

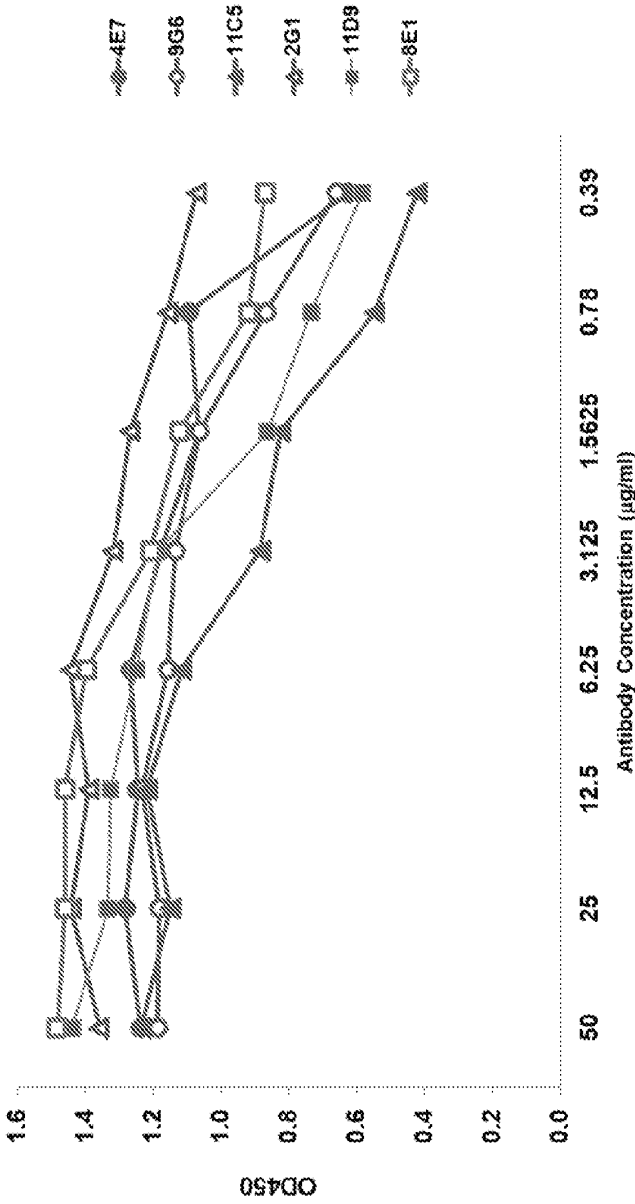


Figure 1

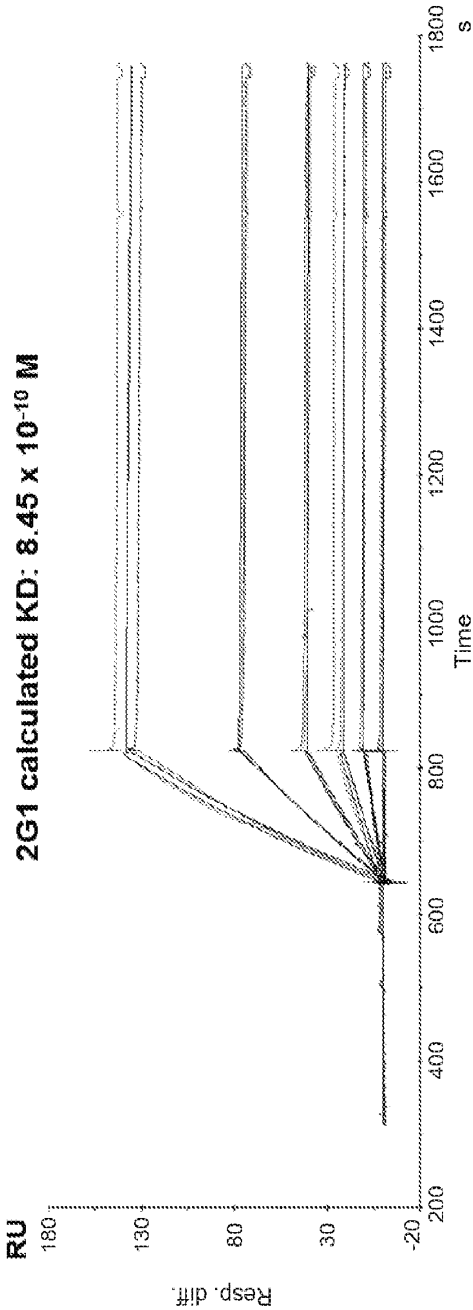


Figure 2

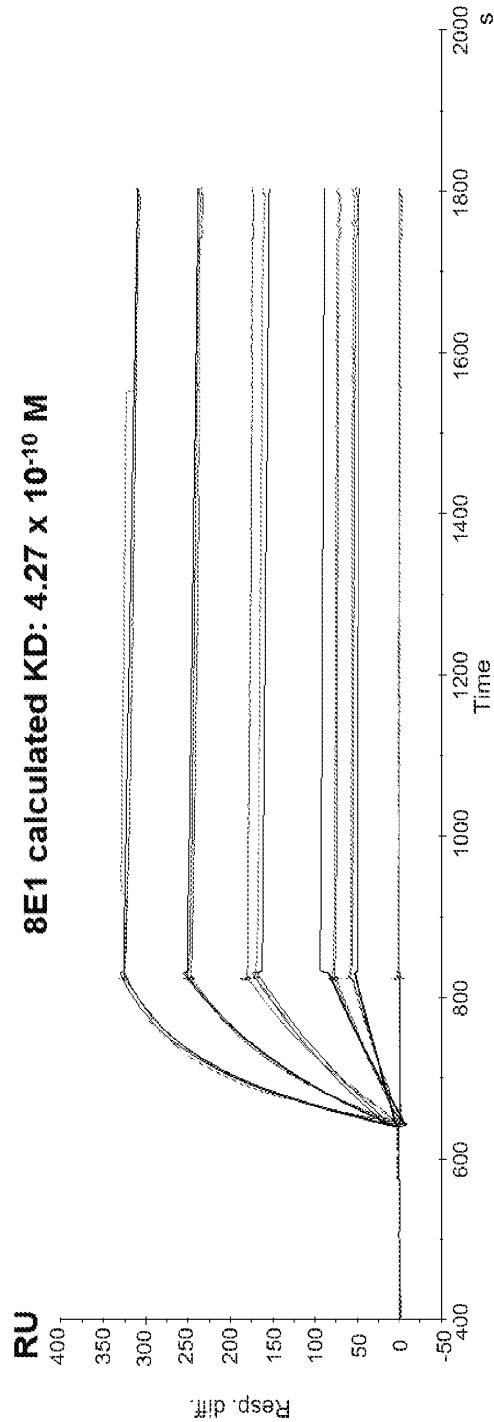


Figure 3

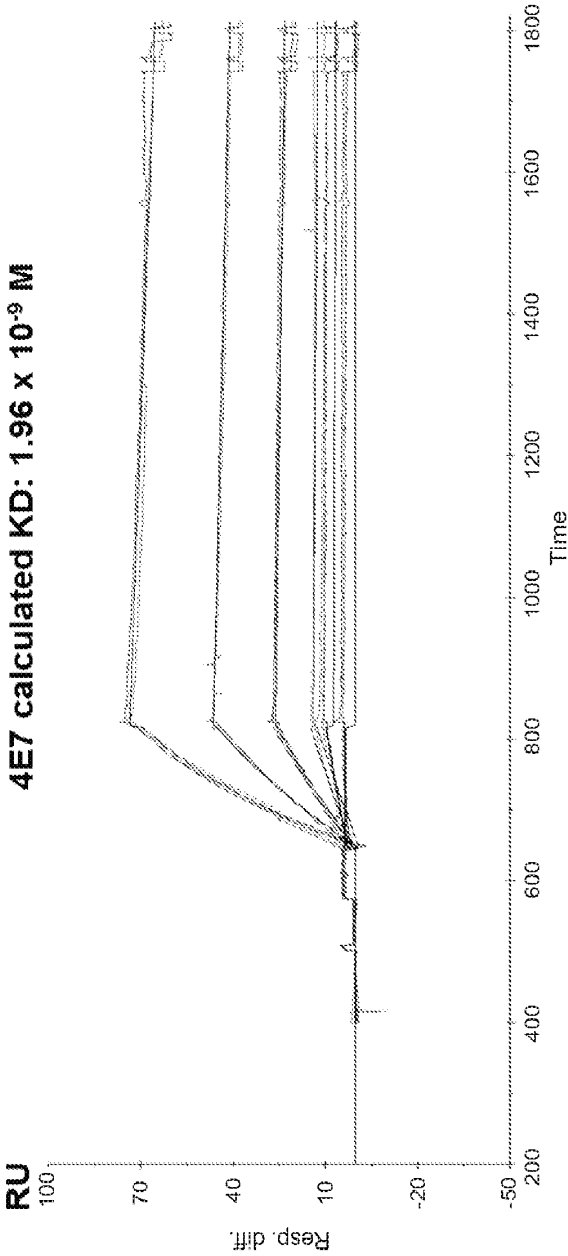


Figure 4

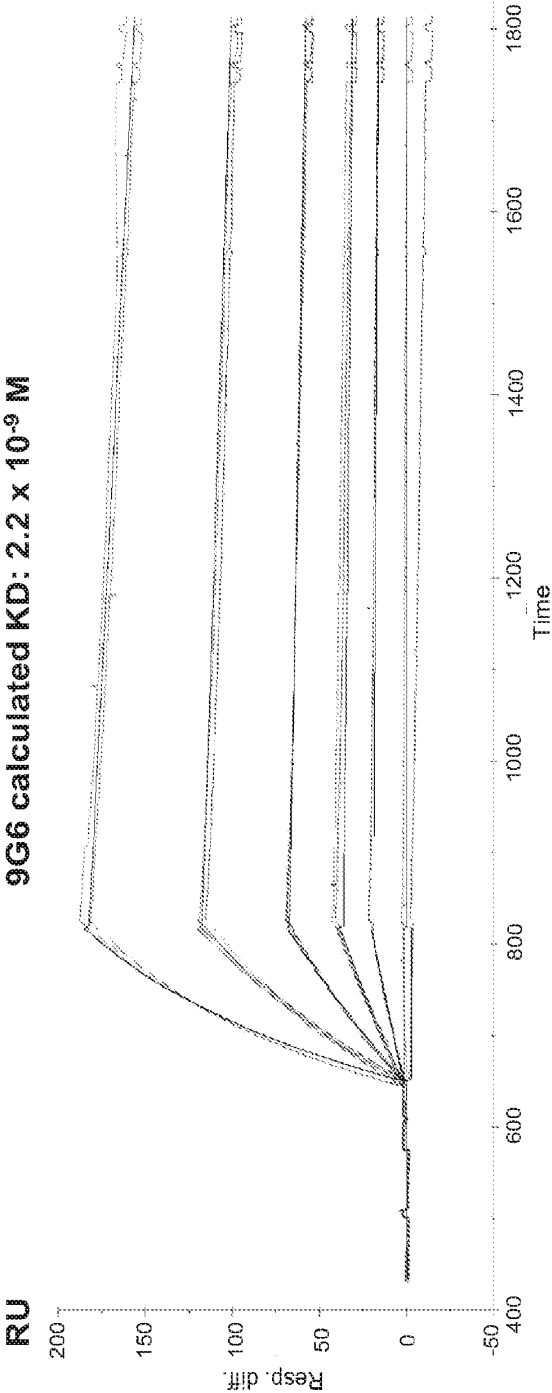


Figure 5

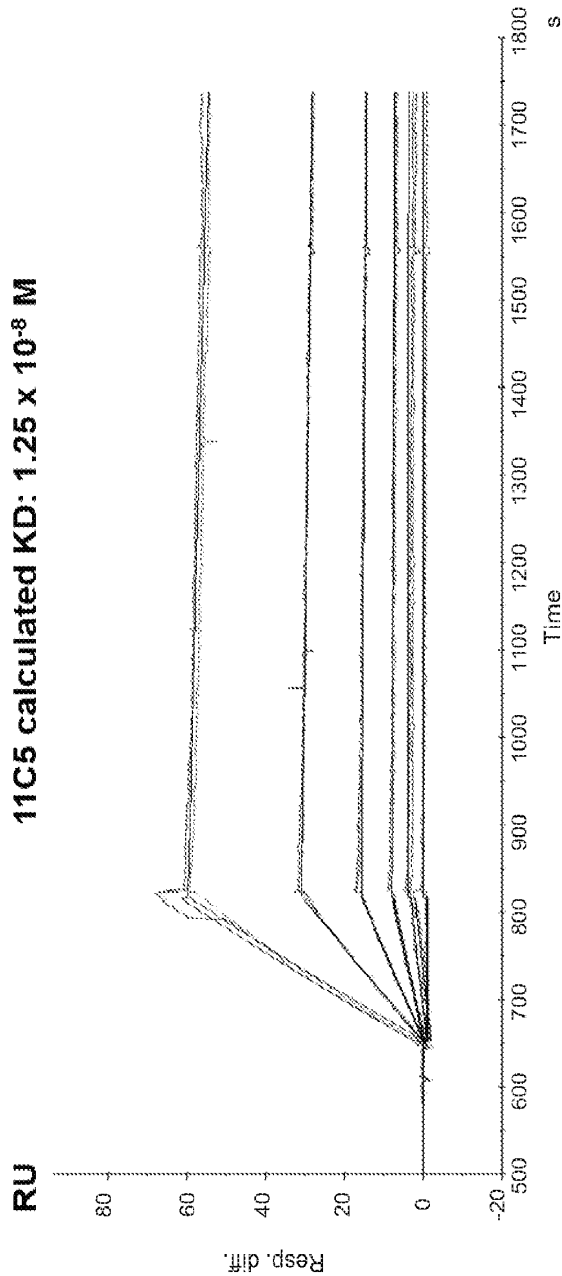


Figure 6

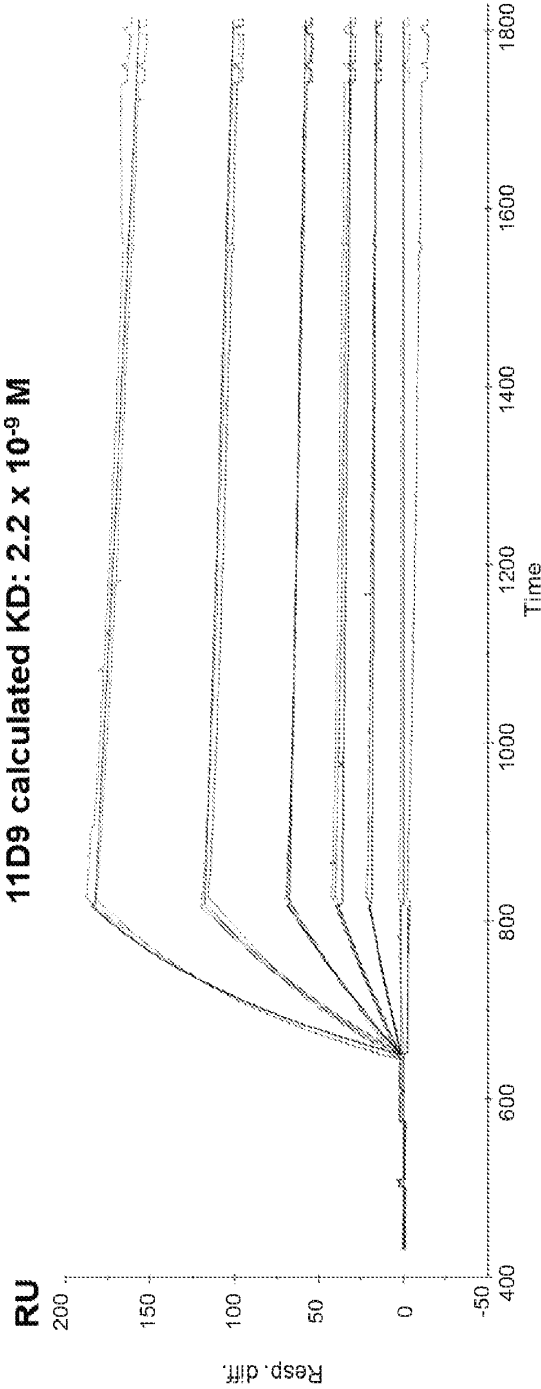


Figure 7

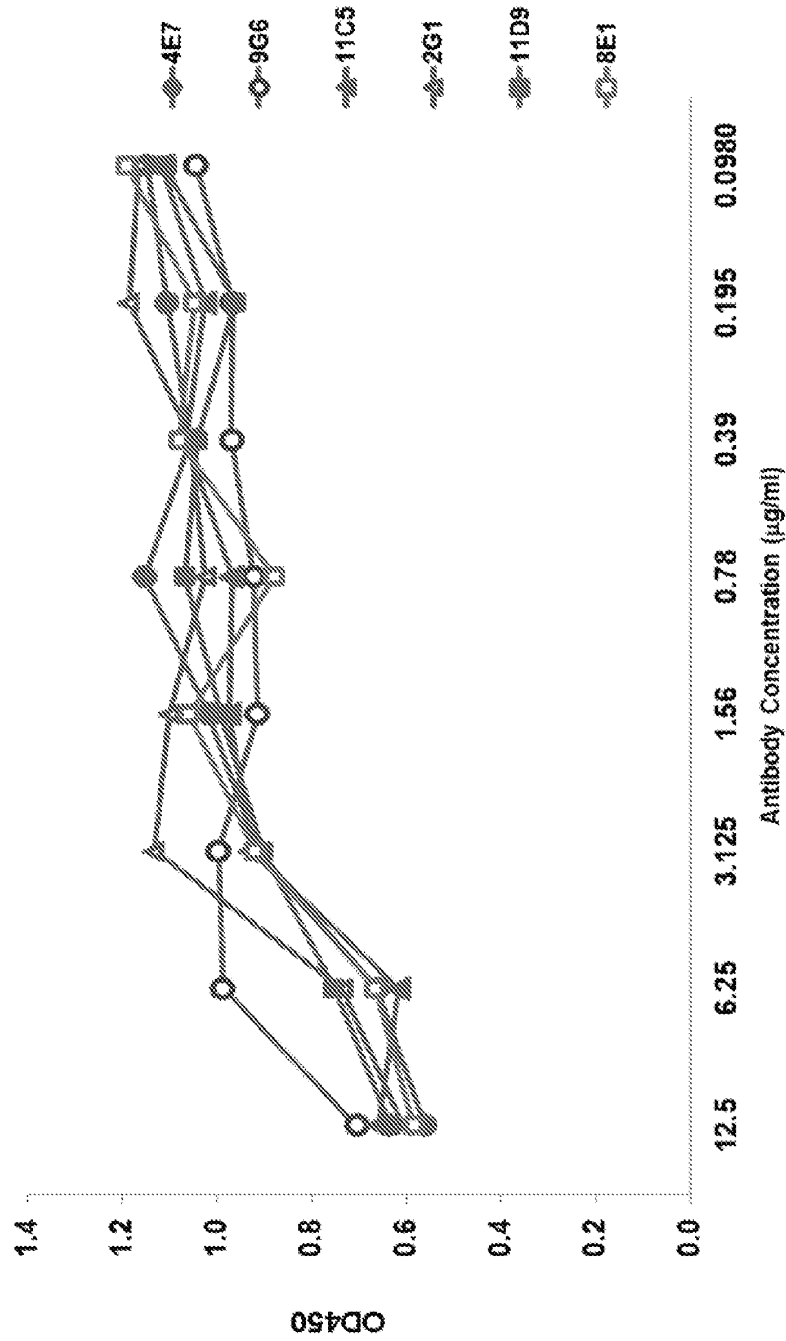


Figure 8

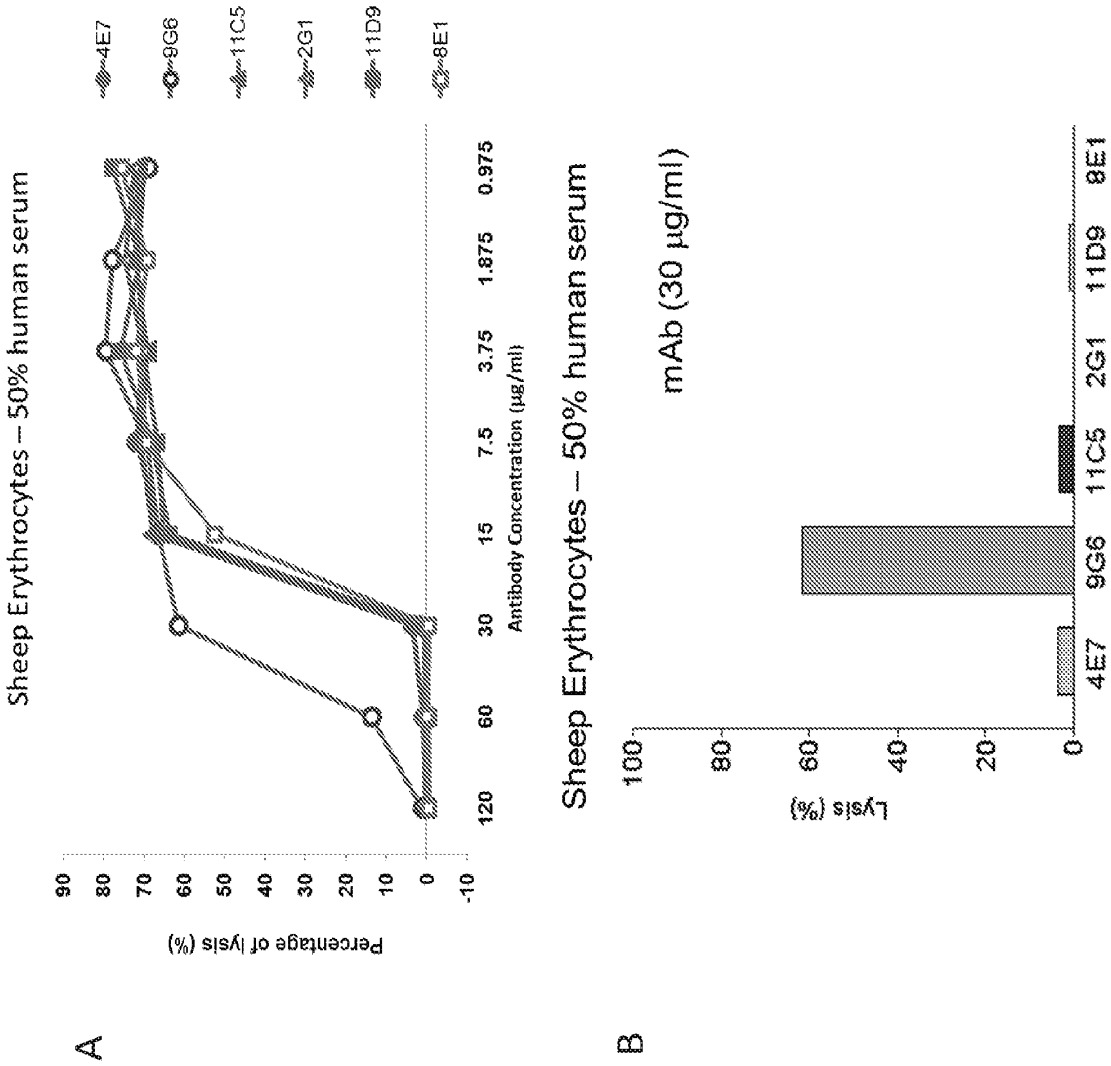


Figure 9

10/33

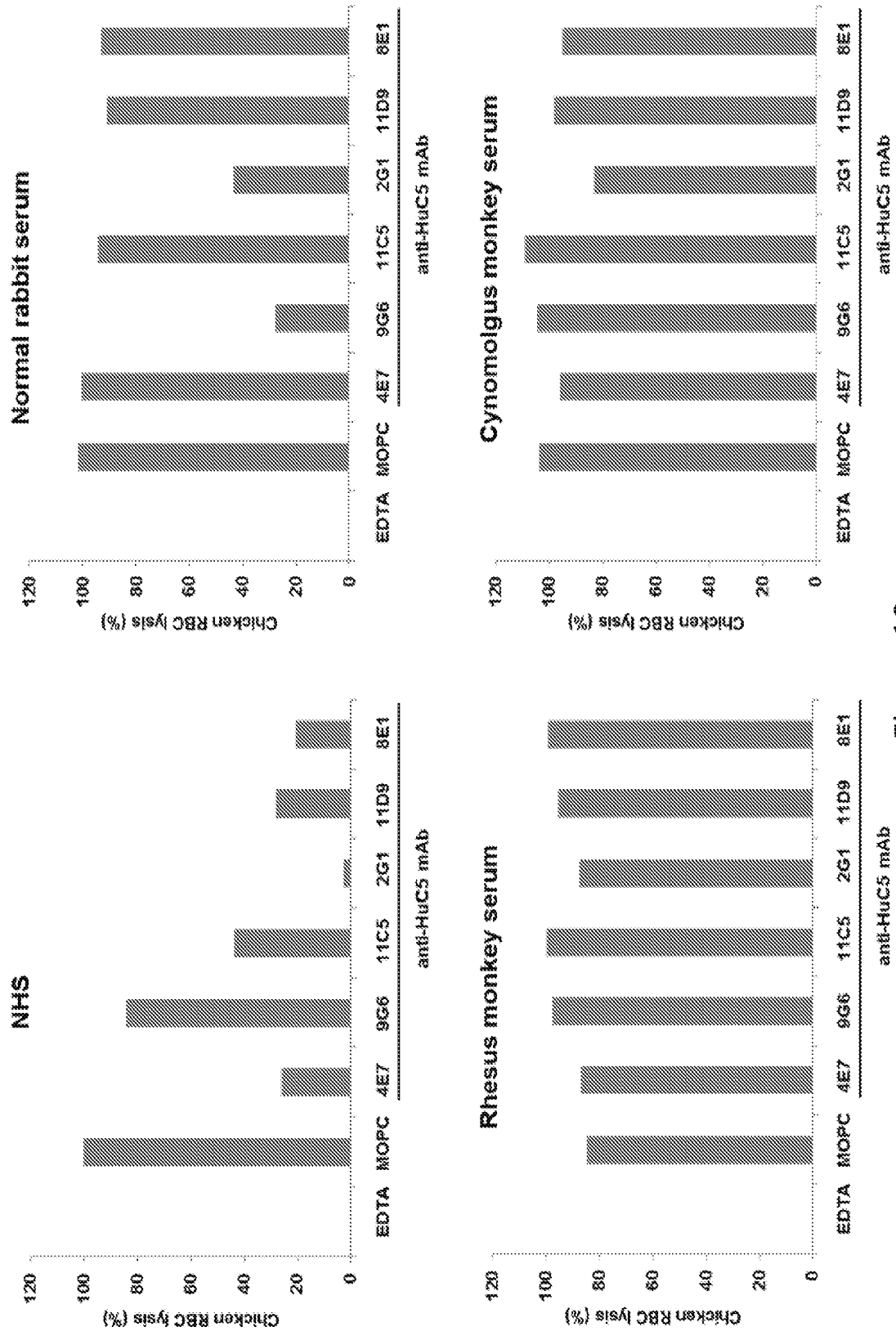


Figure 10

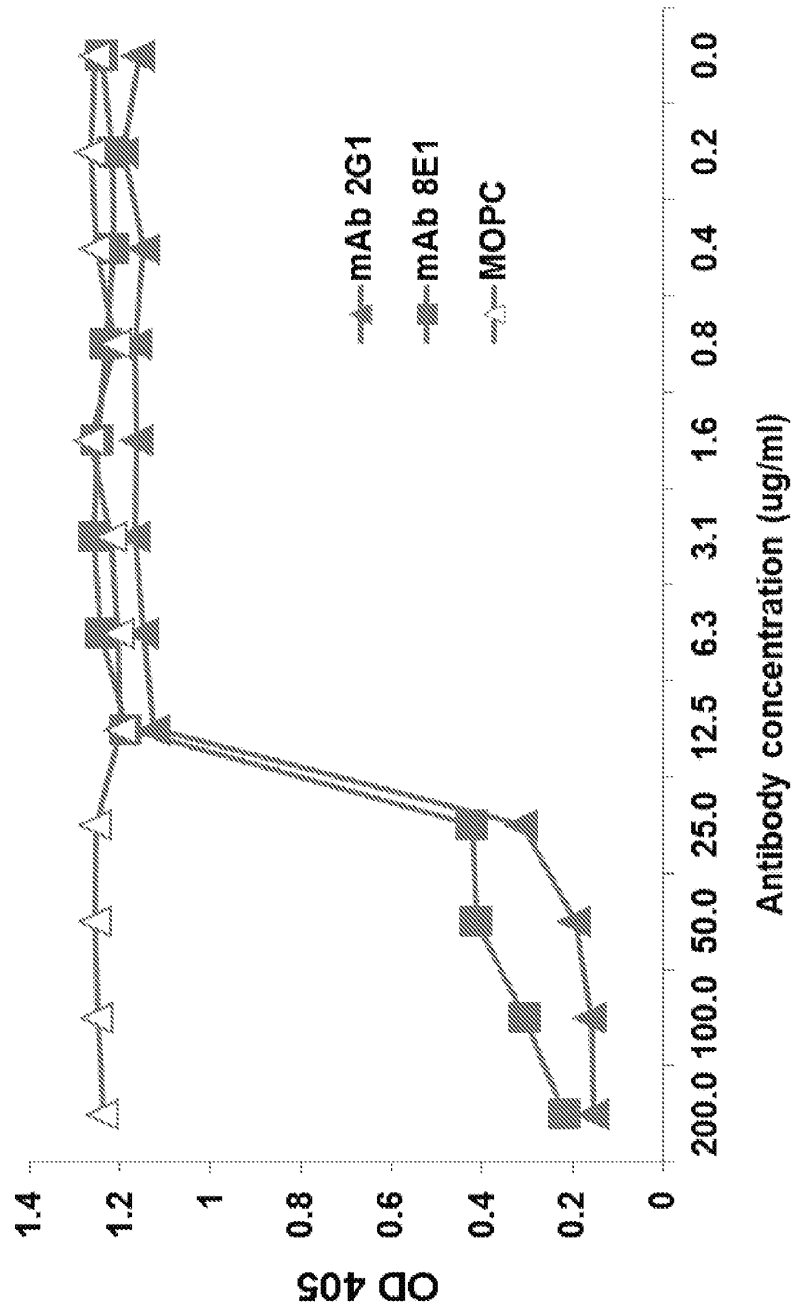


Figure 11

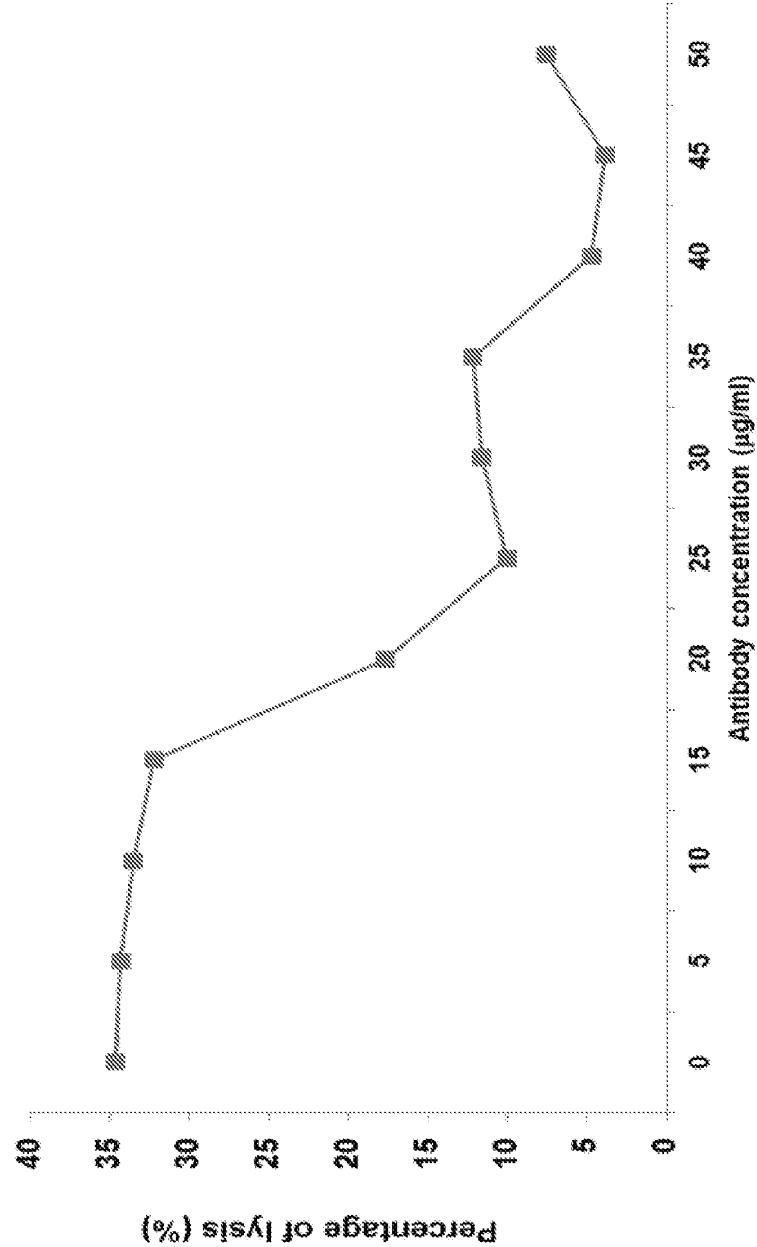


Figure 12

Nucleic acid and amino acid sequence of VH of mAb 2G1. Signal peptide is underlined and CDR1, CDR2 and CDR3 sequences are bolded and highlighted in gray.

VH

AACAACATCTGTCCAAATGTCCTCTCCACAGGCACTGAACACACTGACTCTAACC	
atgggatggagctggatcttctctctctctctctcaggaactgcaggtgtgtctctctctgag	
<u>M G W S W I F L L F L S G T A G V L S E</u>	
gtccagctgcaacagctctggaccagagctggtgaagcctggggcttcagtggaagatatcc	
V Q L Q Q S G P E L V K P G A S V K I S	
tgcaaggcttctggatacacacaatcacagactacaatttggactgggtggaagcagagccat	
