA	FGPGTKLEIK

Legend: A19 leader and AB064054 FW with intercalated 158 VK (grey-shaded) CDRs to generate 158RKAss

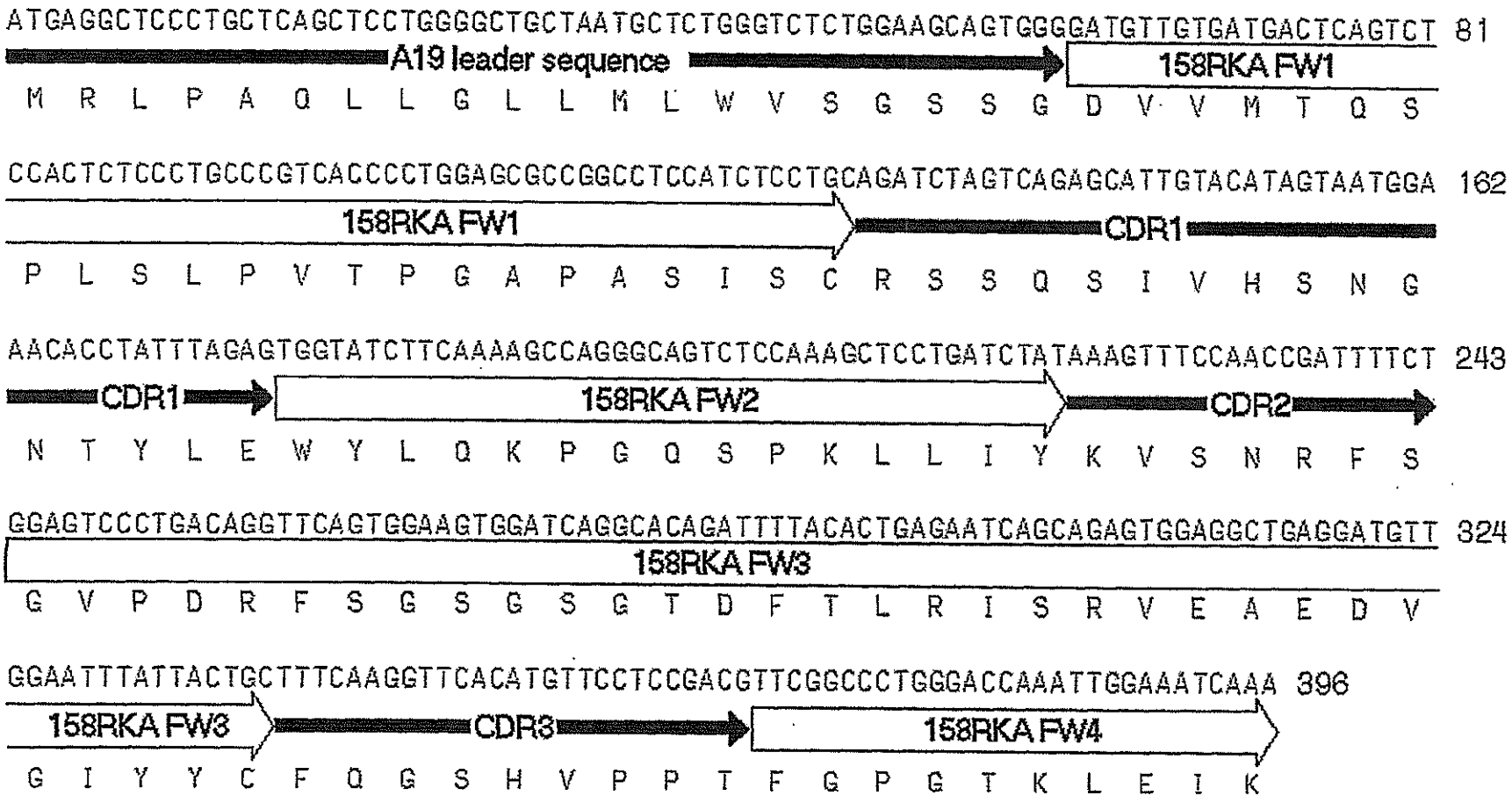
WO 2007/108756 PCT/SE2007/000292

Table 40. 158RKAss DNA sequence



Legend: Splice donor sites predicted by Lasergene 6.0 GeneQuest analysis, together with their score, using the human_ds_2 matrix with a threshold of 4.2.

