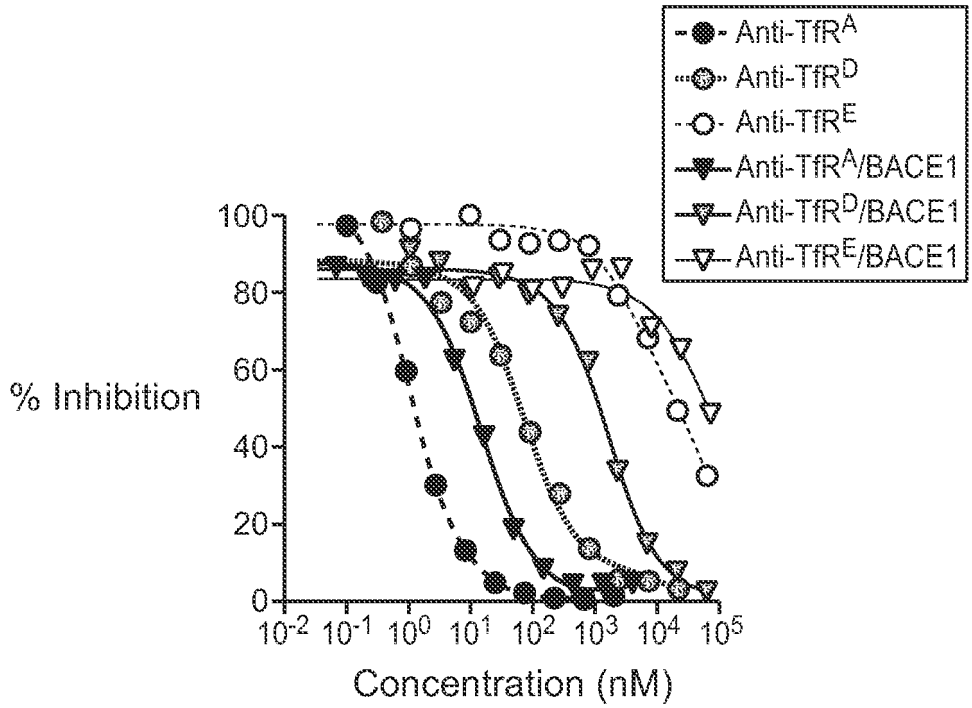

Anti-TfR^A
Anti-TfR^D
Anti-TfR^E
Anti-TfR^A/BACE1
Anti-TfR^D/BACE1
Anti-TfR^E/BACE1
% Inhibition
100
80
60
40
20
0
10^-2 10^-1 10^0 10^1 10^2 10^3 10^4 10^5
Concentration (nM)

FIG. 1A

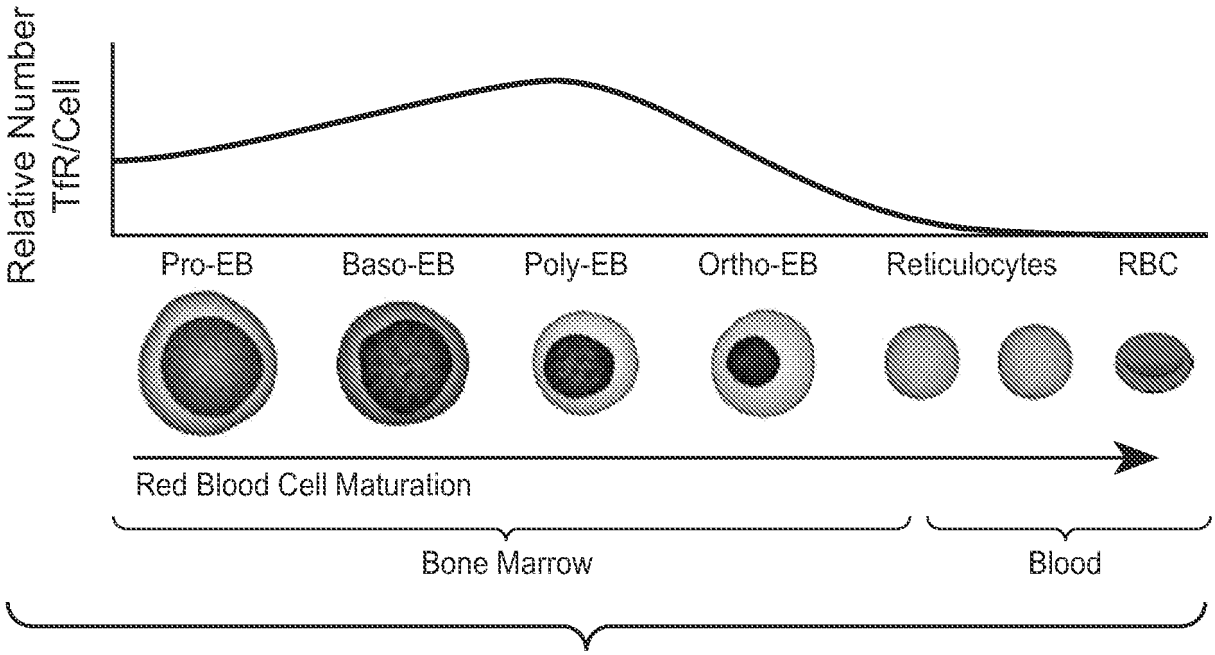

Relative Number TfR/Cell
Pro-EB
Baso-EB
Poly-EB
Ortho-EB
Reticulocytes
RBC
Red Blood Cell Maturation
Bone Marrow
Blood