C K A S G Y T I T D Y N I D W V K Q S H	CDR1 (SEQ ID NO: 3)
ggaaagacottgagtggtggagatattagtccttaactatggttatactatctatacaac	
G K S L E W I G D I S P N Y G Y T I Y N	CDR2 (SEQ ID NO: 4)
cagaaattcaaggacaaggccacacattgactglagacaggtcctccagcagcctacatg	
Q K F K D K A T L T V D R S S S T A Y M	
gagctcgcagcctgacatctgaggaacactgcaggttttattactgtgcagaaggacacatt	
E L R S L T S E D T A V Y Y C A R R D I	CDR3 (SEQ ID NO: 5)
cgttactcggtaattcctacaaatggtacttgcgtgtgtgggcacagggacccaggtc	
R Y S G N S Y K W Y F D Y W G T G T T V	
acgttctcctcagcccaaaacacacagcccatcgtgtctatccactggcc (SEQ ID NO: 1)	
T V S S (SEQ ID NO: 2)	

Nucleic acid and amino acid sequence of VL of mAb 2G1. Signal peptide is underlined and CDR1, CDR2 and CDR3 sequences are bolded and highlighted in gray.

tcagttcctgccaggacacacagtttagatatgaggttccagggttcagggttctgtgggtcctt	
<u>M R F Q V Q V L G L L</u>	
ctgctctggatatcaggtgcccagtgatgtccagataaccacagtcctcatcttctt	
L L W I S G A Q C D V Q I T Q S P S Y L	
gctgcatctcctggagaaccattactatttaattgcaggacaagtaagagcataagcaaa	
A A S P G E T I T I N C R T S K S I S K	CDR1 (SEQ ID NO: 8)
tatttagccttggtatcaagagaaacctgggaaactaataagcttcttactcttggga	
