

FIG. 1A

Murine A1 VH

ATGGATTGGCTGTGGAACCTGCTATTCTGATGGCAGCTGCCCAAAGTAT
CCAAGCACAGATCCAGTTGGTGCAGTCTGGACCTGAGCTGAAGAAGCCTG
GAGAGACAGTCAAGATCTCCTGCAAGGCTTCTGGATATACCTTCACAAAC
TTTGGAAATGAACTGGGTGAAGCAGGGTCCAGGAGAGGGTTTAAAGTGGAT
GGGCTGGATAAACACCAACACTGGAGAGCCAAGATATGCTGAAGAGTTCA
AGGGACGCT (G/T) TGCCTTTTCTTTGGAAACCACTGCCAGCACTGCCTATTTG
CAGATCAACAACCTCAAAAATGAGGACACGGCTACATATTTCTGTGCAAG
AGACTGGGACGGTGCCTACTTCTTTGACTACTGGGGCCAAGGCACCACTC
TCACAGTCTCCTCA (SEQ ID NO:1)

MDNLWNLFLMAAAOSIOAQIQLVQSGPELKKPGETVKISCKASGYFTN
FGMNWVKQGPGEGLKWMGWINTNTGEPRYAEFPKGR (C/F) APSLETTASTAYL
QINNLKNEATATYFCARDWDGAYFFDYWGQGTTLTVSS (SEQ ID NO:2)

Murine A1 VL

ATGAAGTCACAGACCCAGGTCTTCGTATTTCTACTGCTCTGTGTGTCTGG
TGCTCATGGGAGTATTGTGATGACCCAGACTCCCAAATTCCTGCTTGTTT
CAGCAGGAGACAGGGTGACCATTAACCTGCAAGGCCAGTCAGAGTGTGAGT
AATGATGTAGCTTGGTACCAACAGAGCCAGGGCAGTCTCCTAAACTGTT
GATAAACTTTGCAACCAATCGCTACACTGGAGTCCCTAATCGCTTCACTG
GCAGTGBATATGGGACGGATTTCACTTTACCATCAGCACTGTGCAGGCT
GAAGACCTGGCACTTTATTTCTGTTCAGCAGGATTATAGCTCTCCGTGGAC
GTTCCGTGGAGGCACCAAGCTGGAAATCAAA (SEQ ID NO:3)

MKSQFOVFVFLLLCVSGAHGSI VMTQTPKFLLVSAQDRVTITCKASQSVS
NDVANYQQKPGQSPKLLINFATNRYTGVPNRFTGSGYGTDFFTISTVQA
BDLALYFCQQDYSSPWTFGGGTKLEIK (SEQ ID NO:4)

FIG. 1B

Murine A2 VH

ATGGAATGGAGGATCTTTCTCTTCATCCTGTCAGGAAGTGCAGGTGTCCA
CTCCAGGTTTCAGCTGCAGCAGTCTAGACCTGAGCTGGTGAAGCCTGGGG
CTTCAGTGAAGATGTCCTGCAAGGCTTCTGGATACACTTTCAGTGAATAT
GTTATAAGCTGGGTGAAGCAGAGAACTGGACAGGGCCTTGAGTGGATTGG
AGAGATTTATCCTGGAAGTAATAGTATTTATTACAATGAGAACTTCAAGG
GCAGGGCCACACTGACTGCAGACAAATCCTCCAGCACAGCCTACATGCAG
CTCAGCAGCCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAATGGG
GGGTAACCTACGGCTTTGACTATTGGGGCCAAGGCACCACTCTCACAGTCT
CCTCA (SEQ ID NO:5)

MEWKIFLFLISGTAGVHSQVQLQQRPELVKPGASVKMSCKASGYTFTDY
VISWVKQRTGQGLEWIGBIYPGSNSIIYNEKFKGRATLTADKSSSTAYMQ
LSSLTSEDSAVYFCAMGGNYGFDYWGQGTTLTVSS (SEQ ID NO:6)

Murine A2 VL

ATGGATTTTCAGGTGCAGATTTTCAGCTTCCTGCTAATCAGTGCCTCAGT
CATAATGTCCAGAGGACAAATTGTTCTCACCCAGTCTCCAGCAATCATGT
CTGCATCTCTAGGGGAACGGGTCACTTGACCTGCACTGCCAGCTCAAGT
GTAAATTCCAATTACTTACACTGGTACCAGCAGAAGCCAGGATCCTCCCC
CAAACCTCTGGATTTATAGCACATCCAACTGGCTTCTGGAGTCCCAGCTC
GCTTCAGTGGCAAGTGGGTCTGGGACCTCTTACTCTCTCACAATCAGCAGC
ATGGAGGCTGAAGATGCTGCCACTTATTACTGCCACCAGTATCATCGTTC
CCCGCTCACGTTCTGGTCTGGGACCAAGCTGGAGCTGAAA (SEQ ID NO:7)

MDFOVQIFSFLLISASVIMSRGQIVLTQSPAIMSASLGERVTLTCTASSS
VNSNYLHWYQQKPGESPKLWIYSTENLASGVPARFSGSGSCTSYSLTISS
MEAEDAATYYCHQYHRSPLTFGAGTKLELK (SEQ ID NO:8)

FIG. 1C

Murine A3 VH

ATGCTGTTGGGGCTGAAGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGT
GCATTGTGAGGTGCAGCTTGTGAGTCTGGTGGAGGATTGGTGCAGCCTA
AAGSGTCATTGAAACTCTCATGTGCAGCCTCTGGATTACCTTCAATACC
TACGCCATGAACTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAATGGT
TGCTCGCATAAGAAGTAAAAGTAATAATTATGCAACATATTATGCCGATT
CAGTGAAGACAGGTTACCATCTCCAGAGATGATTACAAAGCATGCTC
TATCTGCAAATGAACAACTTGAAAAGTGAAGACACAGCCATGTATT (G/A) CTG
TGTGAGACAGTGGGATTACGACCTCAGGGCTATGAACTACTGGGGTCAAG
GAACCTCAGTCACCGTCTCCTCA (SEQ ID NO:9)

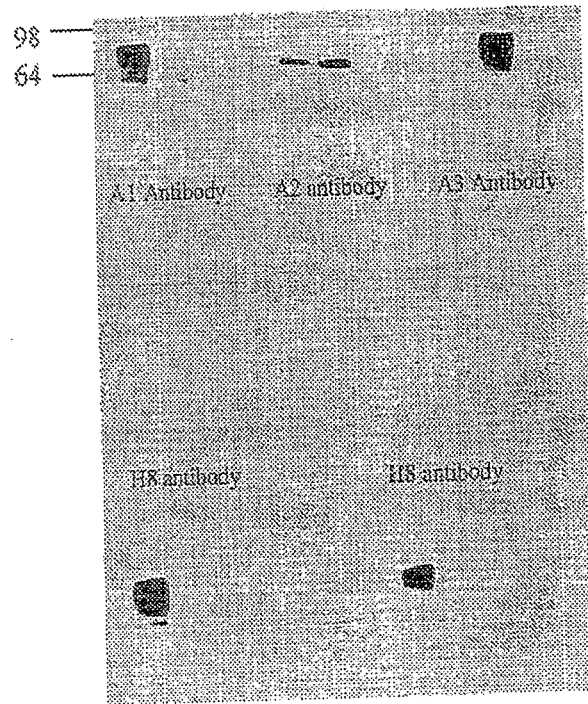
MLLGLKWVFFVVFYOGVHCEVQLVESBGLVQPKGSLKLSCAASGFTFNT
YAMNWVRQAPGKGLEWVARIRSKSNNYATYYADSVKDRFTISRDDSQSML
YLQMNILKTEDTANY (C/Y) CVRQWDYDVRAMNYWGQGTSTVTVSS (SEQ ID
NO:10)

Murine A3 VL

ATGGAGACACATTCTCAGGTCTTTGTATACATGTTGCTGTGGTTGTCTGG
TGTTGAAGGAGACATTGTGATGACCCAGTCTCACATATTCATGTCCACAT
CAGTAGGAGACAGGGTCAGCATCACCTGCAAGGCCAGTCAGGATGTGGAT
ACTGCTGTAGCCTGGTATCAACAGAAACCAGGGCAATCTCCTAACTACT
GATTTACTGGGCATCCACCCGGCTCACTGGAGTCCCTGATCGCTTCACAG
GCAGTGGATCTGGGACGGATTTCACTCTCACCATTAGCAATGTGCAGTCT
GAAGACTTGGCAGATTATTTCTGTCAGCAATATAGCAGCTATCCGTACAC
GTTCCGGAGGGGGGACCAAGCTGGAAATAAAA (SEQ ID NO:11)