FIG. 2A

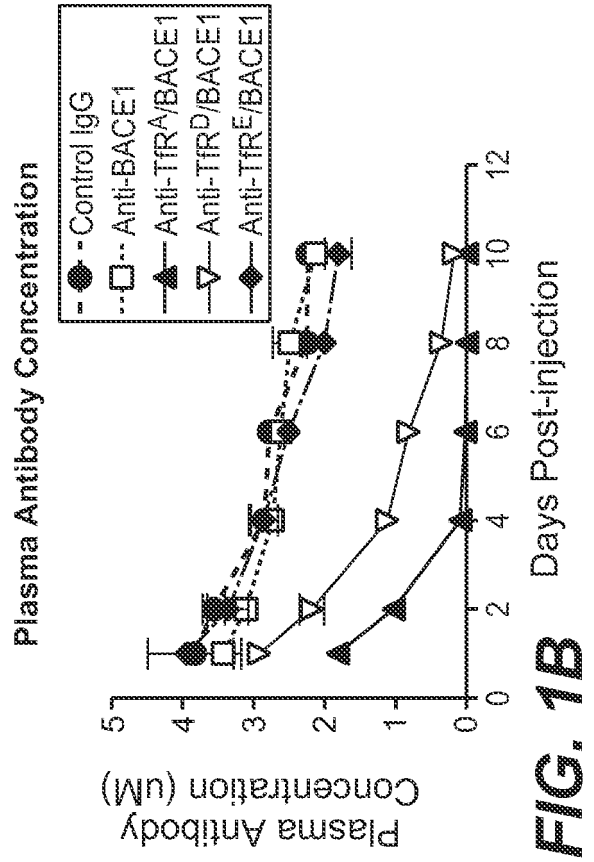


FIG. 1B

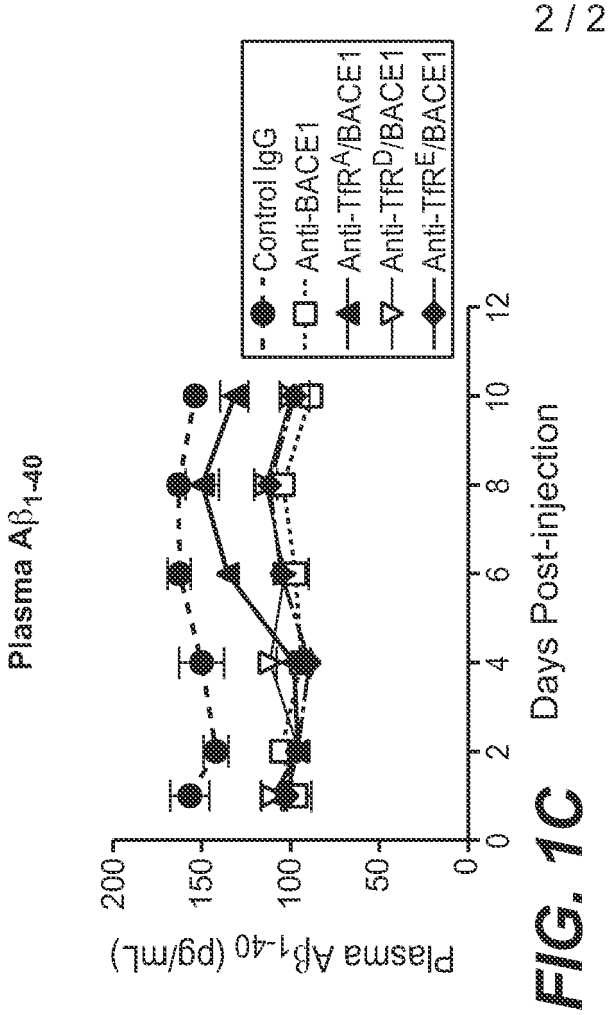


FIG. 1C

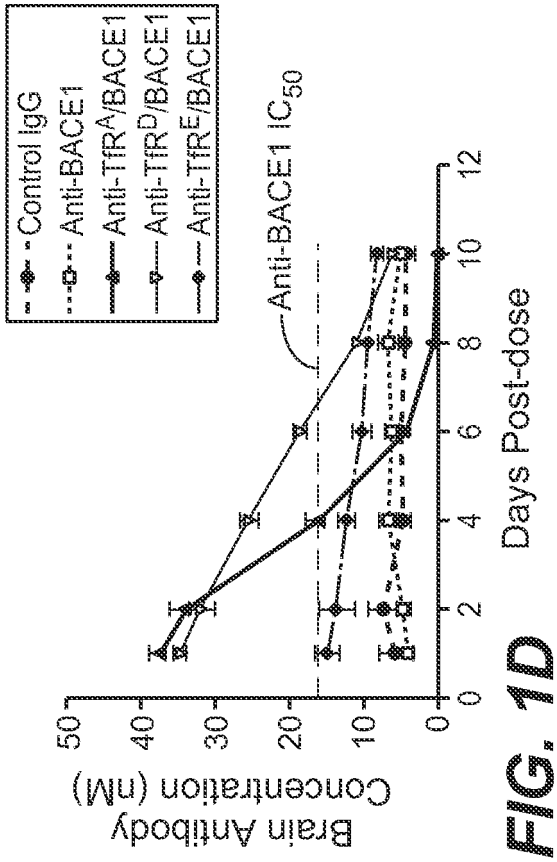


FIG. 1D

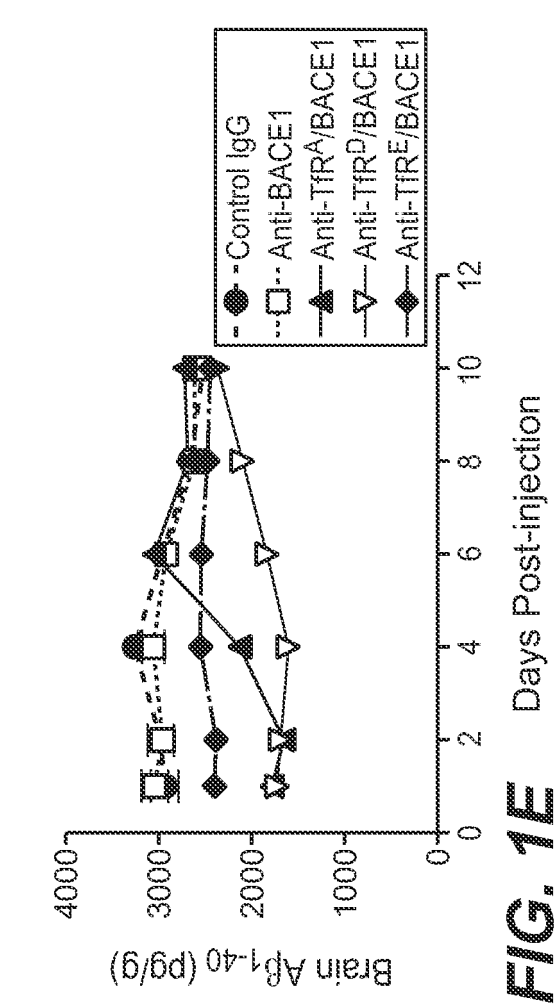


FIG. 1E

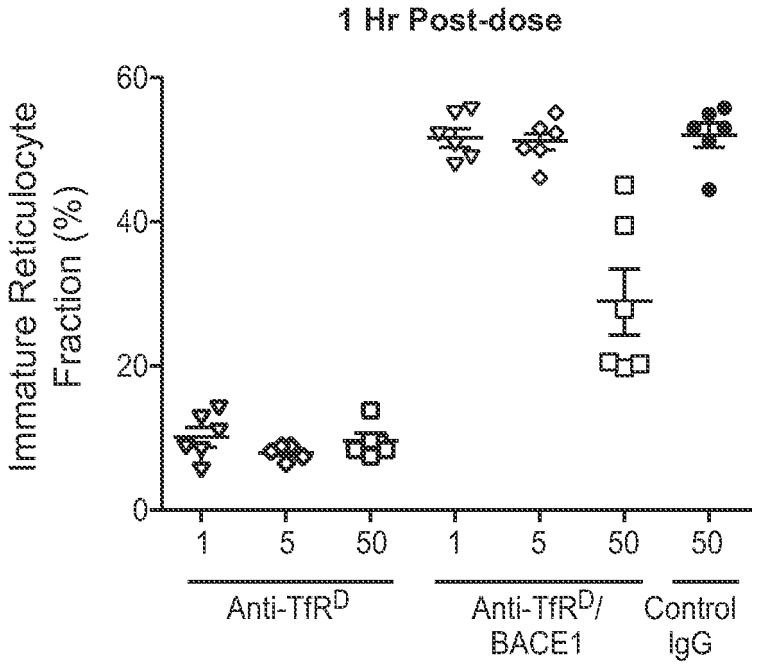

1 Hr Post-dose
Immature Reticulocyte Fraction (%)
60
40
20
0
1
5
50
1
5
50
50
Anti-TfR^D
Anti-TfR^D/ BACE1
Control IgG

FIG. 2B

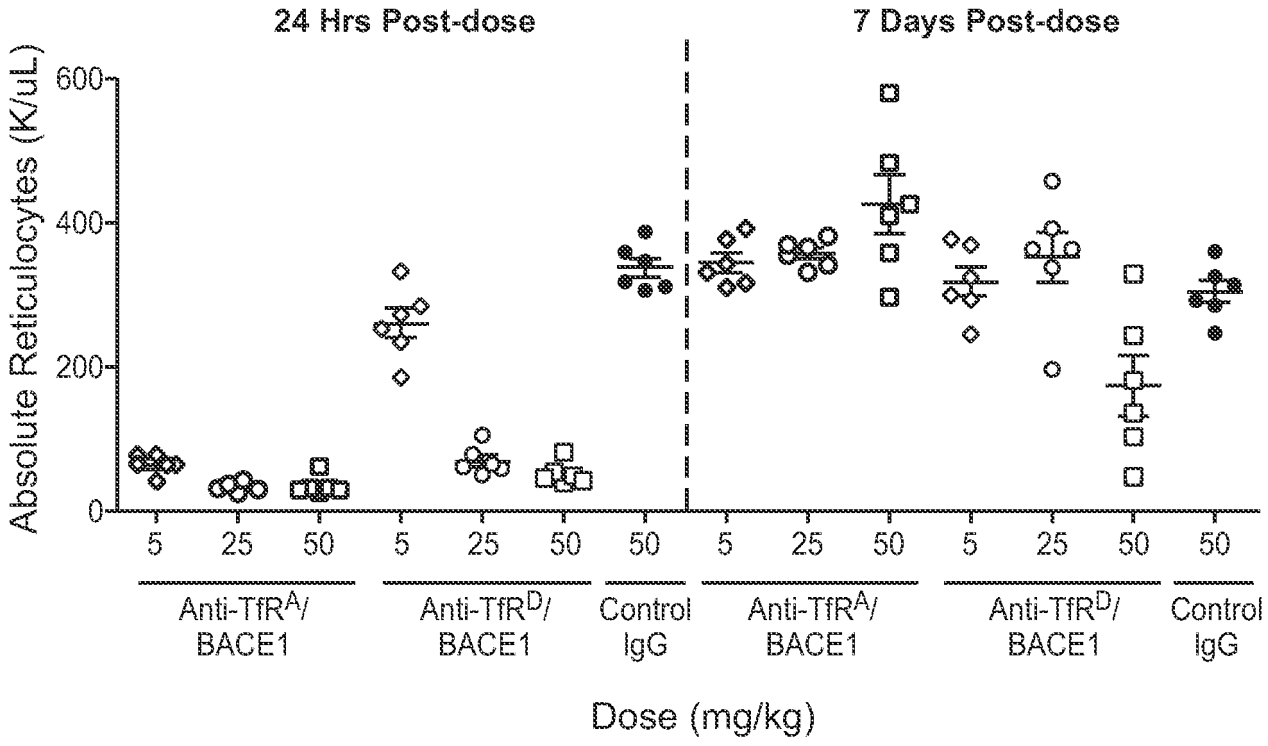

24 Hrs Post-dose
7 Days Post-dose
Absolute Reticulocytes (K/uL)
600
400
200
0
5
25
50
5
25
50
50
5
25
50
5
25
50
50
Anti-TfR^A/ BACE1
Anti-TfR^D/ BACE1
Control IgG
Anti-TfR^A/ BACE1
Anti-TfR^D/ BACE1
Control IgG
Dose (mg/kg)

FIG. 2C

FIG. 2E

FIG. 2D

FIG. 2F

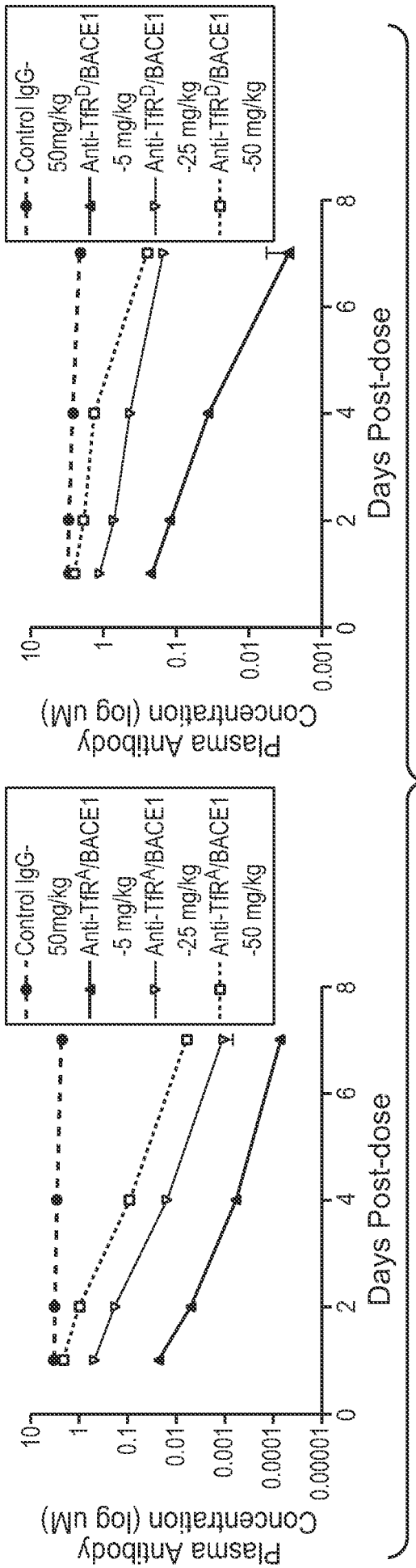

Plasma Antibody Concentration (log uM)
Days Post-dose
Control IgG-50mg/kg
Anti-TfR^A/BACE1 -5 mg/kg
Anti-TfR^A/BACE1 -25 mg/kg
Anti-TfR^A/BACE1 -50 mg/kg
Plasma Antibody Concentration (log uM)
Days Post-dose
Control IgG-50mg/kg
Anti-TfR^D/BACE1 -5 mg/kg
Anti-TfR^D/BACE1 -25 mg/kg
Anti-TfR^D/BACE1 -50 mg/kg