Y L A W Y Q E K P G K T N K L L I Y S G	
tcacacttgcaatctgggaattccatcaaggttcaggggcagtggtggtacagatttc	
S T L Q S G I P S R F R G S G T D F	CDR2 (SEQ ID NO: 9)
actctcaccatcagtagcctggagcctgaagattttgccaatgtattactgtcaacaacat	
T L T I S S L E P E D F A M Y Y C Q Q H	CDR3 (SEQ ID NO: 10)
aatgaataaccgtacacgttctggagggggacccaagctggaaataaaacgggctgatgct	
N E Y P Y T F G G T K L E I K (SEQ ID NO: 7)	
gcacca (SEQ ID NO: 6)	

Figure 13

atyggaagacatctcttccagctctccagatggagacagacacactctgttatgg			
	M E T D T L L W		
gtactgtgtgtgtggcccttagttccgagctcgtgtgacacagctctccttccctta			
V L L L L W A L S S E L V M T Q S P A S L			
gtgttatctctgtgggcagggccaccatctcatgcaggccagcaaggtgtcagtaca			
V V S L G Q R A T I S C R A S K G V S T		CDR1 (SEQ ID NO: 18)	
ctgtgtctacagttatatcactgtgtaccacagaaaccaggacagccaccacaaactcttc			
S V Y S Y M H W Y Q Q K P G Q P K L L			
ctctatctgtgtccatccactagatctgtgggtctcctgcaggttccagtgctgggtct			
I V L A S N L E S G V P A R F S G S G S		CDR2 (SEQ ID NO: 19)	
ggggacagacttctccctccacatccatctctgtggaggaggaggtgtgcaacctattac			
G T D F S L N I H P V E E E D A A T Y Y			
ctgtcagcaaaagtggggagcttccgctcacgttcggtgtctggaccagctgggagctgaaa			