METHSQVFVYMLLWLSQVEGDIVMTQSHIFMSTSVGDRVSITCKASQDVE
TAVAWYQOKPGQSPKLLIYWASTRLTGVPDRFTGSGSGTDFTLTISNVQS
EDLADYFCQYSSYPYTFGGGTKLEIK (SEQ ID NO:12)

FIG. 2



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FIG. 3A

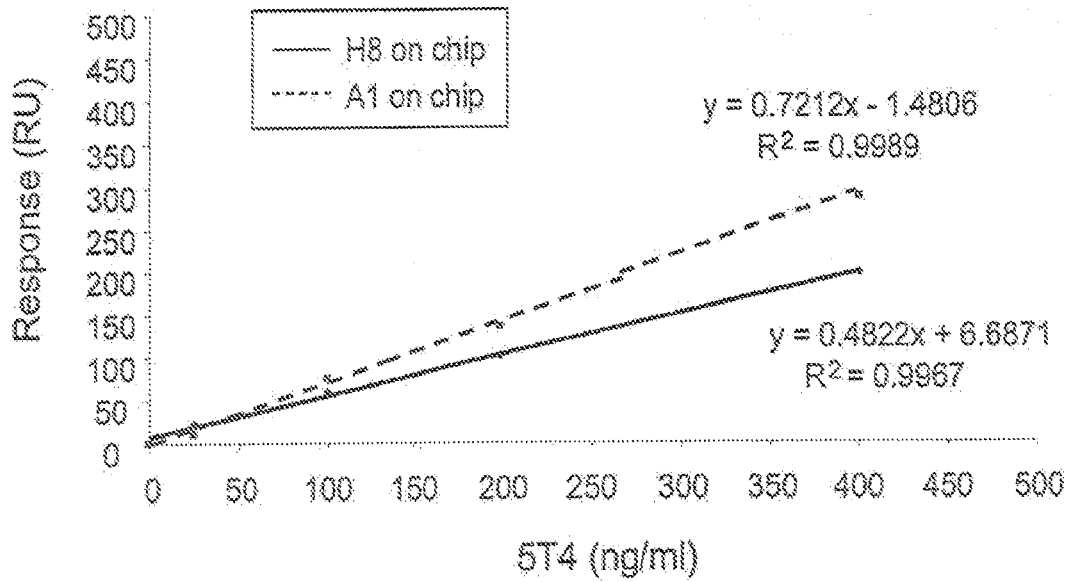
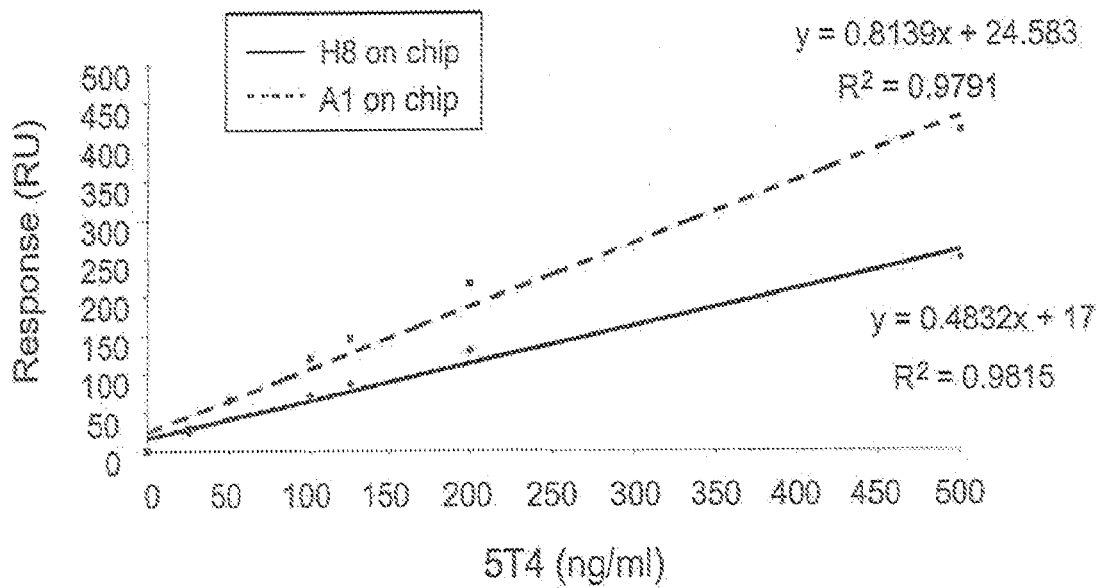