FIG. 2G

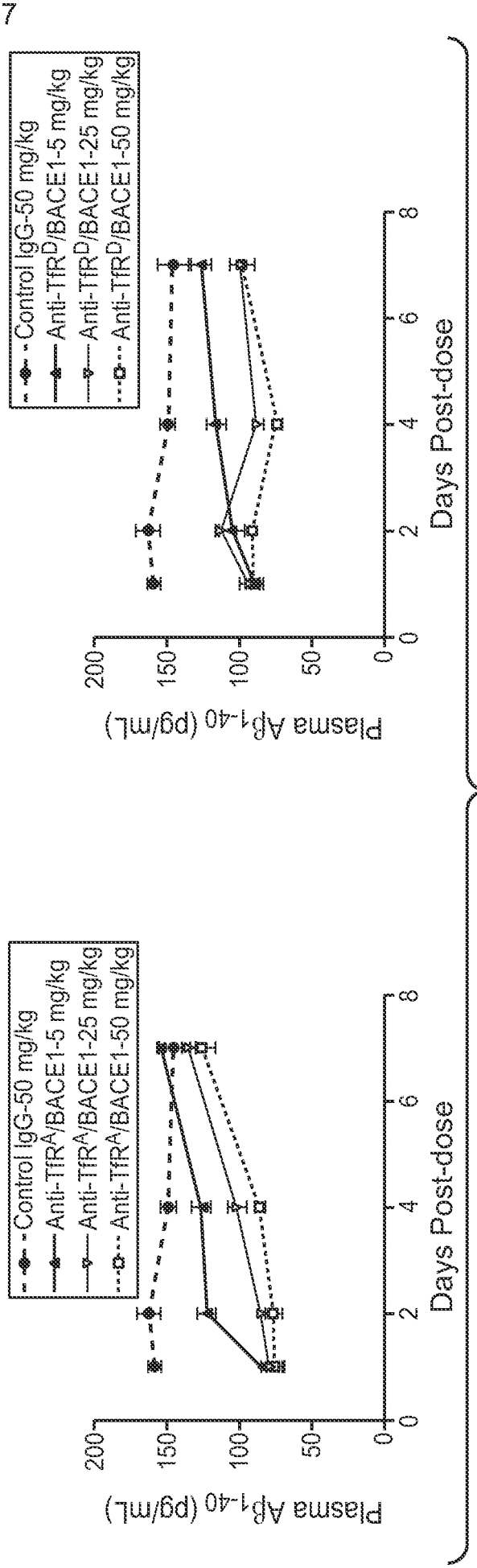
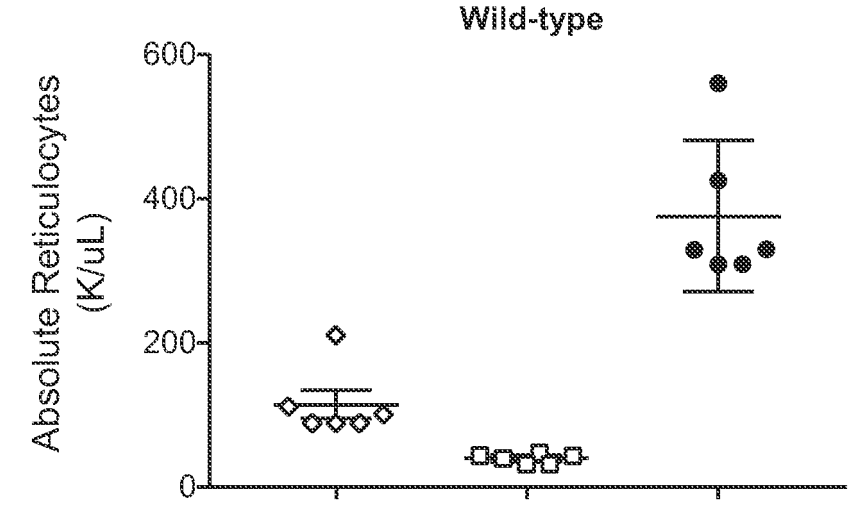
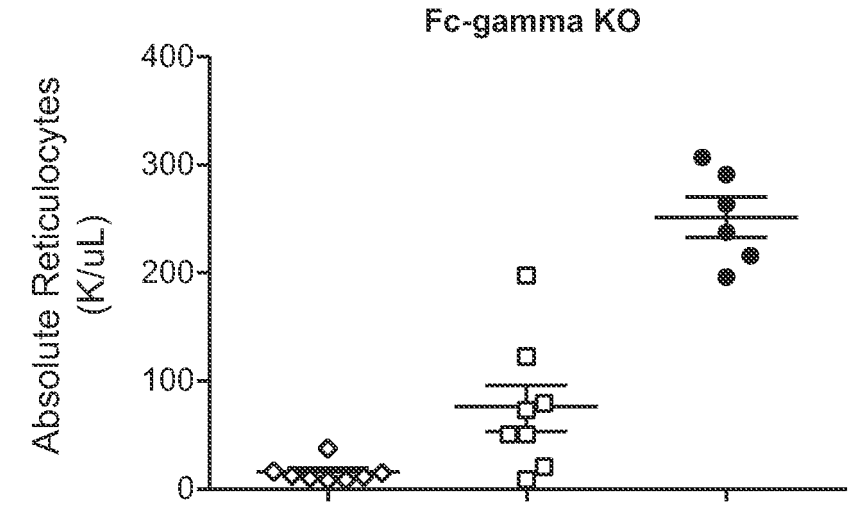

Plasma Aβ1-40 (pg/mL)
Days Post-dose
Control IgG-50 mg/kg
Anti-TfR^A/BACE1-5 mg/kg
Anti-TfR^A/BACE1-25 mg/kg
Anti-TfR^A/BACE1-50 mg/kg
Plasma Aβ1-40 (pg/mL)
Days Post-dose
Control IgG-50 mg/kg
Anti-TfR^D/BACE1-5 mg/kg
Anti-TfR^D/BACE1-25 mg/kg
Anti-TfR^D/BACE1-50 mg/kg

FIG. 2H



Dose (mg/kg)	1	25	25
Antibody	Anti-TfR^D	Anti-TfR^D	Control IgG
Effector Function	-	-	+
Clinical Signs	-	-	-

FIG. 3A



Dose (mg/kg)	25	25	25
Antibody	Anti-TfR^D	Anti-TfR^D/BACE1	Control IgG
Effector Function	+	-	+
Clinical Signs	-	-	-

FIG. 3B

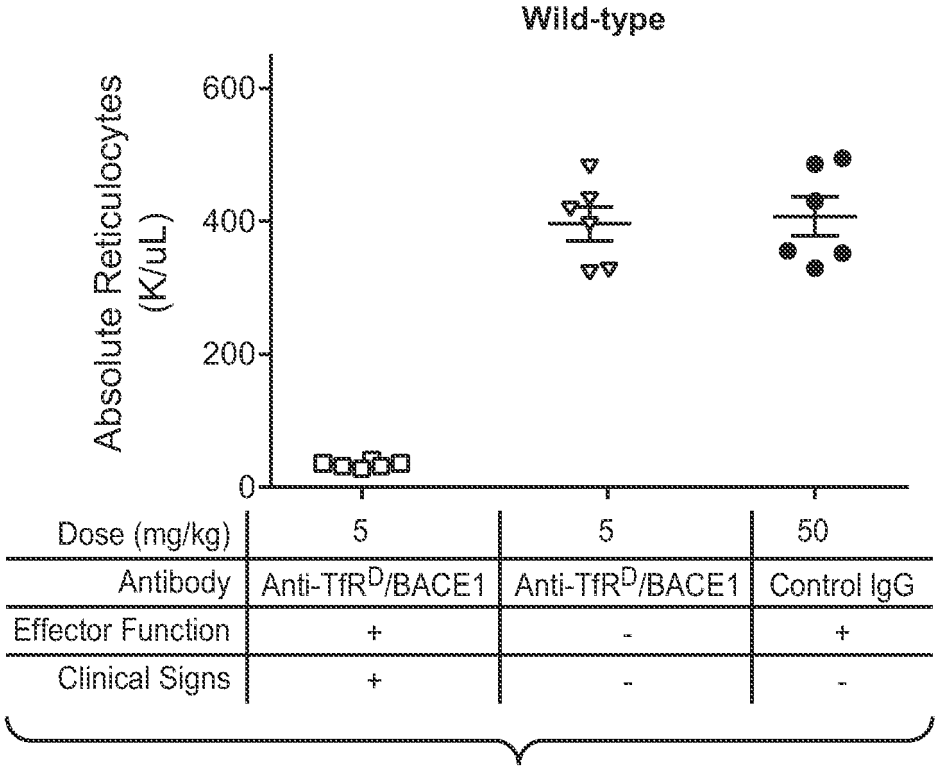

Wild-type
Absolute Reticulocytes (K/uL)
600
400
200
0
Dose (mg/kg) 5 5 50
Antibody Anti-TfR^D/BACE1 Anti-TfR^D/BACE1 Control IgG
Effector Function + - +
Clinical Signs + - -