C Q Q S G E L P L T F C A C T K L E L K			
cgggctgatgctgcaccacaagggc (SEQ ID NO: 16)		CDR3 (SEQ ID NO: 20)	
R (SEQ ID NO: 17)			

Figure 14

File 57

[illegible]

16 June 1963

[illegible]

Nucleic acid and amino acid sequence of VL of mAb 11C5. CDR1, CDR2 and CDR3 sequences are bolded and highlighted in gray.

atgggggtgagccacacaaaactcagggaaagctcgaagatgggttttccacacotcagatactt
M V F T P Q I L
ggacttatgcttttttggatttcagcctcagaggtgaaattgtgtctcactcagttctcca
G L M L F W I S A S R G E I V L T Q S P
gccacccctgtgtgactccaggagagaggtcaggtctttctctaggggcagccaaagt
A T L S V T P G E S V S L S C R A S Q S
atttagcaacaacctacagtggttatcaacaaaaatcacatgagtctccaaagactttctcact
I S N N L Q W Y Q Q K S H E S P R L L I
aaatatgtctccagtcctatcttggtatccctccctccagttccagtggtggtatcaggg
K Y A S Q S I S G I P S R F S G S G S G
acagatttcactctcagtatcaacagtggtgagactgaagattttgggaattgtattctgt
T D F T L S I N S V E T E D F G M Y F C
caacacagatgaacagctggcctctccagttcgttggtgggaccaaggtggagtgaaacgg (SEQ ID NO: 45)
Q Q S N S W P L T F G G G T K V E L K R CDR3 (SEQ ID NO: 49)
Q Q S N S W P L T F G G G T K V E L K R CDR3 (SEQ ID NO: 46)