FIG. 3B



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FIG. 4A

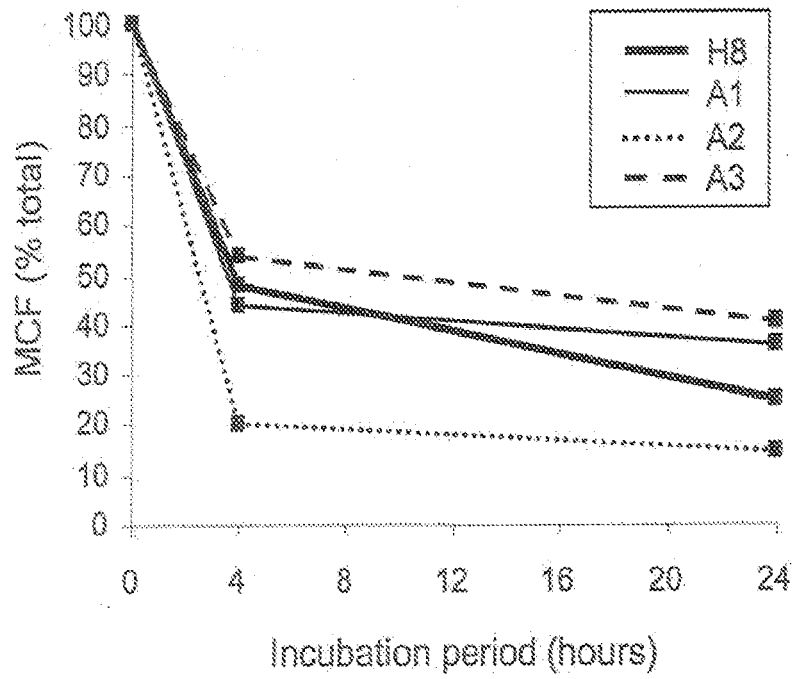


FIG. 4B

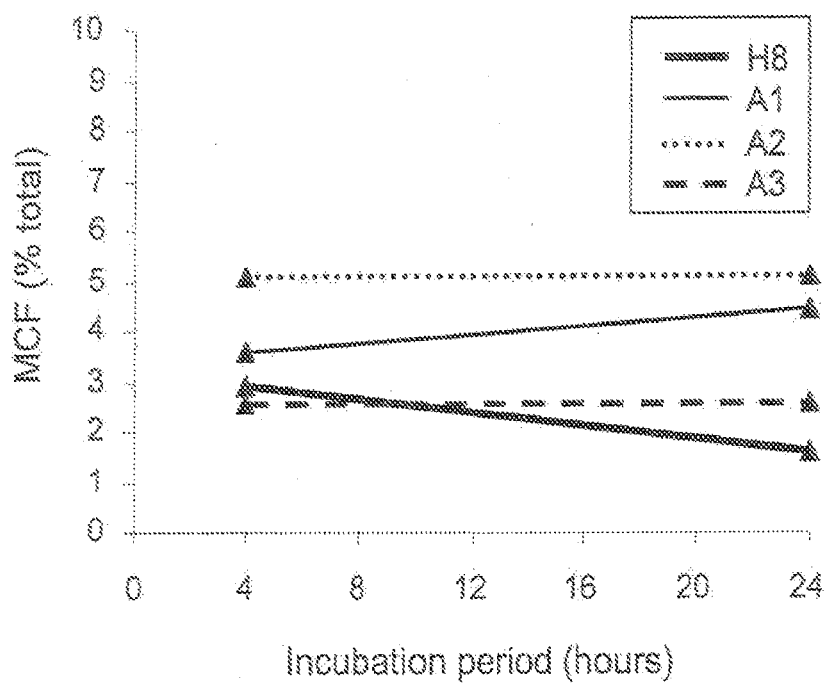