FIG. 3C

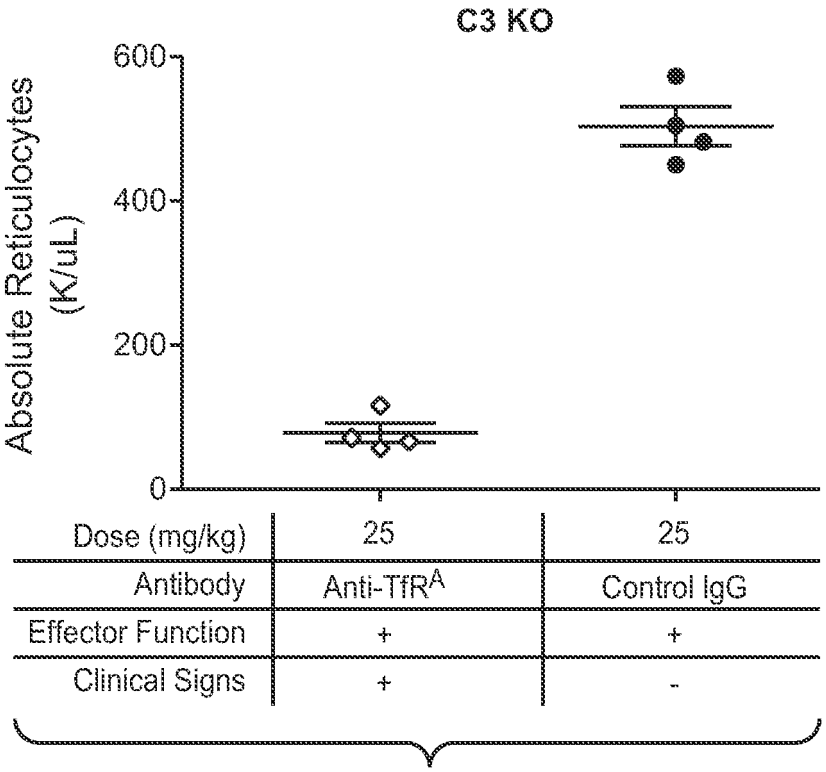

C3 KO
Absolute Reticulocytes (K/uL)
600
400
200
0
Dose (mg/kg) 25 25
Antibody Anti-TfR^A Control IgG
Effector Function + +
Clinical Signs + -

FIG. 3D

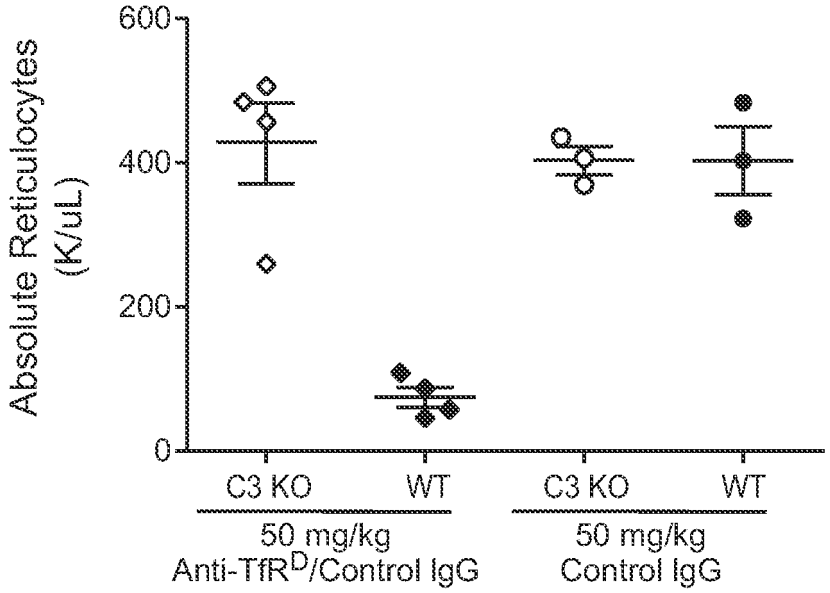

Absolute Reticulocytes (K/uL)
600
400
200
0
C3 KO
WT
C3 KO
WT
50 mg/kg
Anti-TfR^{D}/Control IgG
50 mg/kg
Control IgG

FIG. 3E

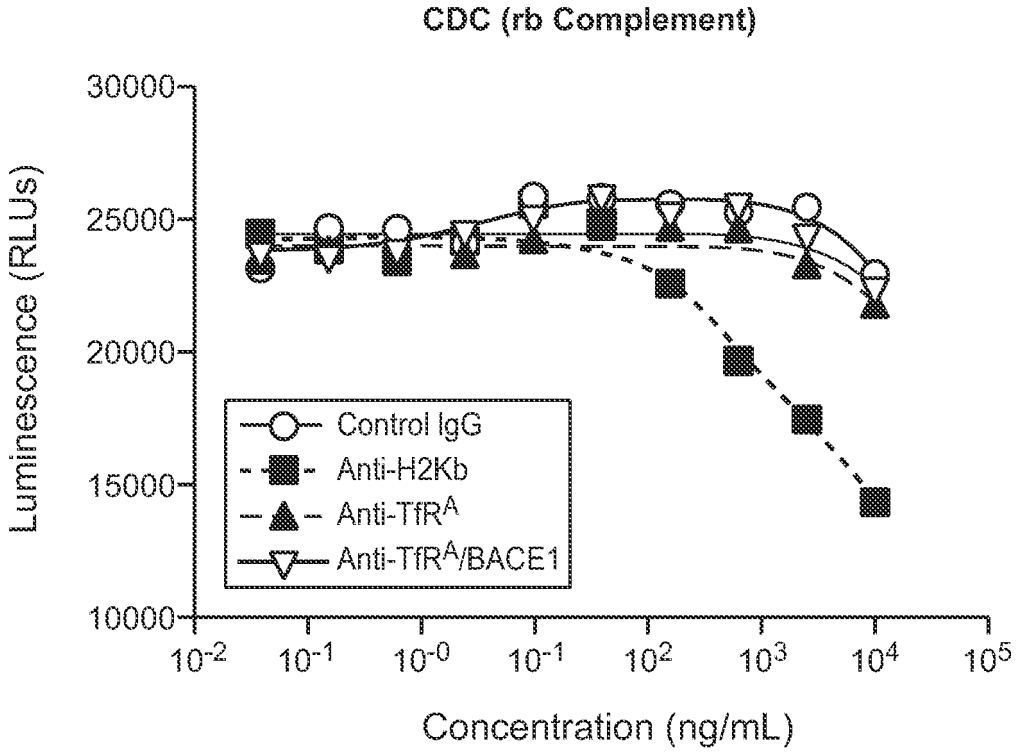

CDC (rb Complement)
Luminescence (RLUs)
30000
25000
20000
15000
10000
Control IgG
Anti-H2Kb
Anti-TfR^{A}
Anti-TfR^{A}/BACE1
10^{-2}
10^{-1}
10^{-0}
10^{-1}
10^{2}
10^{3}
10^{4}
10^{5}
Concentration (ng/mL)

FIG. 4A

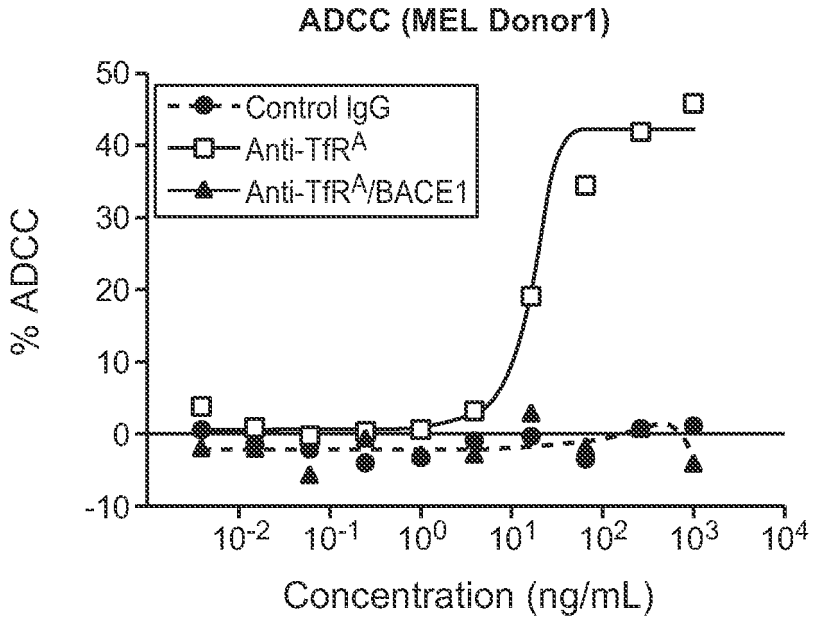

ADCC (MEL Donor1)
% ADCC
50
40
30
20
10
0
-10
Control IgG
Anti-TfR^A
Anti-TfR^A/BACE1
10^-2
10^-1
10^0
10^1
10^2
10^3
10^4
Concentration (ng/mL)

FIG. 4B

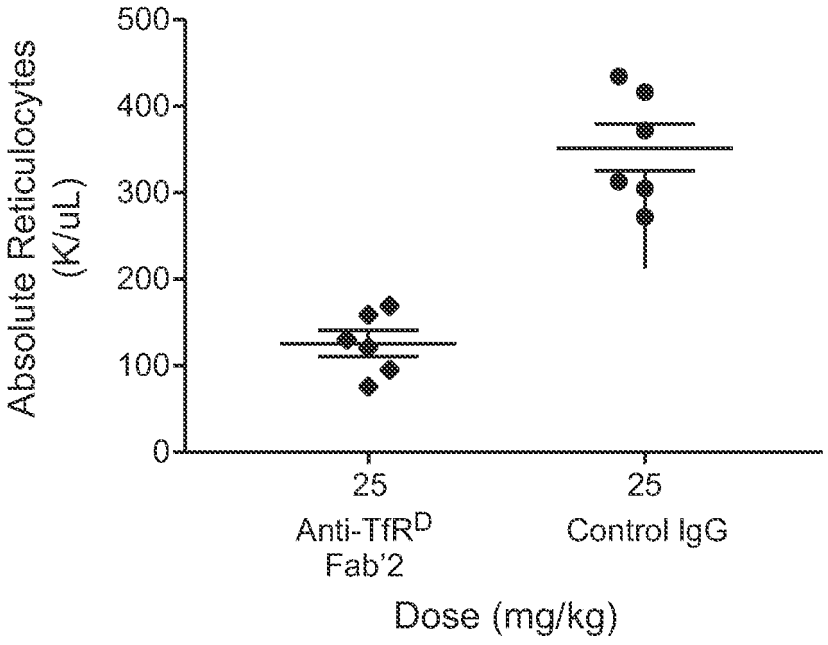

Absolute Reticulocytes (K/uL)
500
400
300
200
100
0
25
Anti-TfR^D Fab'2
25
Control IgG
Dose (mg/kg)