4. Termination

Nucleic acid and amino acid sequence of VH of mAb 11D9. CDR1, CDR2 and CDR3 sequences are bolded and highlighted in gray.

```

atggggacatatgtacaatgtcctcaccacagacactgaacacactgactcttaaccatggga
      M S S P Q T L N T L T L T M G
tgagagtggatctttctctctcctcaggaactgcaggtgtcctctctctgaggtccag
W S W I F L L S G T A G V L S E V Q
ctgcaacaatctggacctgaggtgtgaagcctgggcttcagtgagatatactctgtaag
L Q Q S G P E V V K P G A S V K I S C K
gcttctggatacactgttcactgacttctacatgaactgggtgaacacagagccatggaaag
A S G Y T F T D F Y M N W V K Q S H G K
agccttgagtgattggatatatttaacttaacaatgggtgatactagttacaacagaag
S L E W I G Y I N P N N G D T S Y N Q K
ttcaagggaaggccacatcgactgtgacaggtctcctcaacacagcctacatggagctc
F K G K A T S T V D R S S N T A Y M E L
cgcagcctgacatctgaggactctgcagctctattactgtgcaagactcattctctgtgt
R S L T S E D S A V Y Y C A R L I F Y G
aactggtaactttgatgtctgtgggcaacaggaccacgggtcacogtctcctcagccaaaaca
N W Y F D V W G T G T T V T V S S A K T (SEQ ID NO: 51)
acagccccatcg (SEQ ID NO: 50)

```

CDR1 (SEQ ID NO: 52)

CDR2 (SEQ ID NO: 53)

CDR3 (SEQ ID NO: 54)

Nucleic acid and amino acid sequence of VL of mAb 11D9. CDR1, CDR2 and CDR3 sequences are bolded and highlighted in gray.

```

atgggggaataattagccagagactgagatgggaaacaaatggatttttccagatgcagatt
      M D F Q M Q I
atcagcttgctgataatcagtggtcacagtcatagtgtctaatggagaaaattgtgctcacc
I S L L L I S V T V I V S N G E I V L T
cagttctccacccaccatggctgcattctcccgggggaagaagatcactatcacctgcagtgcc
Q S P P T M A A S P G E K I T I T C S A
agctcaagtataagttccaaattacgtgcattgggtatcagcagaagcaggattctccctc
S S S I S S N Y V H W Y Q Q K P G F S P
aaactcttgattataggacatccaatctgtgtcttggtgagtcaccagttcgtctcagtggc
K L L I Y R T S N L A S G V P V R F S G
agtgggtctgggaactcttactctctcacaattggcaccatggaggtctgaagatgttgcc
S G S G T S Y S L T I G T M E A E D V A
acttactactgcacagcaggtactagataccgtggacgttggtggaggccaccacaggtg
T Y Y C Q Q G T S I F W T F G G G T K V
gaaattaatcgg (SEQ ID NO: 55)
E I N R (SEQ ID NO: 56)

```

CDR1 (SEQ ID NO: 57)

CDR2 (SEQ ID NO: 58)

CDR3 (SEQ ID NO: 59)

Figure 18

These sequences were used to construct chimeric (mouse variable region + human constant region) and humanized (humanized mouse variable region + human constant region) anti-human C5 antibody (2G1).

Amino acid sequence of human IgG4 Constant Heavy chain region with S228P mutation. Proline residue at position 228 is highlighted in gray.

ASTKGPSVFPLAPCSRSTESTALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA
VLQSSGLYSLSVTVPSSSLGTKTYTCNVDPKPSNTKVDKRVESKYGPPCP~~PCP~~
APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEV
HNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISK
AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSPG
K (SEQ ID NO: 60)

Amino acid sequence of human Kappa Constant Light region

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQES
VTEQDSKDSSTYSLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 61)

Figure 19

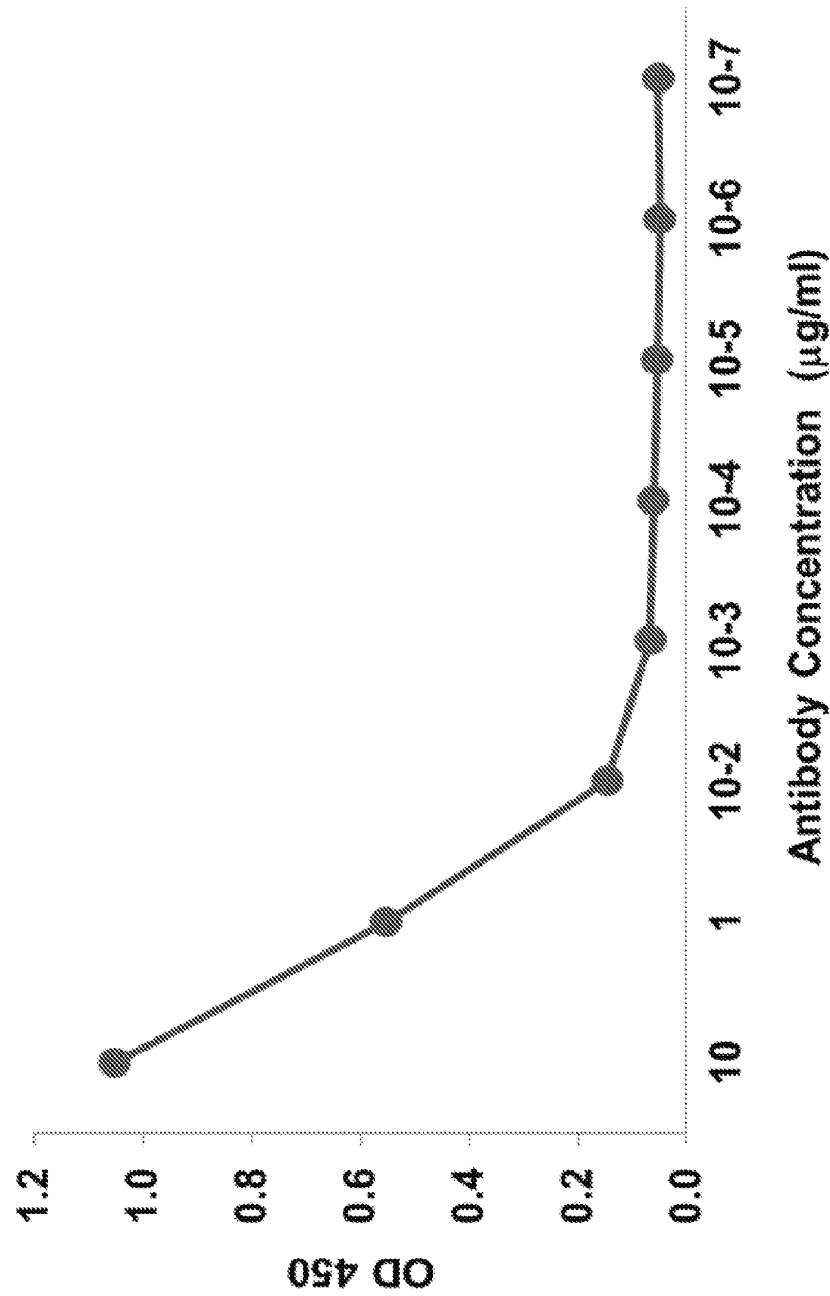


Figure 20

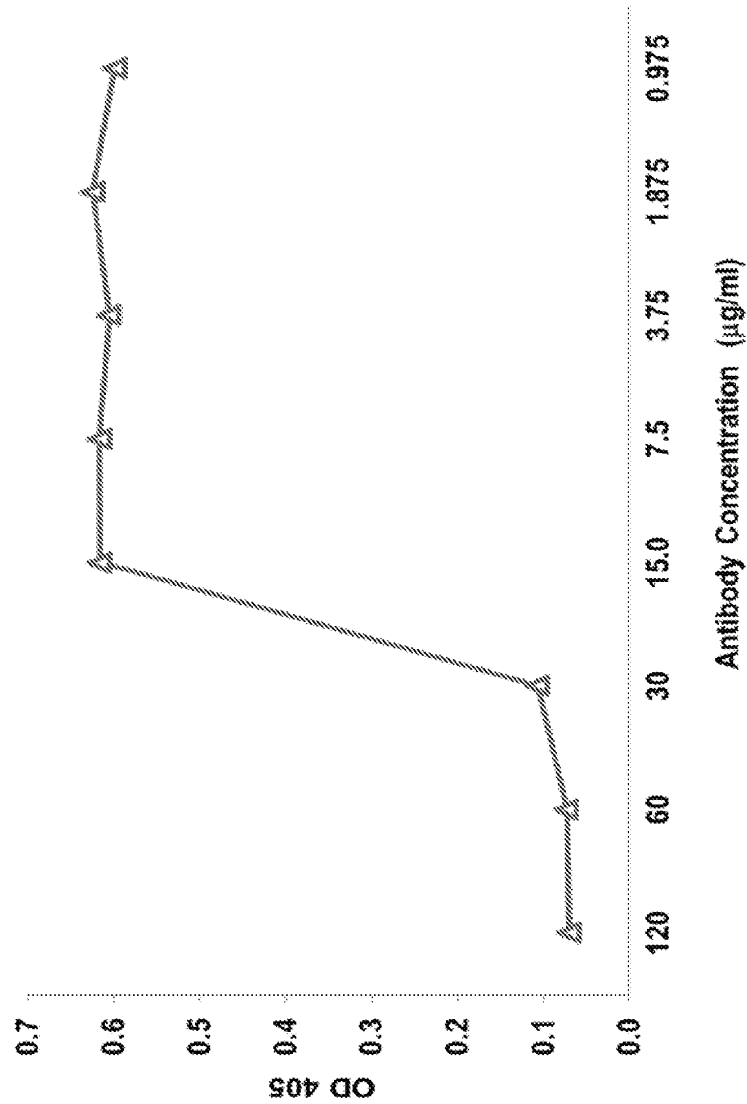


Figure 21

humanized 2G1 VH-11801

cagcatatgatcagtgctcctctccaaagtcccttgaaacatagactctaaccatggactggacc
tggtctctttctctcctcctgtcagtaactgcaggtgtccactcccagggttcagctgggtg
W V F L F L L S V T A G V H S Q V Q L V
cagtcaggagctgaggtgaagaagccctggggccctcagtgaaaggtctcctgcaaggcttct
Q S G A E V K K P G A S V K V S C K A S
ggatacacaatcacagactacaatttgactgggtgagacaggccccctggacaagggtt
G Y T I T D Y N L D W V R Q A P G Q G L
gagtgatgggagatattagtcctaactatgggttatctactatctacaaccagaaattcaag
E W M G D I S P N Y G Y T I Y N Q K F K
gacagagtcaccatgaccacacagacacatccacgagcacagccctacatggagctgaggagc
D R V T M T T D T S T S T A Y M E L R S
ctgagatctgacgacacggccgtgtattactgtgcgagaaggacattcgttactccggt
L R S D D T A V Y C A R R D I R Y S G
aattcctacaaaatgggtactctogatgtctgtgggccaagggacaaatgggtcacccgtctcttca (SEQ ID NO: 62)
N S Y K W Y F D V W G Q G T M V T V S S (SEQ ID NO: 63)