FIG. 4C

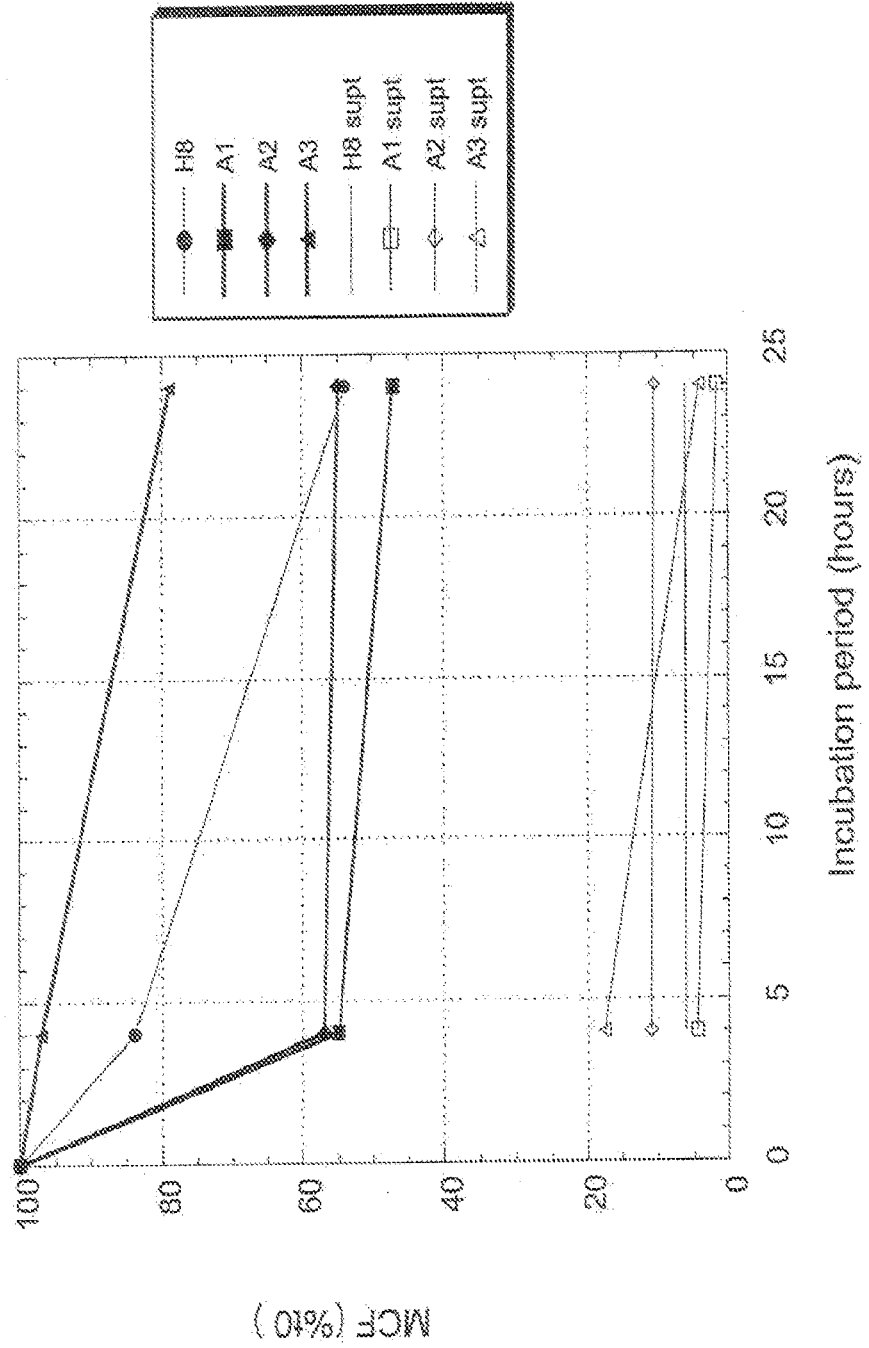
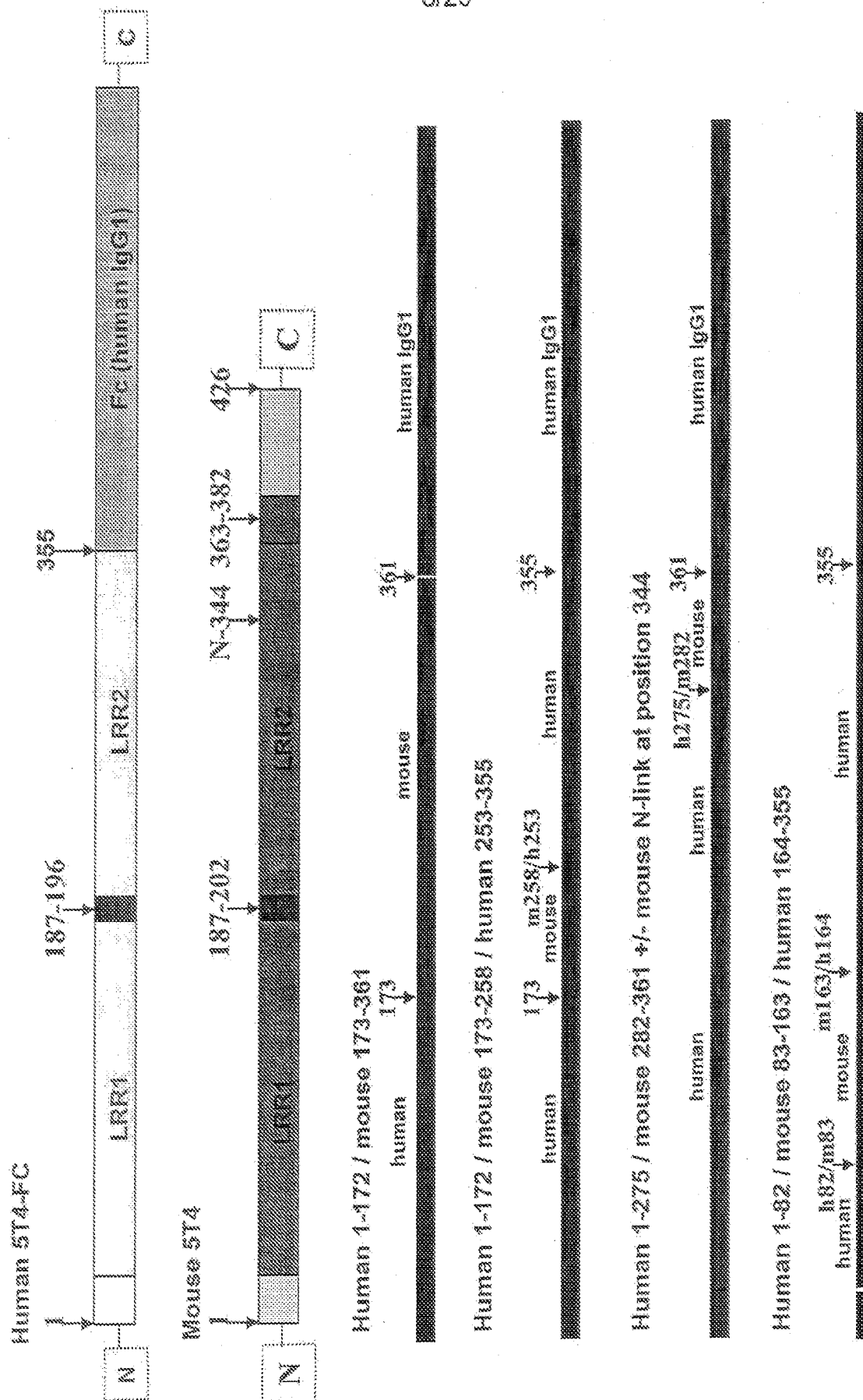
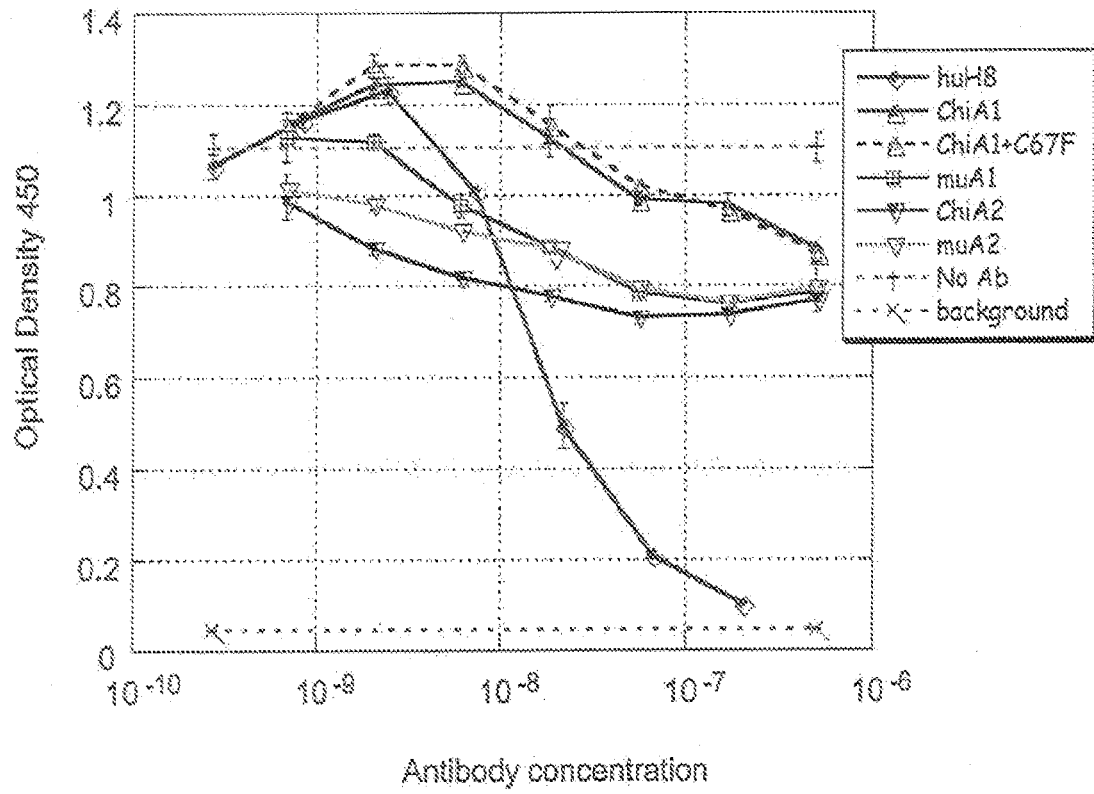