FIG. 5A

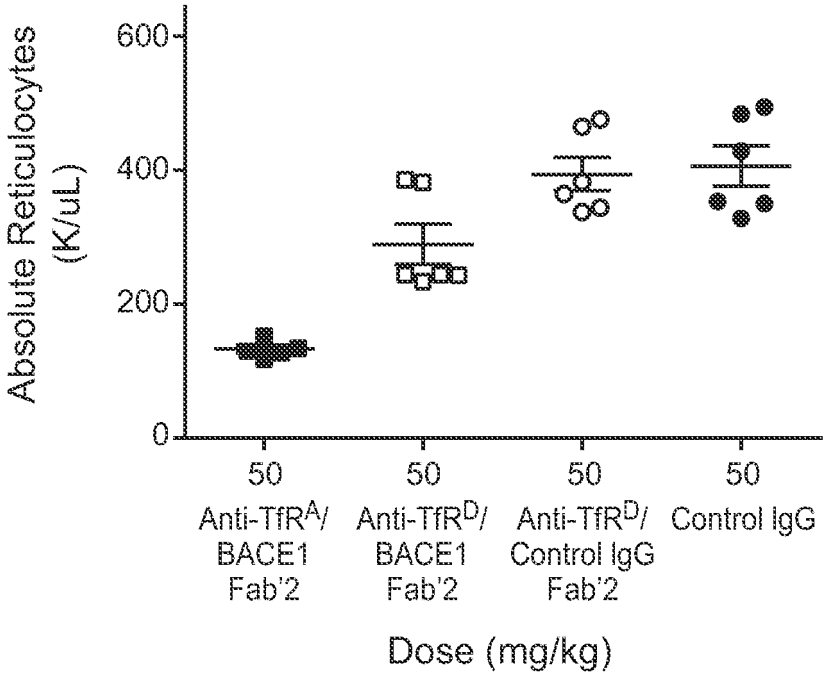

Absolute Reticulocytes (K/uL)
600
400
200
0
50
50
50
50
Anti-TfR^A/ BACE1 Fab'2
Anti-TfR^D/ BACE1 Fab'2
Anti-TfR^D/ Control IgG Fab'2
Control IgG
Dose (mg/kg)

FIG. 5B

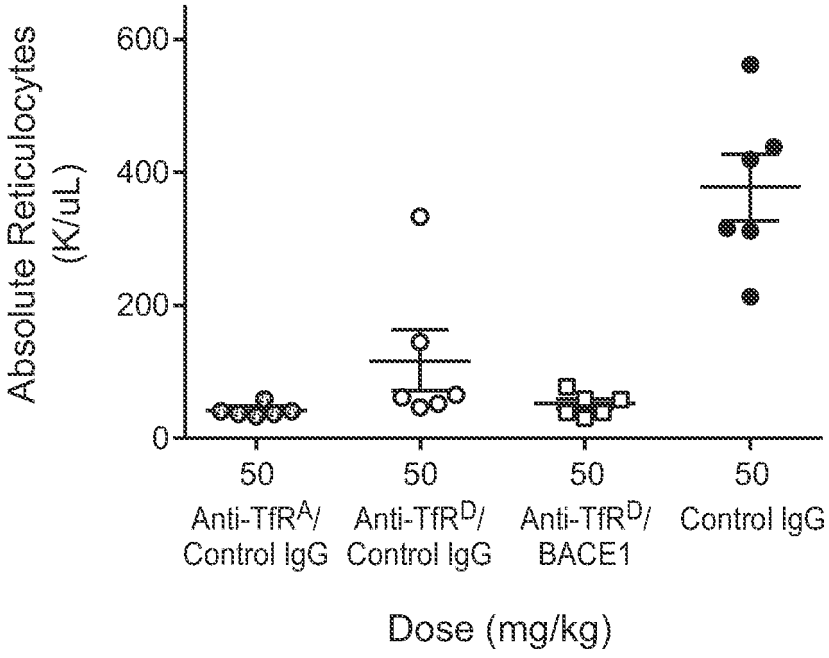

Absolute Reticulocytes (K/uL)
600
400
200
0
50
50
50
50
Anti-TfR^A/ Control IgG
Anti-TfR^D/ Control IgG
Anti-TfR^D/ BACE1
Control IgG
Dose (mg/kg)