CDR1 (SEQ ID NO: 64)

CDR2 (SEQ ID NO: 65)

CDR3 (SEQ ID NO: 66)

Figure 22

humanized 2G1 VH-16901

cagcatatgatcagtgctcctccaaaagtcccttgaacatagactctaaccatggactggacc

WVFLFLLSVTATAGVHSQVLV

MDWT

tggtctcttctcctcctgtcagtaactgcaggtgtccactcccaggtgcagctggtg

cagtcgtgggctgaggtgaagaagcctgggtcctcgtggaaggtctctgcaaggctctct

QSGAEVKPKPGSSSVKVSCKAS

ggatacacaatcacagactacaatttggactgggtgcgacagggccctggacaagggtt

GYTI**TDYNLD**WVRQAPEGGL

gagtgatgggagatattagtcctaactatggttatactatctacaaccagaaattcaag

EWMGDISPNYGYTIYNQKFK

gacagagtcacgattaccgcgacgaatccacgagcacagccctacatggagctgagcagc

DRVTTITADESTSTAAMELS

ctgagatctgaggacacggcgtgtattactgtgcgagaagggaacattcgttactccggt

LRS EDTAVYYCAR**RDIRYSG**

aattcctacaaatggtacttctcgatgtctgtggggcccaagggaacaatggtcacccgtctcttca

NSYKWYFDVWGQGTMTVTS

(SEQ ID NO: 67)

(SEQ ID NO: 68)

CDR1 (SEQ ID NO: 69)

CDR2 (SEQ ID NO: 70)

CDR3 (SEQ ID NO: 71)

Nucleic acid and amino acid sequence of VL of the humanized 2G1. CDR1, CDR2 and CDR3 sequences are bolded and highlighted in gray.

Figure 23

humanized 2G1 VL-1901

gtcagagccctggggagggaactgctcagttagtagccacagagggaaccatgggaagccccagct	
	M E A P A
cagcttctcttcctcctgctactctgtggctcccagataccaccggagacatccagttgacc	
Q L L F L L L L W L P D T T G D I Q L T	
cagtctccatccttcctgtgtcgtatctgttaggagacagagtcaccatcactttgcaggaca	
Q S P S F L S A S V G D R V T I T C R T	CDR1 (SEQ ID NO: 74)
agtaagagcataaagcaaatatttagcctggtatcagcaaaaaaacccagggaagccccctaag	
S K S I S K Y L A W Y Q Q K P G K A P K	
ctcctgatctattctggatccaccttgcaatctgtgggtcccatcaagggttcagcggcagt	
L L I Y S G S T L Q S G V P S R F S G S	CDR2 (SEQ ID NO: 75)
ggatctgggacagaattcactctcacaaatcagcagcctgcagcctgaagattttgcaact	
G S G T E F T L T I S S L Q P E D F A T	
tattactgtcaacaacataatgaatacccggtacacgttttgccaggggaccacgaagctggag	
Y Y C Q Q H N E Y P Y T F G Q G T K L E	CDR3 (SEQ ID NO: 76)
atcaaa (SEQ ID NO: 72)	
I K (SEQ ID NO: 73)	