FIG. 5



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FIG. 6A



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FIG. 6B

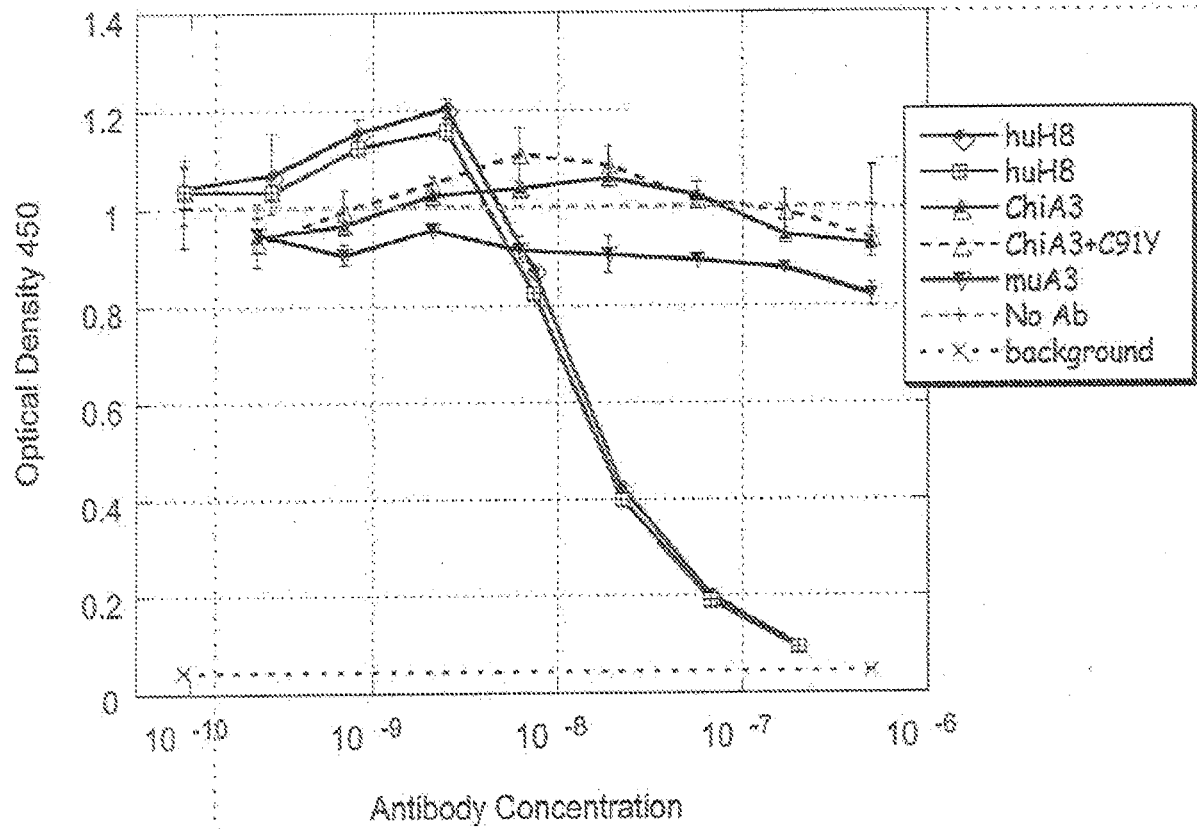


FIG. 7

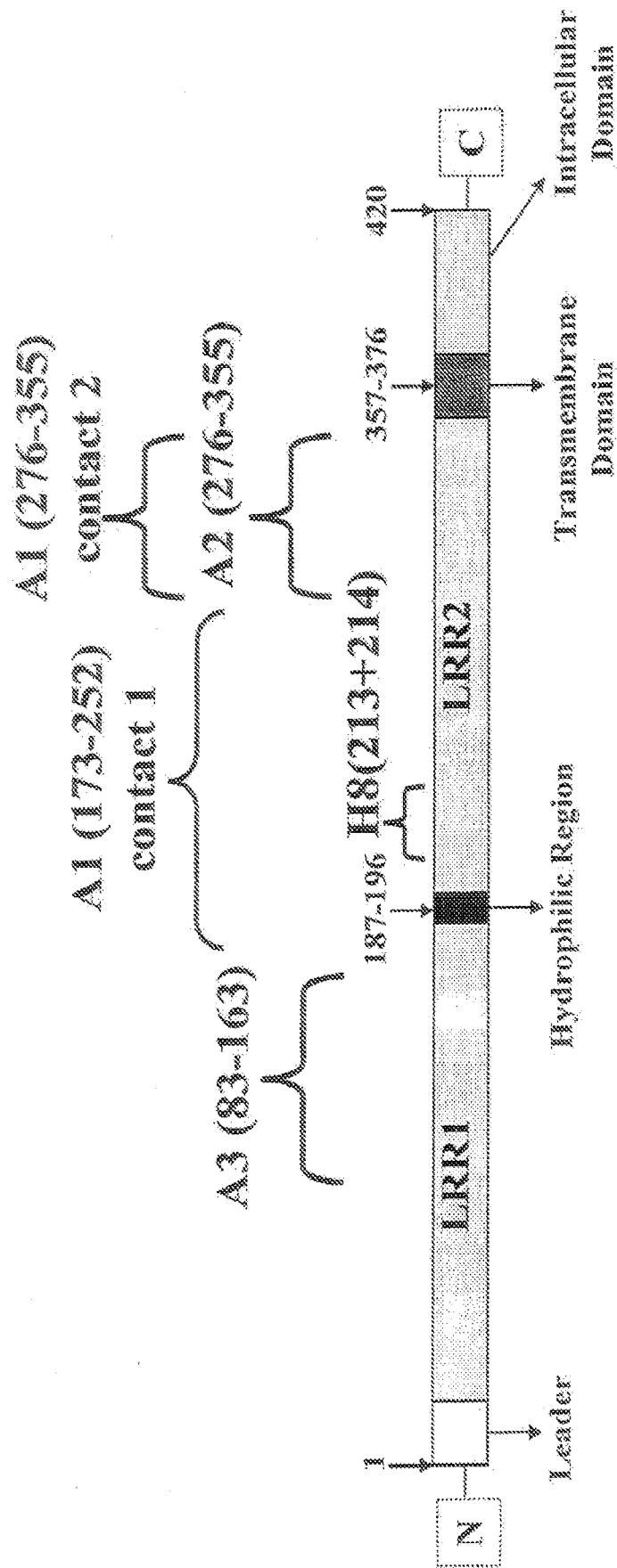


FIG. 8

MDAMB435/5T4

MDAMB435/neo

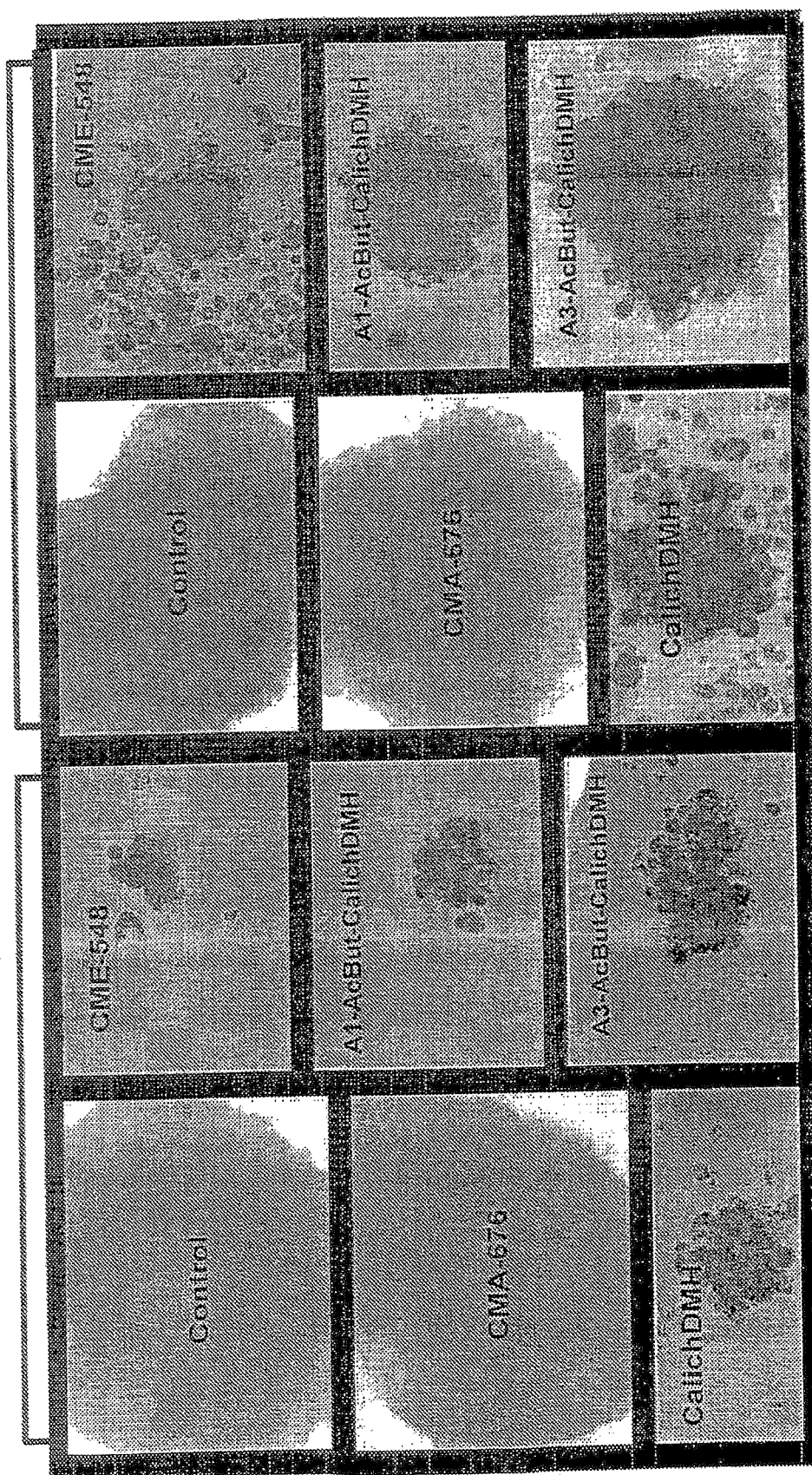


FIG. 9A

Humanized A1 VH-version 1.0 DNA

CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCAGTGAAG
 GTTTCCTGCAAGGCTTCTGGATATACCTTCACAACTTTGGAATGAACTGGGTGCGA
 CAGGCCCTGGACAAGGGCTTAAGTGGATGGGATGGATAAACACCAACTGGAGAG
 CCAAGATATGCTGAAGAGTTCAAGGGACGGTTTGTCTTCTCCTTGGACACCTCTGTC
 AGCACTGCCATATCTGCAGATCTCCAGCCTGAAGGCTGAGGACACTGCCGTGTATTAC
 TGTGCCAGAGACTGGGACGGTGCCTACTTCTTTGACTACTGGGGCCAAGGCACCCCTT
 GTCACAGTCTCCTCA (SEQ ID NO:48)

Humanized A1 VH-version 1.0 Protein

QVQLVQSGSELKKPGASVKVSCKASGYTFNFGMNVVRQAPGQGLKWMGWINTNTGE
PRYAEFFKGRFVFSLDTSVSTAYLQISLKAEDTAVYYCARDWDGAYFFDYWGQGT
 LVTVSS (SEQ ID NO:49)

Humanized A1 VH-version 1.1 DNA

CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCAGTGAAG
 GTTTCCTGCAAGGCTTCTGGATATACCTTCACAACTTTGGAATGAACTGGGTGCGA
 CAGGCCCTGGACAAGGGCTTGAGTGGATGGGATGGATAAACACCAACTGGAGAG
 CCAAGATATGCTGAAGAGTTCAAGGGACGGTTTGTCTTCTCCTTGGACACCTCTGTC
 AGCACTGCCATATCTGCAGATCTCCAGCCTGAAGGCTGAGGACACTGCCGTGTATTAC
 TGTGCCAGAGACTGGGACGGTGCCTACTTCTTTGACTACTGGGGCCAAGGCACCCCTT
 GTCACAGTCTCCTCA (SEQ ID NO:50)

Humanized A1 VH-version 1.1 Protein

QVQLVQSGSELKKPGASVKVSCKASGYTFNFGMNVVRQAPGQGLEWMGWINTNTGE
PRYAEFFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARDWDGAYFFDYWGQGT
 LVTVSS (SEQ ID NO:51)

Humanized A1 VH-version 1.2 (CDR grafted into the DP-21 germline, VH7 sub-group)

QVQLVQSGSELKKPGASVKVSCKASGYTFNFGMNVVRQAPGQGLEWMGWINTNTGE
PRYAEFFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARDWDGAYFFDYWGQGT
 LVTVSS (SEQ ID NO:52)

Any of the following amino acids could be substituted at these designated positions
 K46, C67, S82a and N82a.

FIG. 9B

Humanized A1 VH-version 2.0 DNA

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGA
 CTCTCCTGTGCAGCCTCTGGATATACCTTCACAACTTTGGAATGAACTGGGTCCGC
 CAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCTGGATAAACACCAACACCGGTGAG
 CCAAGATATGCTGAAGAGTTCAAGGGACGATTACCATCTCCAGAGACAACGCCAAG
 AACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACCGCTGTGTATTAC
 TGTGCCAGAGACTGGGACGGTGCCTACTTCTTTGACTACTGGGGCCAAGGCACCCTT
 GTCACAGTCTCCTCA (SEQ ID NO:53)

Humanized A1 VH-version 2.0 Protein (CDR grafted into the DP-54 germline, VH3 sub-group)

EVQLVESGGGLVQPGGSLRLSCAASGYTFTNFGMNWVRQAPGKGLEWVAVINTNTGE
 PRYAEFFKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDWDGAYFFDYWGQGL
 VTVSS (SEQ ID NO:54)

Any of the following amino acids could be substituted at these designated positions
 K46, M48, G49, C67, L71, T73, T74, A75, S76 and A78.