FIG. 5C

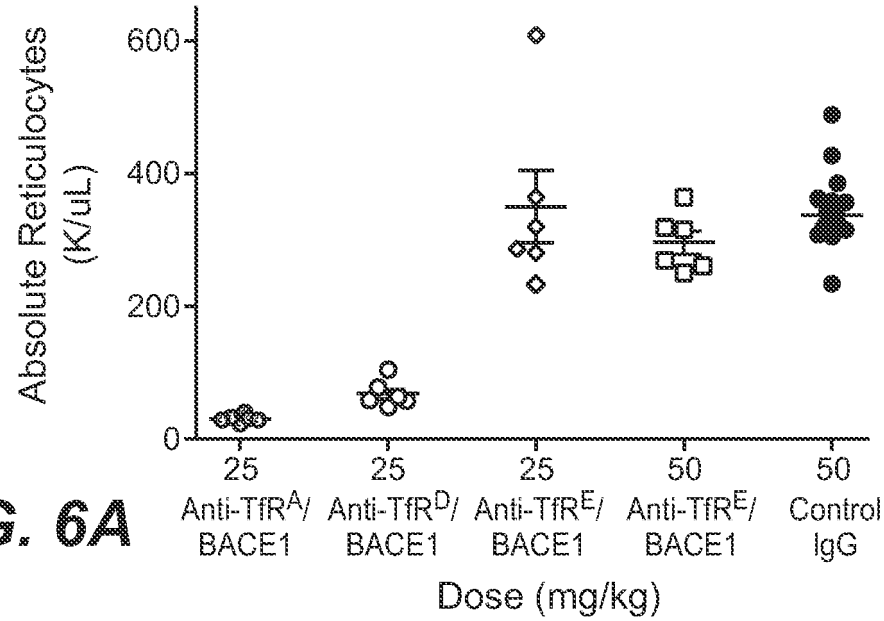


FIG. 6A

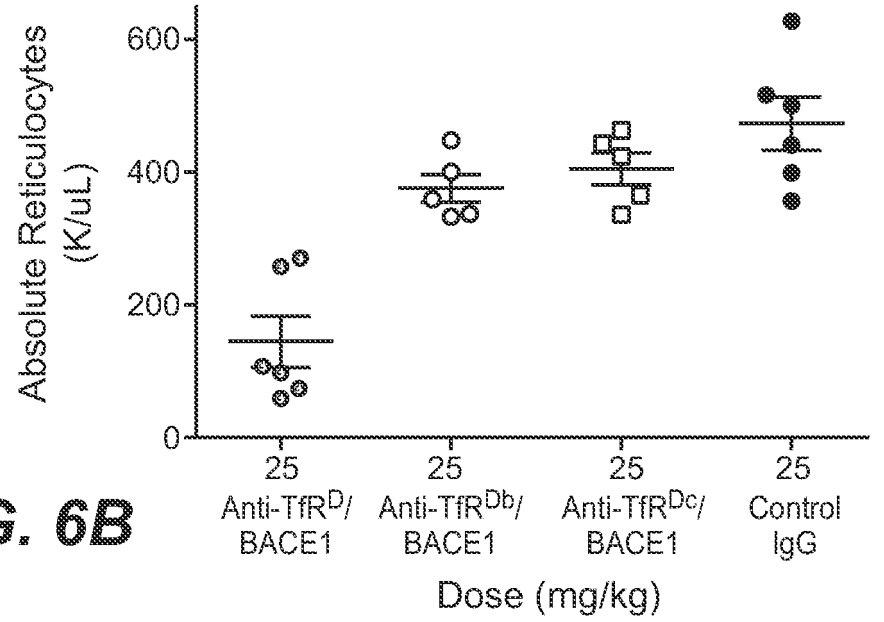


FIG. 6B

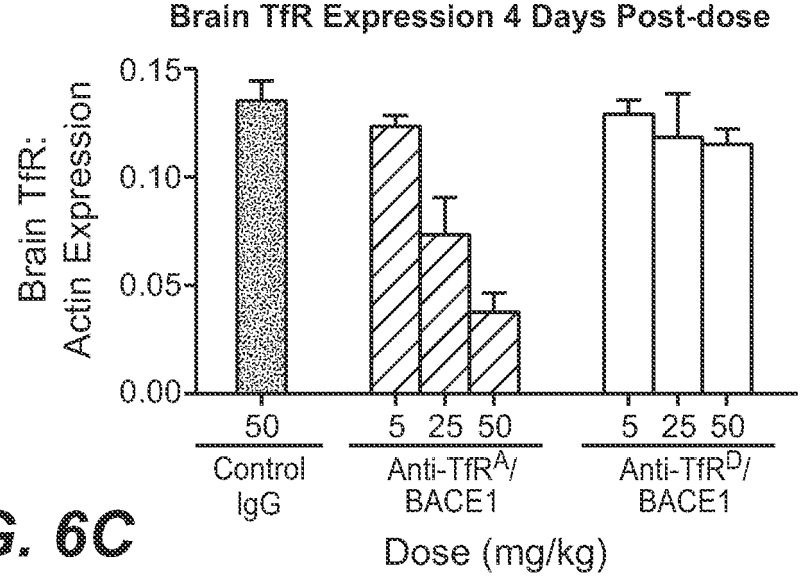


FIG. 6C

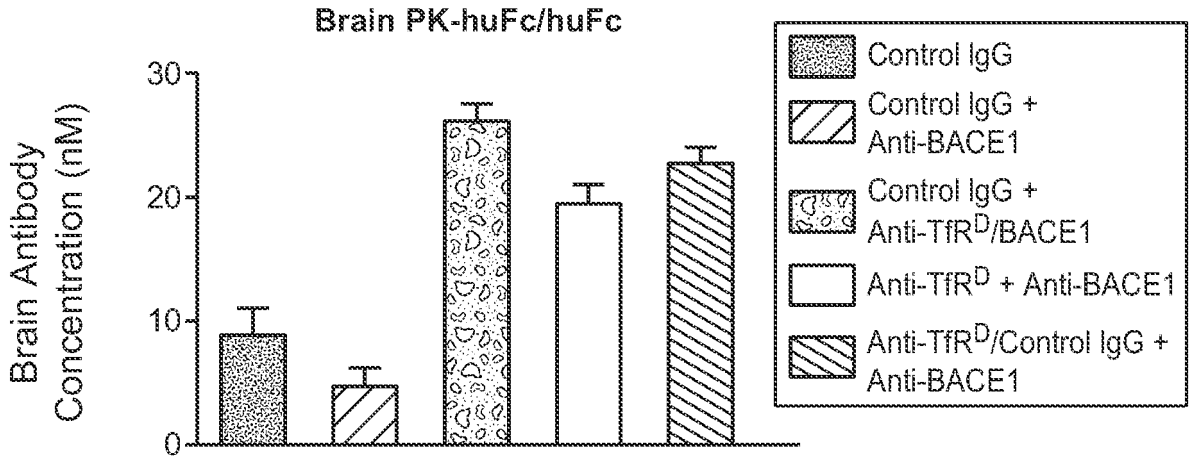


FIG. 7A

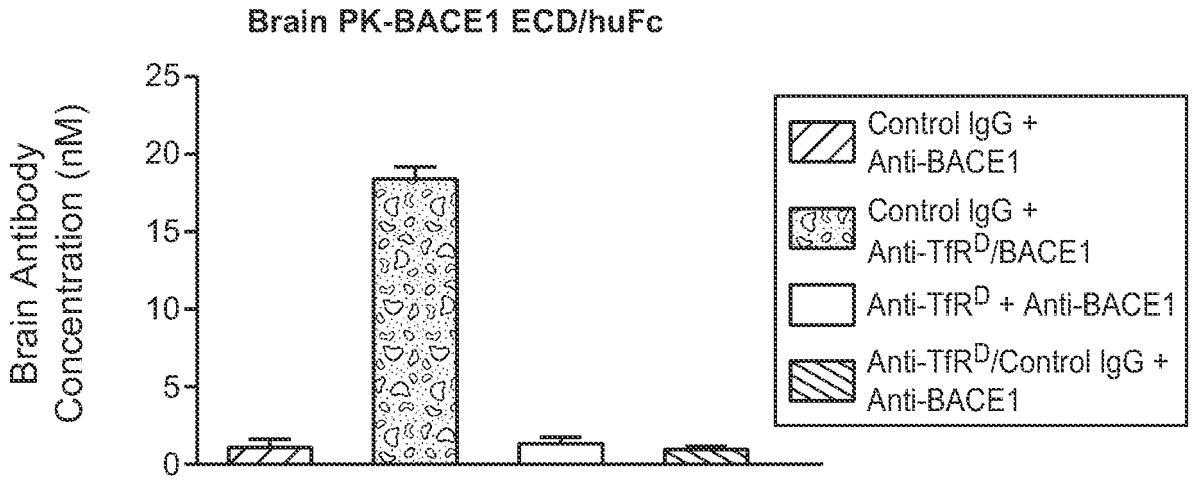


FIG. 7B

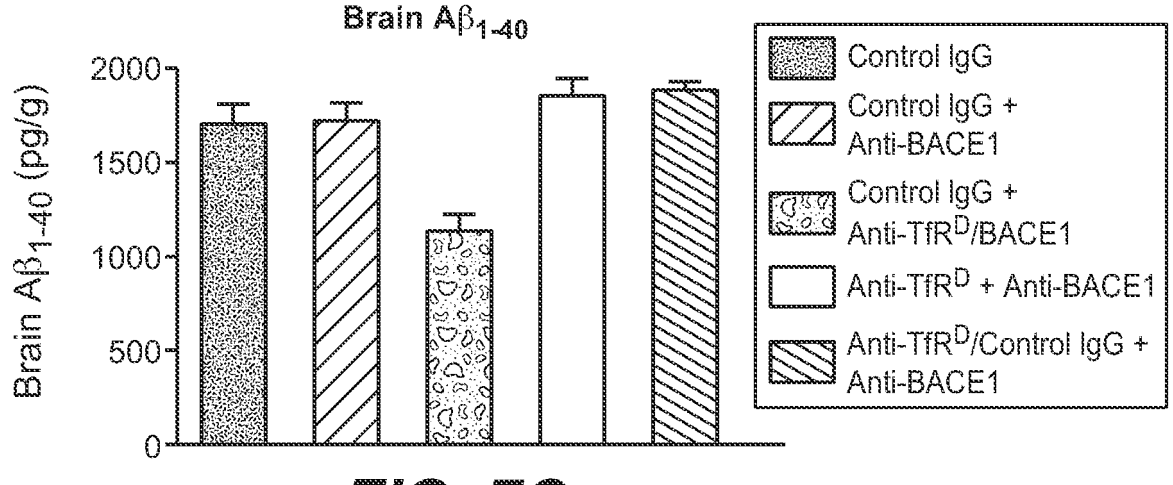


FIG. 7C

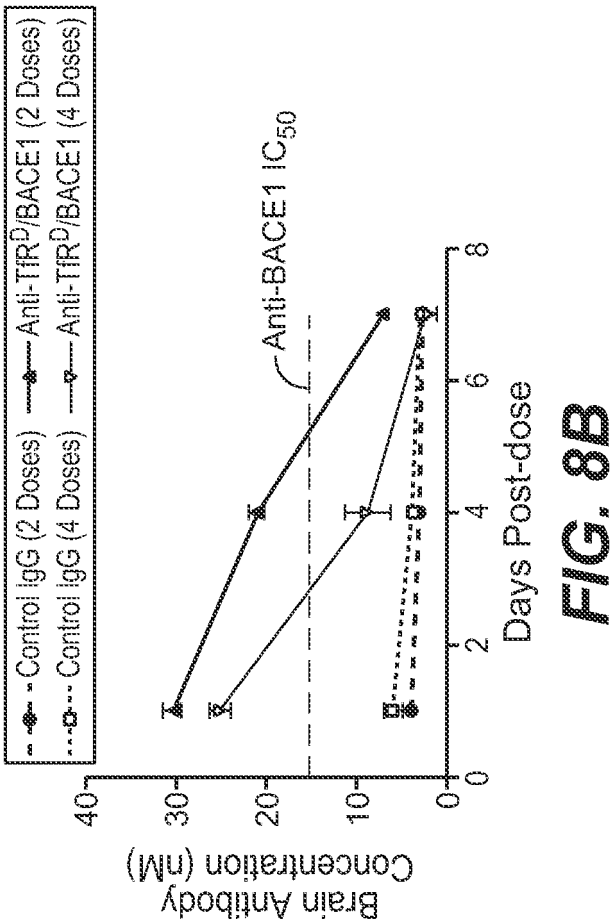


FIG. 8A

FIG. 8B

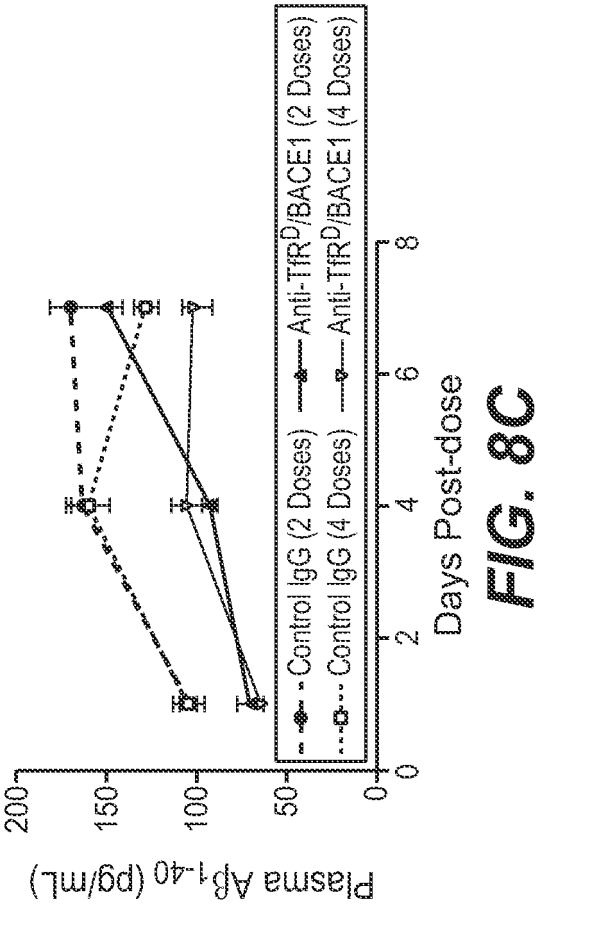


FIG. 8C

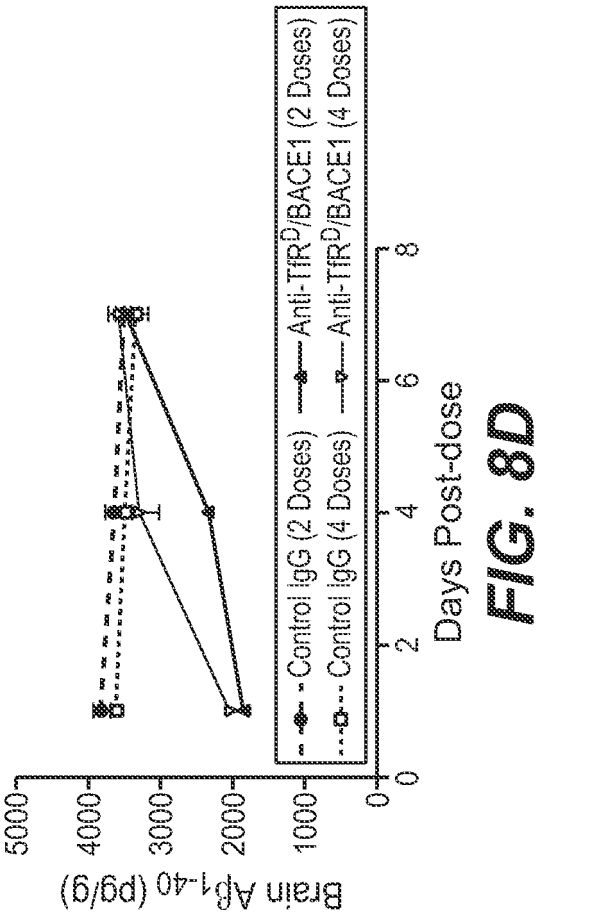


FIG. 8D

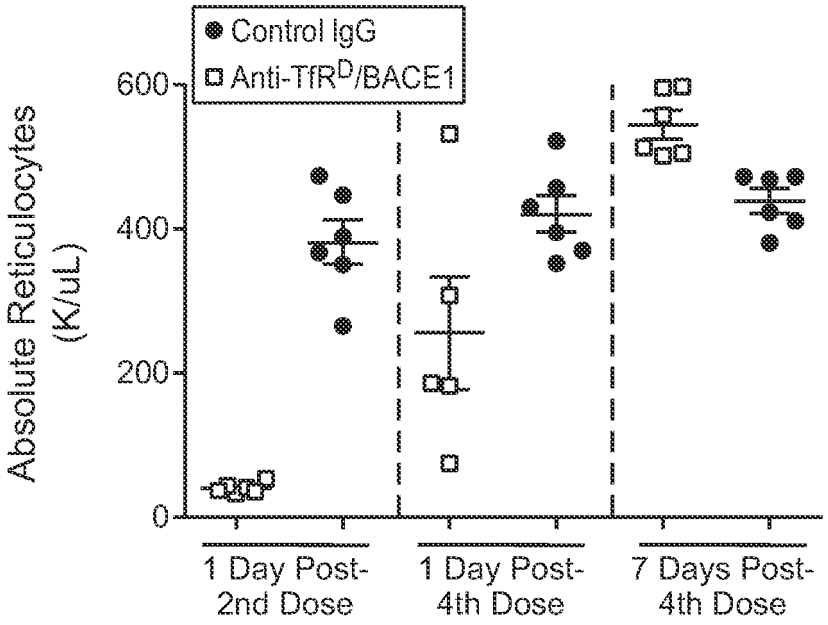

Control IgG
Anti-TfR^D/BACE1
Absolute Reticulocytes (K/uL)