Figure 24

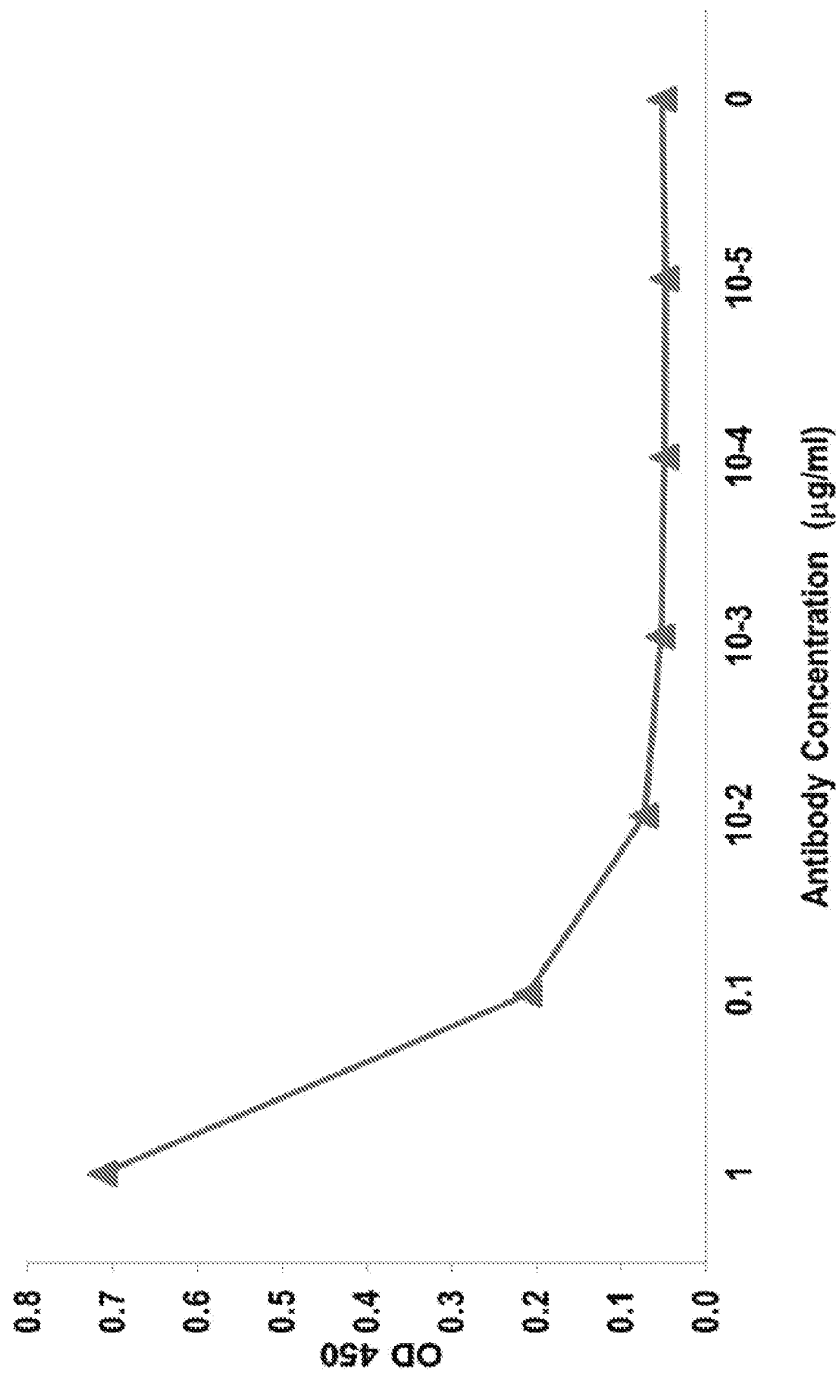


Figure 25

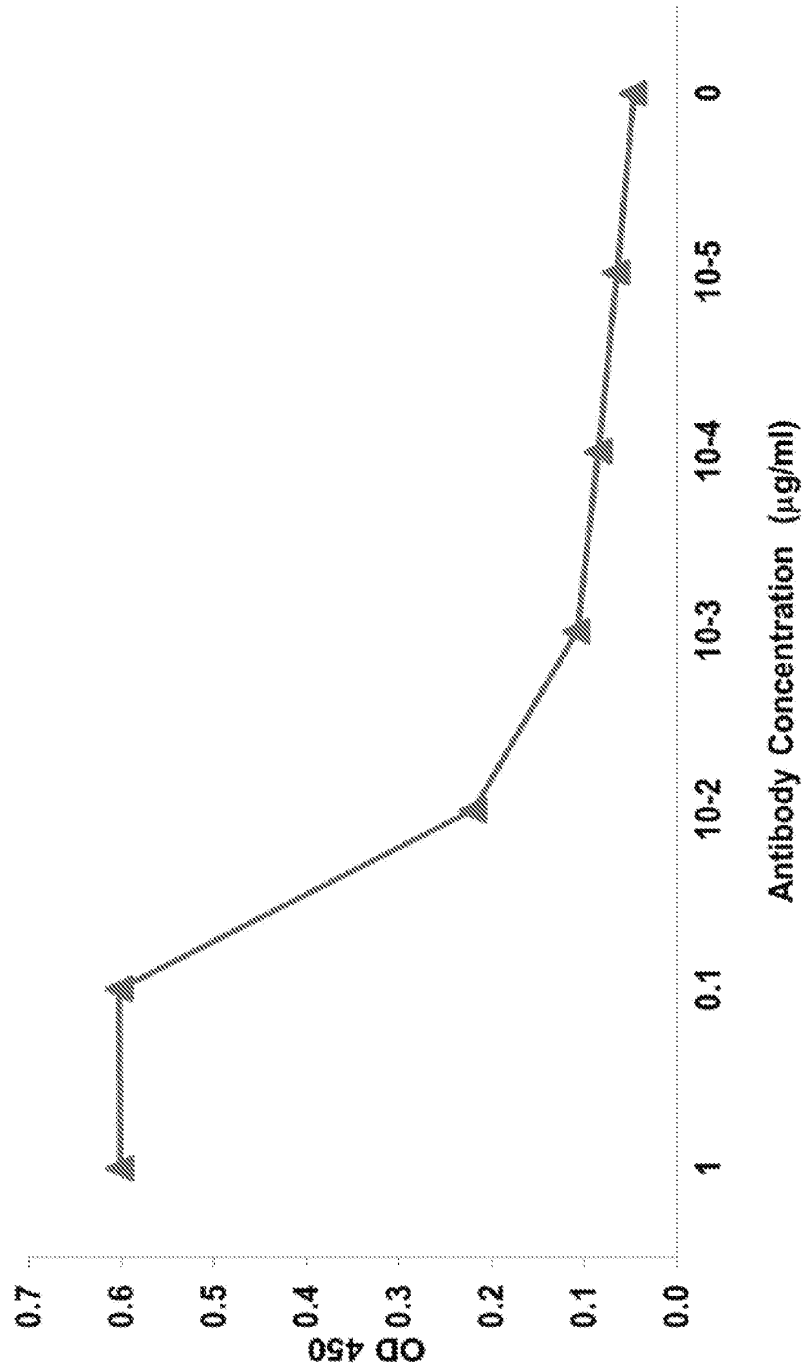


Figure 26

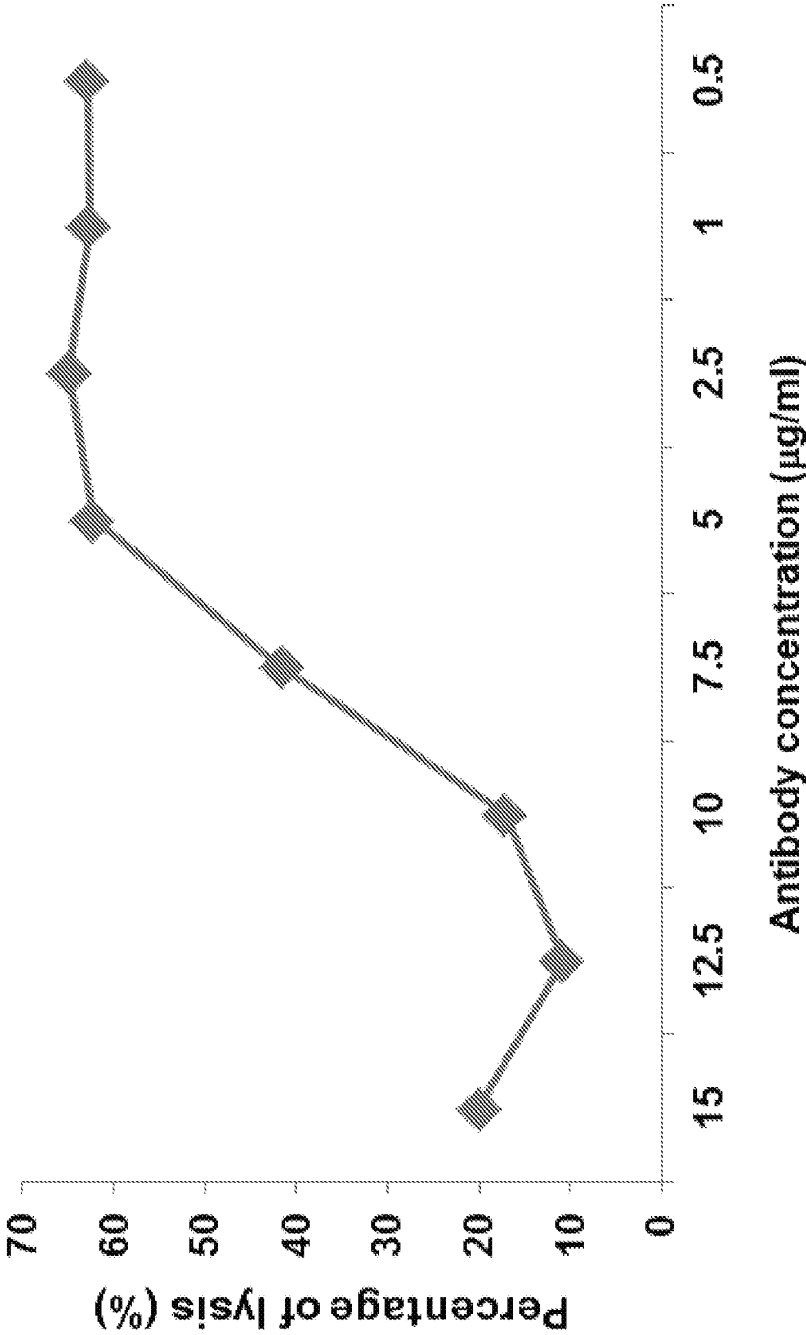


Figure 27

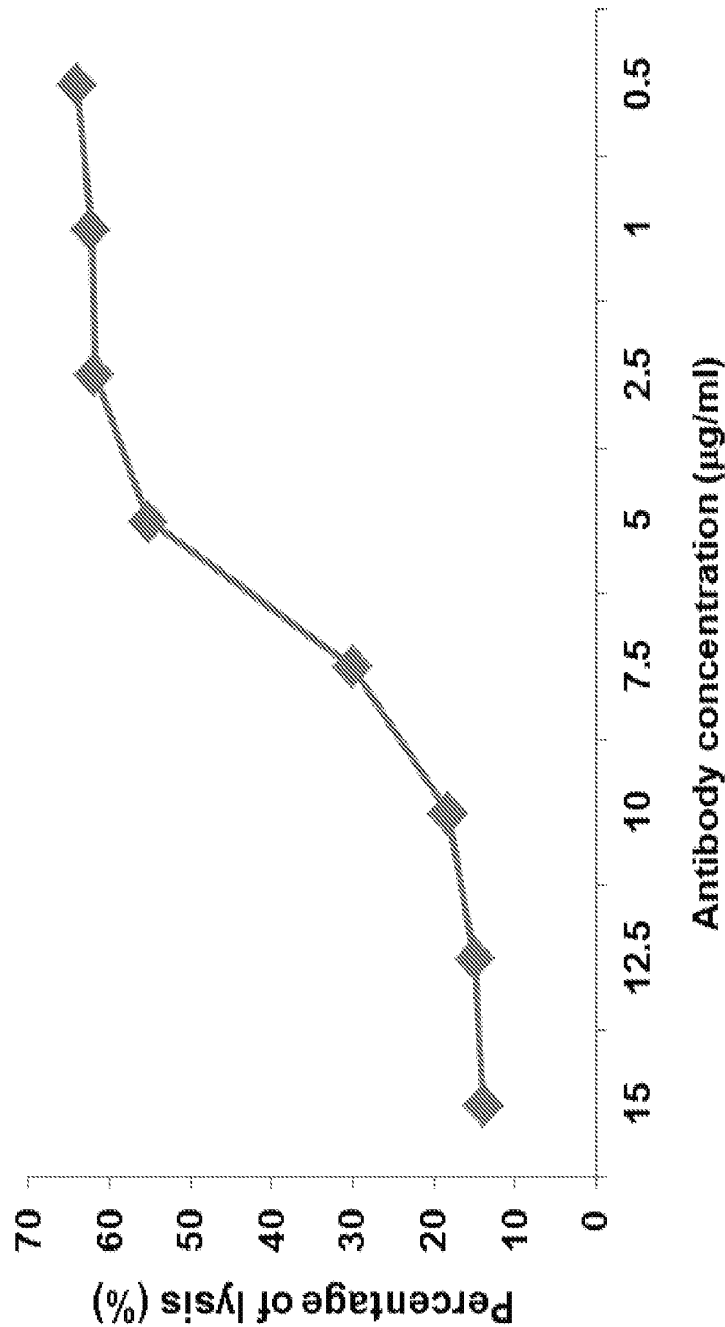


Figure 28

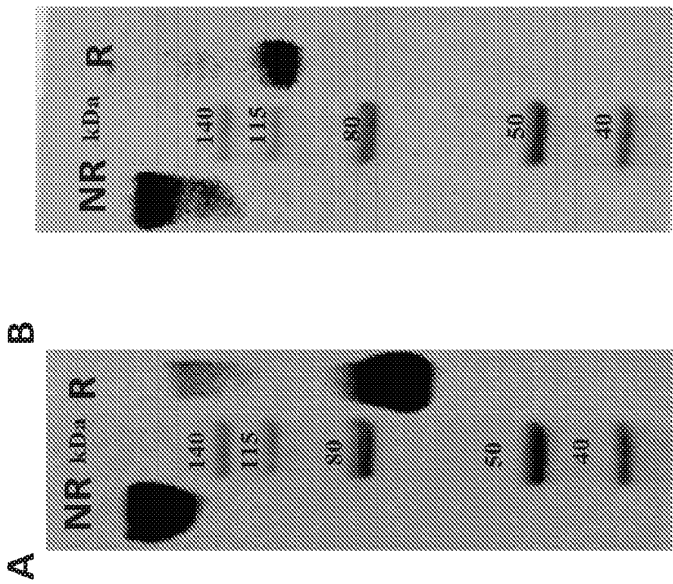


Figure 29

A

MG1	MG2	MG3	MG4	MG5	MG6	C5a	MG7	CUB	C5d	CUB	MG8	C345C
C5 β-chain							C5 α-chain					

B

MG1 :
QEQTYYISAPKIFRVGASENIVIQVGYTEAFDATISIKSYDPDKKFSYSSGHVHLSSENKFQNSAIL
TIQPKQLPGGQNPVSYYLEVVSKEHFSKSRMPITYD (SEQ ID NO:84)

MG2 :
NGELFIHTDKPVYTPDQSVKVRVYSLNDDLKPAKRETVLTFIDPEGSEVDMVEEIDHIGIISFPDFK
IPSNPRYGMWTIKAKYKEDFSTGTAYFEVKEYV (SEQ ID NO:85)