Table 42. DNA and protein sequence of 158RKA



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Table 43. Further version of humanized 158VHA (158RHB,158RHC,158RHD)

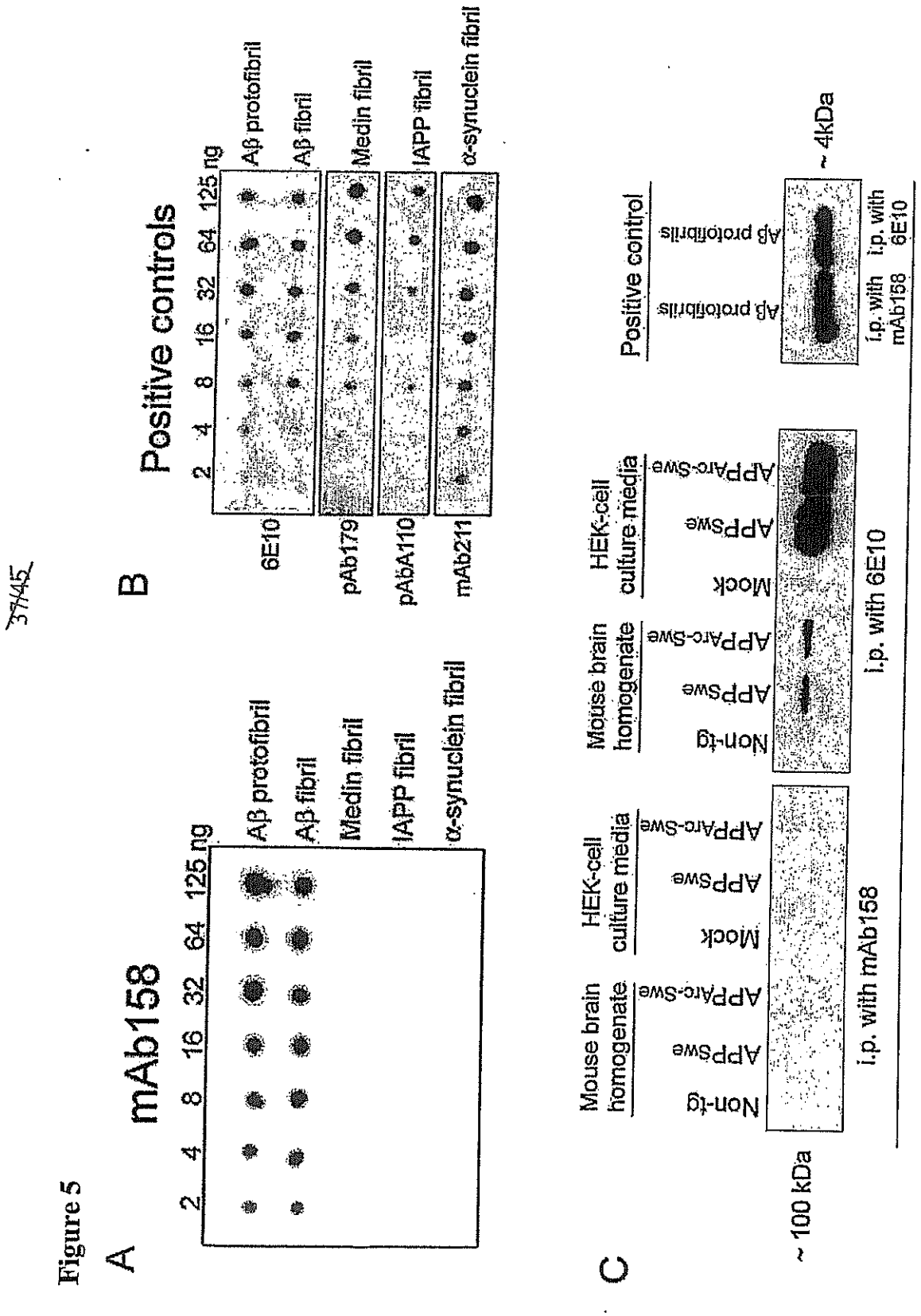
Kabat number[6]	1 2 3 4 5 6 7 8 9 10 11 12345678901234567890123456789012345678901234567890123456789012A3456789012345678901234567890123456789012ABC3456789012345678901234567890ABCDEFv1234567890123
158RHA	EVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSSTIYYGDTVKGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCAREGGYYYGRSYYTMDYWGQGTTVTVS
158RHB	DVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSSTIYYGDTVKGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCAREGGYYYGRSYYTMDYWGQGTTVTVS
158RHC	EVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSSTIYYGDTVKGRFTISRDNEKNSLFLQMSSLRAEDTAVYYCAREGGYYYGRSYYTMDYWGQGTTVTVS
158RHD	EVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSSTIYYGDTVKGRFTISRDNAKNSLFLQMESLRAEDTAVYYCAREGGYYYGRSYYTMDYWGQGTTVTVS

Table 44. Further version of humanized 158VKA (158RKB,158RKC)

Kabat number	1 2 3 4 5 6 7 8 9 10 12345678901234567890123456789012345678901234567890123456789012345678901234567890123456789012345678901234567
158RKA	DVVMTQSPLSLPVTPGAPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLRISRVEAEDVGIYYCFQGSHVPPTFGPGTKLEIK
158RKB	DVLMTQSPLSLPVTPGAPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLRISRVEAEDVGIYYCFQGSHVPPTFGPGTKLEIK
158RKC	DVVMTQSPLSLPVTPGAPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLRISRVEAEDVGIYYCFQGSHVPPTFGEGTKLEIK

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Figure 5



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Figure 6