600
400
200
0
1 Day Post-2nd Dose
1 Day Post-4th Dose
7 Days Post-4th Dose

FIG. 8E

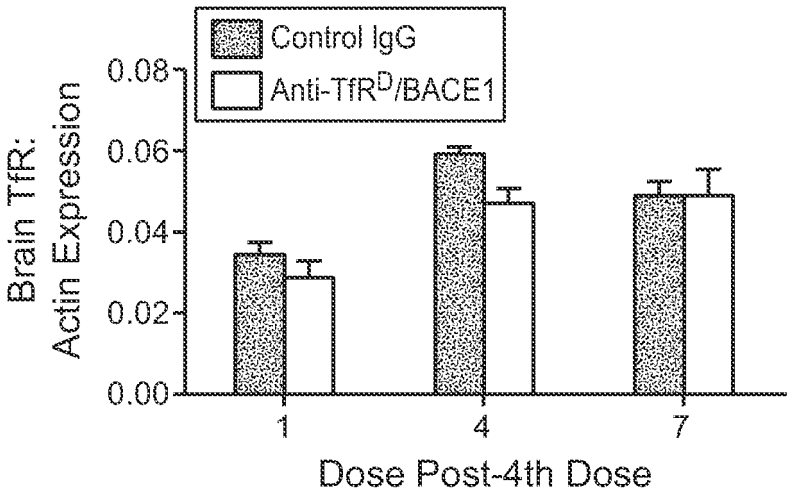

Control IgG
Anti-TfR^D/BACE1
Brain TfR: Actin Expression
0.08
0.06
0.04
0.02
0.00
1
4
7
Dose Post-4th Dose

FIG. 8F

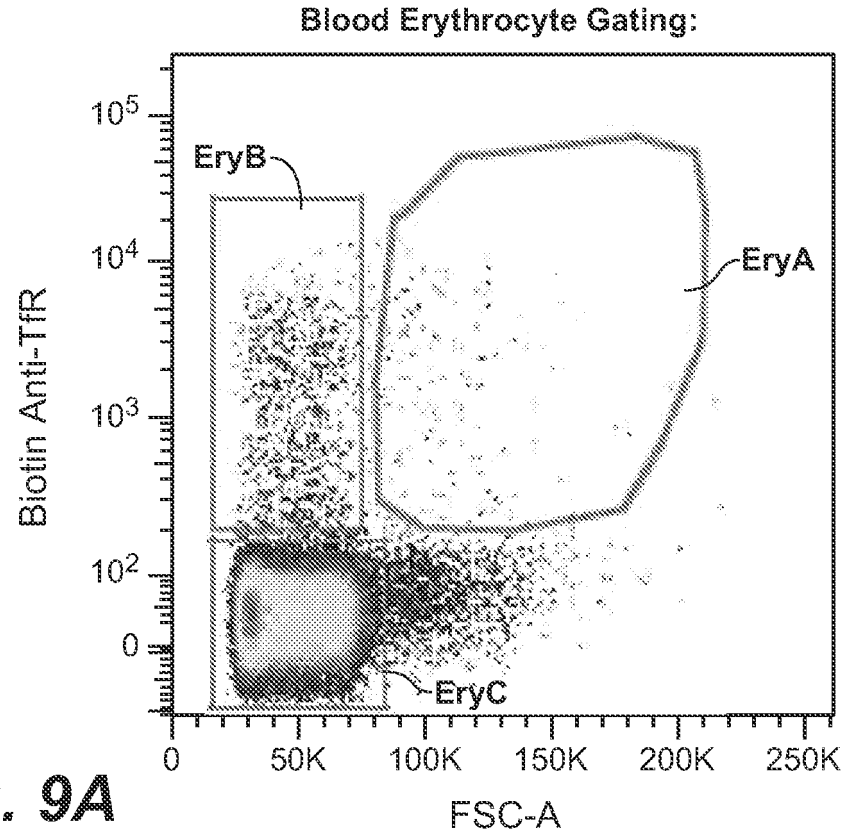

Blood Erythrocyte Gating:
EryB
EryA
EryC
Biotin Anti-TfR
10^5
10^4
10^3
10^2
0
0
50K
100K
150K
200K
250K
FSC-A

FIG. 9A

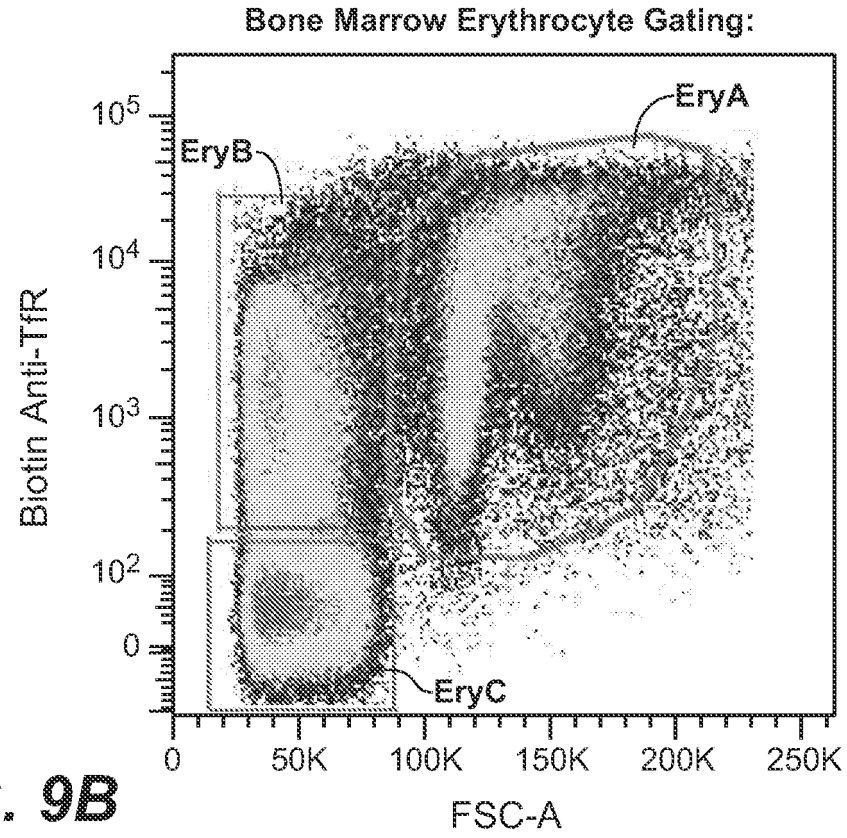

Bone Marrow Erythrocyte Gating:
EryA
EryB
EryC
Biotin Anti-TfR
10^5
10^4
10^3
10^2
0
0
50K
100K
150K
200K
250K
FSC-A