MG3 :
LPHFSVSIIEPEYNFIGYKNFKNFEITIKARYFYNKVVTEADVYITFGIREDLKDDQKEMMQTAMQNT
MLINGIAQVTFDSETAVKELSYSLEDLNNKYLYIAVTVIESTGGFSEEAIEPGIKYVLS (SEQ
ID NO:86)

MG4 :
PYKLNLVATPLFLKPGIPYPIKVQVKDSLQLVGGVPVTLNAQTIDVNQETSDLDPSKSVTRVDDGV
ASFVLNLP SGVTVLEFNVKTDAPDLPEENQAREGYRAIAYS (SEQ ID NO:87)

MG5 :
SLSQSYLYIDWTDNHHKALLVGEHLNIIIVTPKSPYIDKITHYNYLILSKGKIIHFGTREKFSASYQS
INIPVTQNMVPSRLLVYYIVTGEQTAELVSDSVWLNIEEK (SEQ ID NO:88)

MG6 :
CGNQLQVHLSPDADAYS PGQT VSLNMTGMDSWVALAAVDSAVYGVQRGAKKPLERVVFQFLEKSDLG
CGAGGGLNNANVFHLAGLTFILTANADDSQENDEPCKEIL (SEQ ID NO:89)

Figure 30

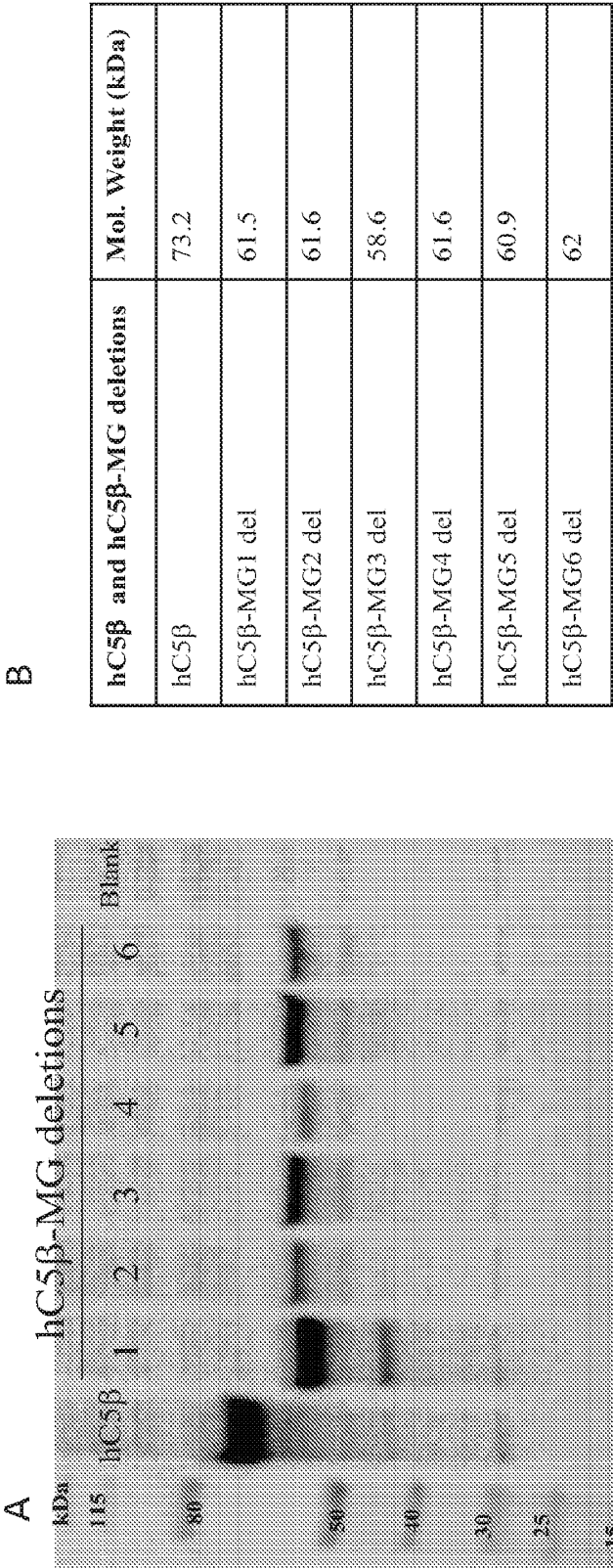


Figure 31

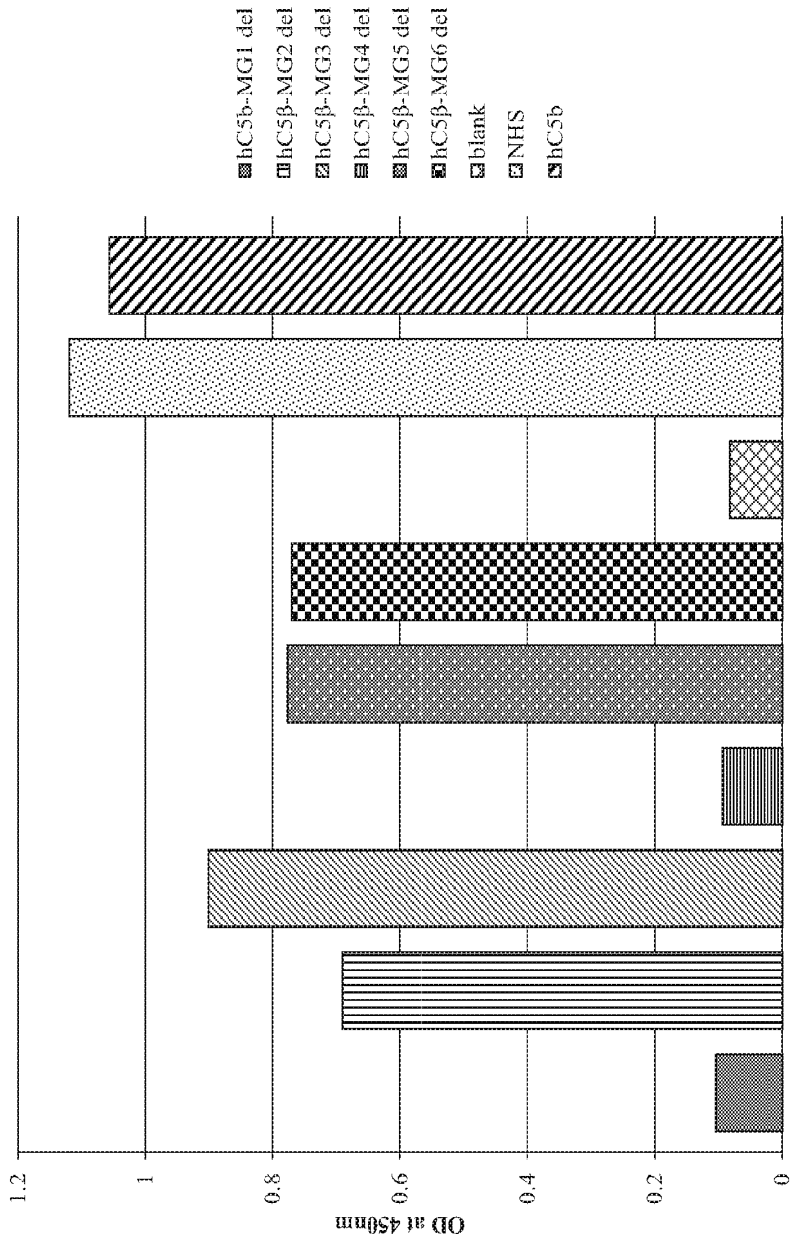


Figure 32

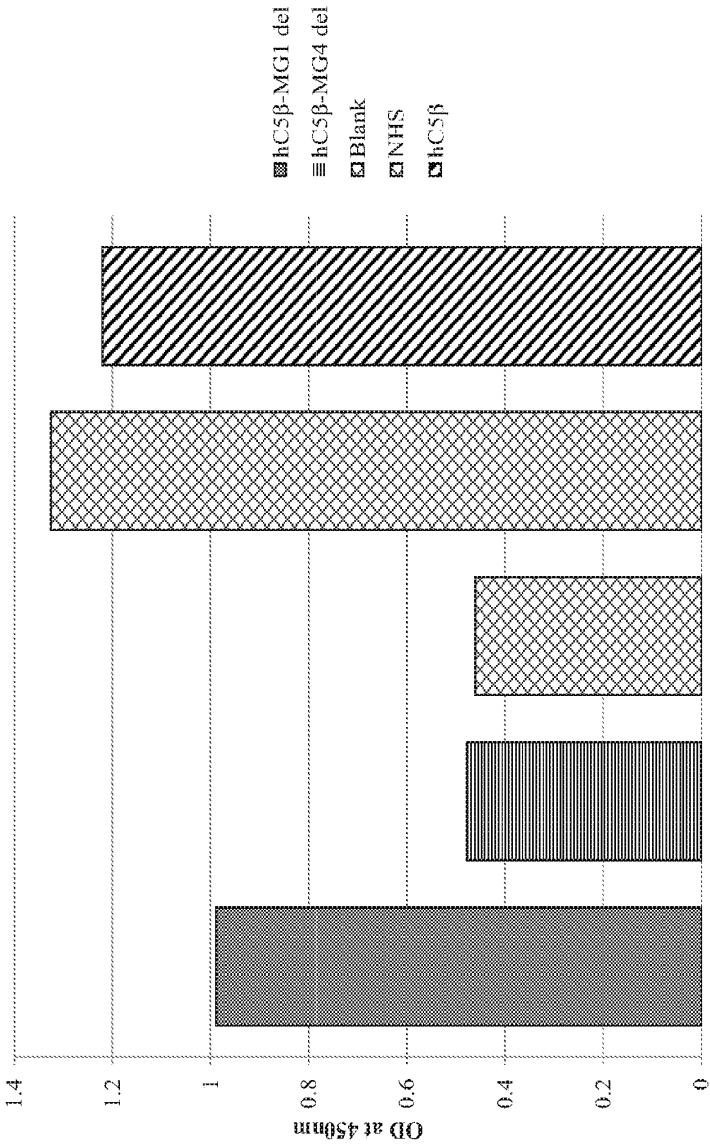


Figure 33