Humanized A1 VH-version 2.1 DNA

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGA
 CTCTCCTGTGCAGCCTCTGGATATACCTTCACAACTTTGGAATGAACTGGGTCCGC
 CAGGCTCCAGGGAAGGGGCTGAAGTGGATGGGCTGGATAAACACCAACACCGGTGAG
 CCAAGATATGCTGAAGAGTTCAAGGGACGATTACCATCTCCCTGGACAACGCCAAG
 TCCTCAGCCTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACCGCTGTGTATTAC
 TGTGCCAGAGACTGGGACGGTGCCTACTTCTTTGACTACTGGGGCCAAGGCACCCTT
 GTCACAGTCTCCTCA (SEQ ID NO:55)

Humanized A1 VH-version 2.1 Protein

EVQLVESGGGLVQPGGSLRLSCAASGYTFTNFGMNWVRQAPGKGLKWMGWINTNTGE
 PRYAEFFKGRFTISLDNAKSSAYLQMNSLRAEDTAVYYCARDWDGAYFFDYWGQGL
 VTVSS (SEQ ID NO:56)

FIG. 9C

Humanized A1 VL-version 1.0 DNA

GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGCC
 ACCATCAACTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTACCAGCAG
 AAACCAGGACAGCCTCCTAAGCTGCTCATTTACTTTGCAACCAATCGCTACACTGGA
 GTCCCTGACCGCTTCTCCGGCAGCGGATCCGGCACAGATTTCACTCTCACCATCAGC
 AGCCTGCAGGCTGAAGATGTGGCAGTTTATTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:57)

Humanized A1 VL-version 1.0 Protein (CDR grafted into the DPK24 germline, VKIV sub-group)

DIVMTQSPDSLAVSLGERATINCKASQSVSNDAVWYQQKPGQPPKLLIYPATNRYTG
 VPDRLFSGSGTDFLTITISLQAEDVAVYYCQDYSSPWFPGQGTKVEIK (SEQ ID
 NO:58)

Any of the following amino acids could be substituted at these designated positions
 S43, N49, N60, T63, Y67, F73, L85 and F87.

Humanized A1 VL-version 1.1 DNA

GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGCC
 ACCATCAACTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTACCAGCAG
 AAACCAGGACAGCCTCCTAAGCTGCTCATTTACTTTGCAACCAATCGCTACACTGGA
 GTCCCTGACCGCTTCTCCGGCAGCGGATACGGCACAGATTTCACTCTCACCATCAGC
 AGCCTGCAGGCTGAAGATGTGGCAGTTTATTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:59)

Humanized A1 VL-version 1.1 Protein

DIVMTQSPDSLAVSLGERATINCKASQSVSNDAVWYQQKPGQPPKLLIYPATNRYTG
 VPDRLFSGSGYGTDFLTITISLQAEDVAVYYCQDYSSPWFPGQGTKVEIK (SEQ
 ID NO:60)

Humanized A1 VL-version 2.0 DNA

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGAGACAGAGTC
 ACCATCACTTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTATCAGCAG
 AAACCAGGCAAAGCCCCCTAAGCTCCTGATCTATTTTGCAACCAATCGCTACACTGGA
 GTCCCATCCCGCTTCAGCGGCAGCGGATCCGGCACAGATTTCACTCTCACCATCAGC
 AGCCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:61)

FIG. 9D

Humanized A1 VL-version 2.0 Protein (CDR grafted into the DPK9 germline, VKI sub-group)

DIQMTQSPSSLSASVGDRVITITCKASQSVSNDAVWYQOKPGKAPKLLIYFATNRYTG
VPSRFGSGSGTDFTLTISSLQPEDFATYYCQDDYSSPWTFGQGTKVEIK (SEQ
ID NO:62)

Any of the following amino acids could be substituted at these designated positions
V3, Q42, S43, N49, N60, Y67, F73, L85 and F87.

Humanized A1 VL-version 2.1 DNA

GACATCCAGATGACCCAGTCTCCATCCTCCCTGCTCTGCATCTGTCCGAGACAGAGTC
ACCATCACTTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTATCAGCAG
AAACCAGGCAAATCCCCTAAGCTCCTGATCTATTTTGCAACCAATCGCTACACTGGA
GTCCCATCCCGCTTCAGCGGCAGCGGATCCGGCACAGATTTCACTCTCACCATCAGC
AGCCTGCAACCTGAAGATTTTGCAACTTACTACTGTCTCAGCAGGATTATAGCTCTCCC
TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:63)

Humanized A1 VL-version 2.1 Protein

DIQMTQSPSSLSASVGDRVITITCKASQSVSNDAVWYQOKPGKSPKLLIYFATNRYTG
VPSRFGSGSGTDFTLTISSLQPEDFATYYCQDDYSSPWTFGQGTKVEIK (SEQ
ID NO:64)

Humanized A1 VL-version 2.2 DNA

GACATCCAGATGACCCAGTCTCCATCCTCCCTGCTCTGCATCTGTCCGAGACAGAGTC
ACCATCACTTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTATCAGCAG
AAACCAGGCAAAGCCCCCTAAGCTCCTGATCAATTTTGCAACCAATCGCTACACTGGA
GTCCCATCCCGCTTCAGCGGCAGCGGATCCGGCACAGATTTCACTCTCACCATCAGC
AGCCTGCAACCTGAAGATTTTGCAACTTACTACTGTCTCAGCAGGATTATAGCTCTCCC
TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:65)

Humanized A1 VL-version 2.2 Protein

DIQMTQSPSSLSASVGDRVITITCKASQSVSNDAVWYQOKPGKAPKLLINPATNRYTG
VPSRFGSGSGTDFTLTISSLQPEDFATYYCQDDYSSPWTFGQGTKVEIK (SEQ
ID NO:66)

FIG. 9E

Humanized A1 VL-version 2.3 DNA

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTCCGAGACAGAGTC
 ACCATCACTTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTATCAGCAG
 AAACCAGGCAAAGCCCCCTAAGCTCCTGATCTATTTTGCAACCAATCGCTACACTGGA
 GTCCCAAACCGCTTCAGCGGCAGCGGATCCGGCACAGATTTCACTCTCACCATCAGC
 AGCCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:67)

Humanized A1 VL-version 2.3 Protein

DIQMTQSPSSLSASVGDRTITCKASQSVSNDAWYQQKPGKAPKLLIYFATNRYTG
 VPNRFGSGSGTDFTLTISSLQPEDFATYYCQDYSSPWTFGGGTKVEIK (SEQ
 ID NO:68)

Humanized A1 VL-version 2.4 DNA

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTCCGAGACAGAGTC
 ACCATCACTTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTATCAGCAG
 AAACCAGGCAAAGCCCCCTAAGCTCCTGATCTATTTTGCAACCAATCGCTACACTGGA
 GTCCCATCCCGCTTCAGCGGCAGCGGATACGGCACAGATTTCACTCTCACCATCAGC
 AGCCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:69)

Humanized A1 VL-version 2.4 Protein

DIQMTQSPSSLSASVGDRTITCKASQSVSNDAWYQQKPGKAPKLLIYFATNRYTG
 VPSRFSGSGYGTDFLTISSLQPEDFATYYCQDYSSPWTFGGGTKVEIK (SEQ
 ID NO:70)

Humanized A1 VL-version 2.5 DNA

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTCCGAGACAGAGTC
 ACCATCACTTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTATCAGCAG
 AAACCAGGCAAAGCCCCCTAAGCTCCTGATCTATTTTGCAACCAATCGCTACACTGGA
 GTCCCATCCCGCTTCAGCGGCAGCGGATCCGGCACAGATTTCACTTTTACCATCAGC
 AGCCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:71)

Humanized A1 VL-version 2.5 Protein

DIQMTQSPSSLSASVGDRTITCKASQSVSNDAWYQQKPGKAPKLLIYFATNRYTG
 VPSRFSGSGSGTDFTFTISSLQPEDFATYYCQDYSSPWTFGGGTKVEIK (SEQ
 ID NO:72)

FIG. 9F

Humanized A1 VL-version 3.0 DNA

GAAATTGTGATGACACAGTCTCCAGCCACCCTGTCCCTGTCTCCAGGCGAAAGAGCC
 ACCCTCTCCTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTACCAGCAG
 AAACCTGGGGCAGGCTCCCAGGCTGCTGATCTATTTTGCAACCAATCGCTACACTGGC
 ATCCCAGCCCCGCTTCTCCGGCAGCGGCTCCGGCACAGACTTCACTCTCACCATCAGC
 AGCCTGCAGCCTGAAGATTTTGCAGTTTATTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:73)

Humanized A1 VL-version 3.0 Protein (CDR grafted into the DPK23 germline, VKIII sub-group)

EIVMTQSPATLSLSPGERATLSCKASQSVSNDAVANYQOKPGQAPRLLIYFATNRYTG
 IPARFSGSGSGTDFTLTISSLQPEDFAVYYCQDYSSFWTFGGGTKVEIK (SEQ
 ID NO:74)

Any of the following amino acids could be substituted at these designated positions
 F10, S43, N49, V58, N60, Y67, F73, L85 and F87.

Humanized A1 VL-version 3.1 DNA

GAAATTGTGATGACACAGTCTCCAGCCACCCTGTCCCTGTCTCCAGGCGAAAGAGCC
 ACCCTCTCCTGCAAGGCCAGTCAGAGTGTGAGTAATGATGTGGCTTGGTACCAGCAG
 AAACCTGGGGCAGGCTCCCAGGCTGCTGATCTATTTTGCAACCAATCGCTACACTGGC
 ATCCCAGCCCCGCTTCTCCGGCAGCGGCTACGGCACAGACTTCACTCTCACCATCAGC
 AGCCTGCAGCCTGAAGATTTTGCAGTTTATTACTGTCAGCAGGATTATAGCTCTCCC
 TGGACCTTCGGTCAGGGCACCAAGGTGGAAATCAAA (SEQ ID NO:75)

Humanized A1 VL-version 3.1 Protein

EIVMTQSPATLSLSPGERATLSCKASQSVSNDAVANYQOKPGQAPRLLIYFATNRYTG
 IPARFSGSGYGTDFTLTISSLQPEDFAVYYCQDYSSFWTFGGGTKVEIK (SEQ
 ID NO:76)

FIG. 9G

huA2 VH Version 1.0 (CDR grafted into the DP-75 germline, VH1 subgroup)

QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYVISWVRQAPGQGLEWMGEIYPGSNS
IYYNEKFVKGRVTMTRDPSISSTAYMELSRLRSDDTAVYYCARGGNYGFDYWGQGT
 VSS (SEQ ID NO:77)

Any of the following amino acids could be substituted at these designated positions
 K38, R40, T41, I48, I69, T75, Q81, S82b, E85 and M94.

huA2 VH Version 2.0 (CDR grafted into the DP-54 germline, VH3 subgroup)

EVQLVESGGGLVQPGGSLRLSCAASGYTFTDYVISWVRQAPGKGLEWVAEIYPGSNS
IYYNEKFVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARGGNYGFDYWGQGT
 VSS (SEQ ID NO:78)

Any of the following amino acids could be substituted at these designated positions
 K38, R40, T41, I48, G49, A67, A71, K73, S74, S76, A78 and M94.

huA2 VL Version 1.0 (CDR grafted into the DPK20 germline, VKIII subgroup)

EIVLTQSPATLSLSPGERATLSCITASSESVNSNYLHWYQQKPGAPRLLIYSTNLA
SLPDRFSGSGSGTDFTLTISRLEPEDFAVYYCHQYHRSPLTFGGGTKVEIK (SEQ
 ID NO:79)

Any of the following amino acids could be substituted at these designated positions
 S43, W47, A60, S70, S77, M78, and A80.

huA2 VL Version 2.0 (CDR grafted into the DPK9 germline, VKI subgroup)

DIQMTQSPSSLSASVGDRVTITCTASSESVNSNYLHWYQQKPGKAPKLLIYSTNLA
SLPDRFSGSGSGTDFTLTISLQPEDFATYYCHQYHRSPLTFGGGTKVEIK (SEQ
 ID NO:80)

Any of the following amino acids could be substituted at these designated positions
 V3, L4, S43, W47, S70, and M78.

FIG. 9H

huA3 VH Version 1.0 (CDR grafted into the DP-29 germline, VH3 subgroup)

EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIIRSKSNN
YATYYADSVKDRFTISRDDSKNSLYLQMNSLKTEDTAVYYCARQWDYDVRAMNYWGQ
 GTLVTVSS (SEQ ID NO: 81)

Any of the following amino acids could be substituted at these designated positions
 A49, Q75, S76, M89, C91 and V93.

huA3 VH Version 2.0 (CDR grafted into the DP-54 germline, VH3 subgroup)

EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKSNN
YATYYADSVKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCARQWDYDVRAMNYWGQ
 GTLVTVSS (SEQ ID NO: 82)

Any of the following amino acids could be substituted at these designated positions
 D73, Q75, S76, M89, C91 and V93.

huA3 VL Version 1.0 (CDR grafted into the DPK24 germline, VKIV sub-group)

DIVMTQSPFDSLAVSLGERATINCKASQDQDVTAVAWYQOKPGQPPKLLIYWASTRLTG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQCYSSYPYTFGQGTKLEIK (SEQ
 ID NO: 83)

Any of the following amino acids could be substituted at these designated positions
 S43, D85 and F87.

huA3 VL Version 2.0 (CDR grafted into the DPK9 germline, VKI subgroup)

DIQMTQSPFSSLSASVGDRTTITCKASQDQDVTAVAWYQOKPGKAPKLLIYWASTRLTG
VPDRFSGSGSGTDFTLTISSLQPEDFATYYCQCYSSYPYTFGQGTKLEIK (SEQ
 ID NO: 84)

Any of the following amino acids could be substituted at these designated positions
 3V, Q42, S43, D60, D85 and F87.

FIG. 10A

	FR1	CDR1	FR2	SEQ ID NO.
VH1 consensus	QVQLVQSGAEVKKPGASVKVSCKASGYTFT		WVRQAPGQGLEWMG	25-27
VH1 locus				
1-3 1-02	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	G--YYMH	WVRQAPGQGLEWMG	14
1-3 1-03	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	S--YAMH	WVRQAPGQGLEWMG	15
1-3 1-08	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	S--YDIN	WVRQATGQGLEWMG	16
1-2 1-18	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	S--YGIS	WVRQAPGQGLEWMG	17
1-U 1-24	QVQLVQSGAEVKKPGASVKVSCKVSGYTLT	E--LEMH	WVRQAPGKGLEWMG	18
1-3 1-45	QMQLVQSGAEVKKPGASVKVSCKASGYTFT	Y--RYLH	WVRQAPGQALEWMG	19
1-3 1-46	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	S--YYMH	WVRQAPGQGLEWMG	20
1-3 1-58	QMQLVQSGAEVKKPGTSVKVSCKASGYTFT	S--SAVQ	WVRQARGQRLIEWIG	21
1-2 1-69	QVQLVQSGAEVKKPGSSVKVSCKASGGTFS	S--YAIS	WVRQAPGQGLEWMG	22
1-2 1-e	QVQLVQSGAEVKKPGSSVKVSCKASGGTFS	S--YAIS	WVRQAPGQGLEWMG	23
1-2 1-f	EVQLVQSGAEVKKPGATVKISCKVSGYITFT	D--YYMH	WVQQAPEGKLEWMG	24

FIG. 10A-1

SEQ ID NO.

FR3

CDR2

VH1 consensus

VH1 locus

22/29

RVTITRDTSTSTAYMELSSLRSEDTAVYYCAR 25-27

1-3	1-02	WINE--NSCGTNYAOKFQG	RVTMTRDTSISTAYMELSRLESDDTAVYYCAR	14
1-3	1-03	WINA--GNGNTKYSQKFG	RVTITRDTSASTAYMELSSLRSEDTAVYYCAR	15
1-3	1-08	WMNP--NSCNTGYAOKFQG	RVTMTRNTSISTAYMELSSLRSEDTAVYYCAR	16
1-2	1-18	WISA--YNGCNTNYAOKLQG	RVTMTTDTSTSTAYMELSRLESDDTAVYYCAR	17
1-0	1-24	GFDP--EDGETIYAOKFQG	RVTMTEDTSTDTAYMELSSLRSEDTAVYYCAT	18
1-3	1-45	WITP--FNGCNTNYAOKFQD	RVTITRDRSMSTAYMELSSLRSEDTAVYYCAR	19
1-3	1-46	LINE--SGGSTSYAOKFQG	RVTMTRDTSISTVYMELSSLRSEDTAVYYCAR	20
1-3	1-58	WIVV--GSCNTNYAOKFOE	RVTITRDMSTSTAYMELSSLRSEDTAVYYCAA	21
1-2	1-69	GIIP--IFGTANYAOKFQG	RVTITADESTSTAYMELSSLRSEDTAVYYCAR	22
1-2	1-e	GIIP--IFGTANYAOKFQG	RVTITADKSTSTAYMELSSLRSEDTAVYYCAR	23
1-2	1-f	LVDP--EDGETIYAOKFQG	RVTITADTSTDTAYMELSSLRSEDTAVYYCAT	24

FIG. 10B

Amino acid sequences of human germline genes of VH 7 subgroup

DP-21 (VH 7) GenBank Accession No. CAA43346 (SEQ ID NO:88)

QVQLVQSGSELKKPGASVKVSCKASGYTFTSYAMNWVRQAPGQGLEWMG
WIN
TNTGNFTYAQGFTGRFVPSLDTSVSTAYLQISSLKAEDTAVYYCARDSESGYSY
DFWSGYFYYYMDVWGKGITVTVSS

Amino acid sequences of human germline genes of VH 3 subgroup

DP-54 (VH 3-07) GenBank Accession No. AB019440 (SEQ ID NO:89)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANI
KQDGSEKYYVDSVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCAR

DP-47 (VH3-23) GenBank Accession No. AB019439 (SEQ ID NO:90)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAK

DP-49 (VH 3-30) GenBank Accession No. AB019439 (SEQ ID NO:91)

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVI
SYDGSNKYYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAR

DP-53 (VH3-74) GenBank Accession No. AB019437 (SEQ ID NO:92)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYWMHWVRQAPGKGLVWVSRI
NSDGSSTSYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAR

DP-48 (VH3-13) GenBank Accession No. AB019440 (SEQ ID NO:93)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYDMHWVRQATGKGLEWVSAI
GTAGDTYYPGSVKGRFTISRDNKNTLYLQMNSLRAGDTAVYYCAR

FIG. 11

SEQ ID NO.	CDR1									
	L16_germline	...	EIVNTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
29	L16_germline	...	EIVNTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
30	L2_germline	...	EIVNTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
31	A27_germl_VL	...	EIVLTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
32	L6_germl_VL	...	EIVLTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
33	L10_germl_VL	...	EIVNTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
34	L25_germl_VL	...	EIVNTQS	PATLSVSPGE	RATLSQ	SVSS	NLAWY	QOKPGQAPRL		
	CDR2									
	L16_germline	LIYGASTRAT								
29	L16_germline	LIYGASTRAT								
30	L2_germline	LIYGASTRAT								
31	A27_germl_VL	LIYGASTRAT								
32	L6_germl_VL	LIYGASTRAT								
33	L10_germl_VL	LIYGASTRAT								
34	L25_germl_VL	LIYGASTRAT								
	CDR3									
	L16_germline	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				
29	L16_germline	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				
30	L2_germline	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				
31	A27_germl_VL	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				
32	L6_germl_VL	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				
33	L10_germl_VL	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				
34	L25_germl_VL	GIPIAFSGSG	SGTEFTLTIS	SLQSEDFAVY	YCCQYNNWPP	TV				

FIG. 12

SEQ ID NO.	FR1	CDR1	FR2
35	O12 DIQMTQSPSSLSASVGDRVITTC	RASQSISS	WYQQKPGKAPKLLIY
36	O2 DIQMTQSPSSLSASVGDRVITTC	RASQSISS	WYQQKPGKAPKLLIY
37	O18 DIQMTQSPSSLSASVGDRVITTC	QASQDISN	WYQQKPGKAPKLLIY
38	O8 DIQMTQSPSSLSASVGDRVITTC	QASQDISN	WYQQKPGKAPKLLIY
39	A20 DIQMTQSPSSLSASVGDRVITTC	RASQGISN	WYQQKPGKVPKLLIY
40	L1 DIQMTQSPSSLSASVGDRVITTC	RASQGISN	WFQQKPGKAPKSLIY
41	L15 DIQMTQSPSSLSASVGDRVITTC	RASQGISS	WYQQKPEKAPKSLIY
42	L8 DIQLTQSPSPFLSASVGDRVITTC	RASQGISS	WYQQKPGKAPKLLIY
43	L12 DIQMTQSPSTLSASVGDRVITTC	RASQSISS	WYQQKPGKAPKLLIY
44	L11 AIQMTQSPSSLSASVGDRVITTC	RASQSISS	WYQQKPGKAPKLLIY

FIG. 12-1

SEQ ID NO.	CDR2	FR3	CDR3
35	O12 AASSLQS	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQSYSTP
36	O2 AASSLQS	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQSYSTP
37	O18 DASNLET	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQYDNLFP
38	O8 DASNLET	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQYDNLFP
39	A20 AASLTQS	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QKYNAP
40	L1 AASSLQS	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQYNSYP
41	L15 AASSLQS	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQYNSYP
42	L8 AASLTQS	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQLNSYP
43	L12 DASSLES	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQYNSYS
44	L11 DASSLES	GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYC	QQYNSYS

FIG. 13

Amino acid sequences of human germline genes of Vk I subgroup

DPK9 (O12, Vk I) GenBank Accession No. X59315 (SEQ ID NO:94)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSL
QSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTP

O2 (O2, Vk I) GenBank Accession No. X59312 (SEQ ID NO:95)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSL
QSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTP

DPK 1 (Vk I,)18) GenBank Accession No. M64856 (SEQ ID NO:96)

DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASN
LETGVPSRFSGSGSGTDFTFTISLQPEDFATYYCQQYDNL

DPK 7 (Vk I, L15) GenBank Accession No. K01323 (SEQ ID NO:97)

DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLIYAASS
LQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQYNSYP

Amino acid sequences of human germline genes of Vk IV subgroup

DPK24 (B3, VkiV) GenBank Accession No. Z00023 (SEQ ID NO:98)

DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPPKL
LIYWASTRESGVPRFSGSGSGTDFTLTISLQAEDVAVYYCQQYYSTP

Amino acid sequences of human germline genes of Vk III subgroup

DPK 23 (Vk-III, L25) GenBank Accession No. X72820 (SEQ ID NO:99)

EIVMTQSPATLSLSPGERATLSCRASQSVSSSYLSWYQQKPGQAPRLLIYGAST
RATGIPARFSGSGSGTDFTLTISLQPEDFAVYYCQQDYNLP

FIG. 14

Human IgG4_mutated (hinge mutation S241P) (SEQ ID NO:45)

ASTKGPSVFPLAFCRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKVDKRVESKYGPPCPFCPAPEF
LGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKP
REEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQV
YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGEFF
LYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSPGK

Human IgG1 (SEQ ID NO:46)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYTCNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA
PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAKGQPRE
PQVYTLPPSRREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG
SPFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

Human Kappa (SEQ ID NO:47)

TVAAPSVEFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 15

Black-tailed Marmoset 5T4

MPGGCSRGPAAGNGRLRLARLALVLLGWVSSSSPTSSASSSSSSAPFLASAVSAQPPLPGQCPA
LCECSEAARTVKCVNRNLTEVPTDLPPYVRNLFLTGNQLAVLPAGAFARVPPLAELAALNLSGS
RLEDVQAGAFEHLPSLRQLDLSHNPLAVLSPFAFSGSNASVSAPSPLVELILNHIVPPEDERNN
RSFEGMVVAALRAGGALHGLHRLELASNHFLYLPRDVLAQLPSLRHLDLSNNSLVSLTYVSFRN
LTHLESLHLEDNALKVLHNGTLAELQGLPHVRVFLDNNPWVCDCHMADMVAWLKETEVVQGYQ
LTCAFPEKMRNRVLLELNSADLDCDPILPPSLQTSYVFLGIVLALIG (SEQ ID NO:85)

Cynomolgus monkey 5T4

MPGGCSRGPAAGDGRLRLARLALVLLGWVSSSSPTSSASSFSSSAPFLASAASAQPPLPDQCPA
LCECSEAARTVKCVNRNLTEVPTDLPLYVRNLFLTGNQLAVLPAGAFARRPPLAELAALNLSGS
RLDEVRAAGAFEHLPSLRQLDLSHNPLAYLSPFAFSGSNASISAPSPLVELILNHIVPPDDKRQN
RSFEGMVAAALVAGRALQGLHLELASNHFLYLPRDVLAQLPSLRYLDLSNNSLVSLTYVSFRN
LTHLESLHLEDNALKVLHNGTLAELQGLPHVRVFLDNNPWVCDCHMADMVTWLKQTEVVQGKDR
LTCAFPEKMRNRVLLELNSADLDCDPILPPSLQTSYVFLGIVLALIGAIFFLLVLYLNRKGIKKW
MHNIRDACRDHMEGYHYRYEINADPRLTNLSSNSDV (SEQ ID NO:86)