FIG. 9B

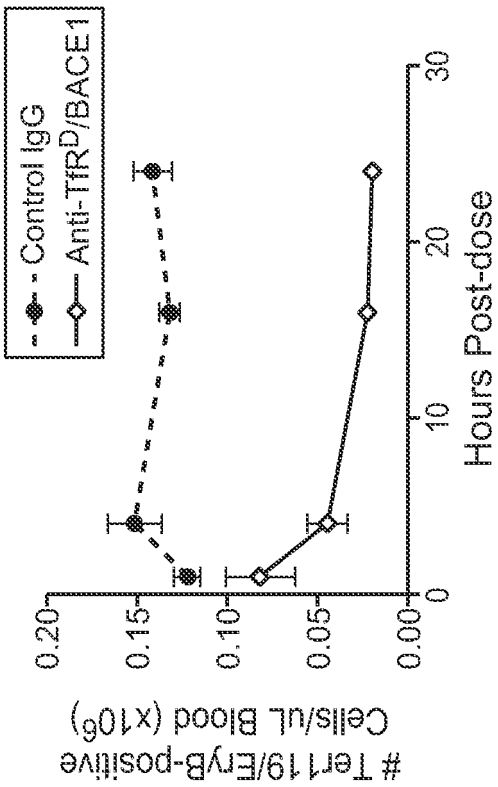


FIG. 9D

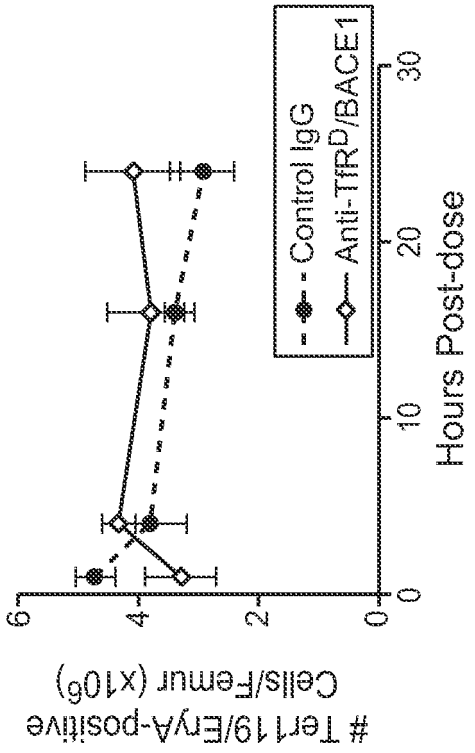


FIG. 10B

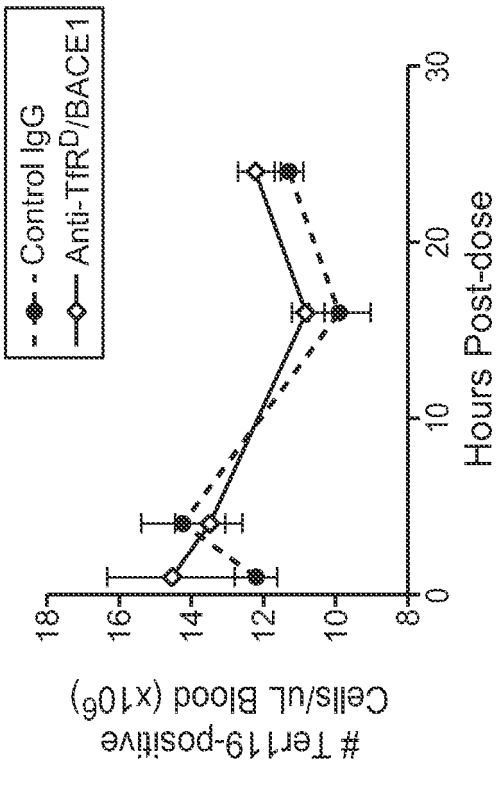


FIG. 9C

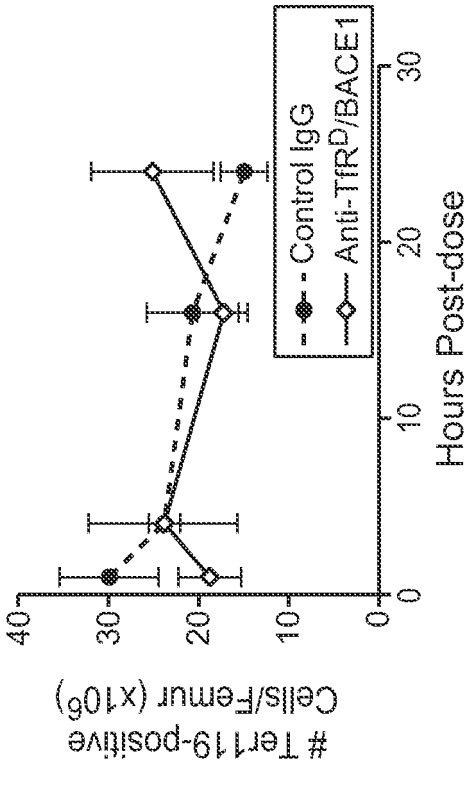


FIG. 10A

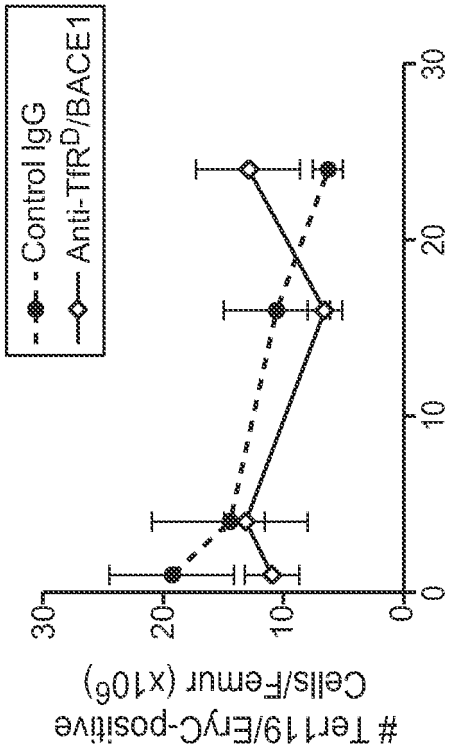


FIG. 10D

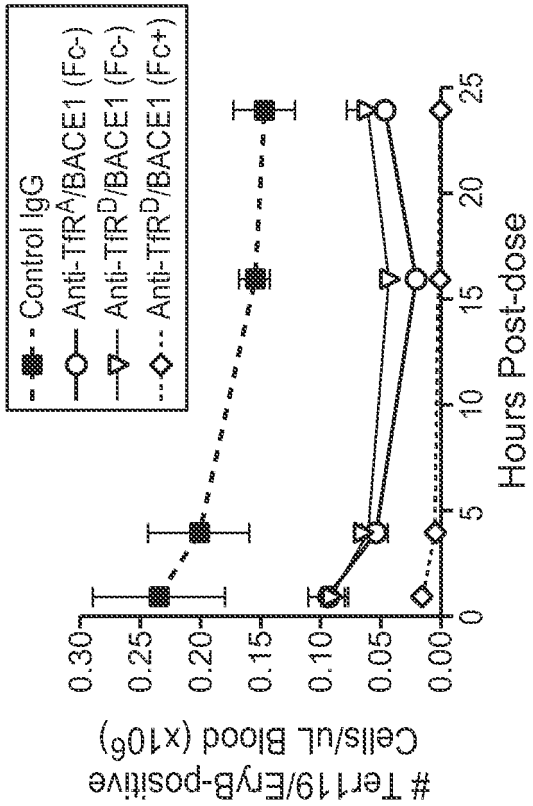


FIG. 11B

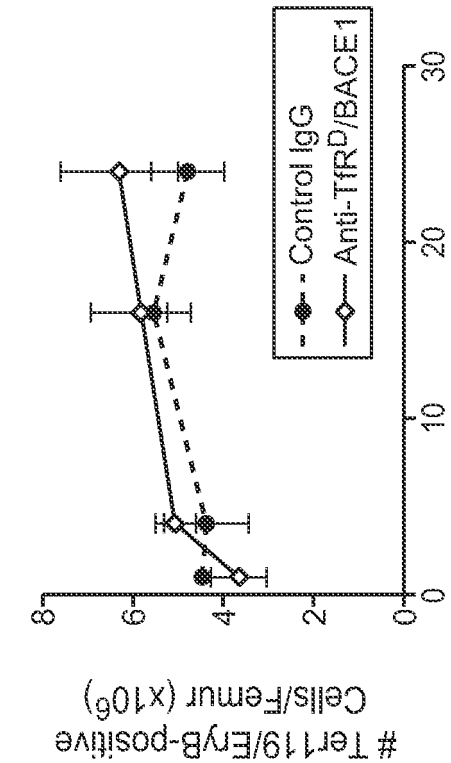


FIG. 10C

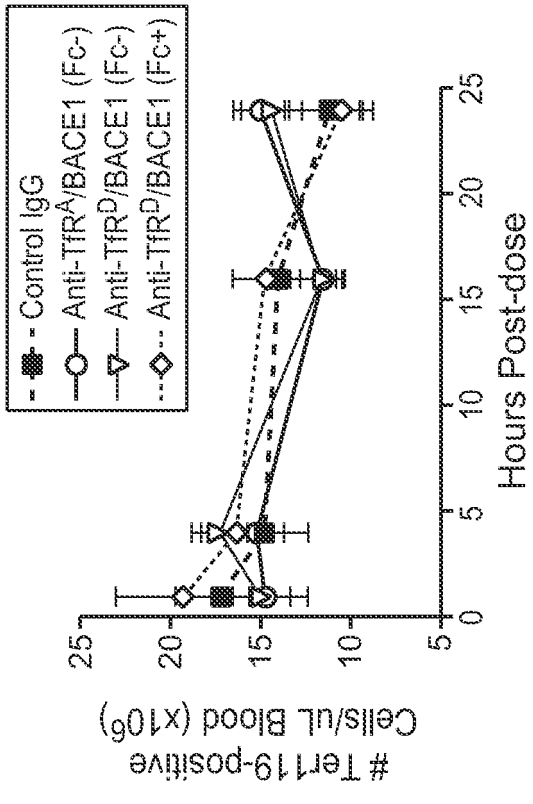


FIG. 11A

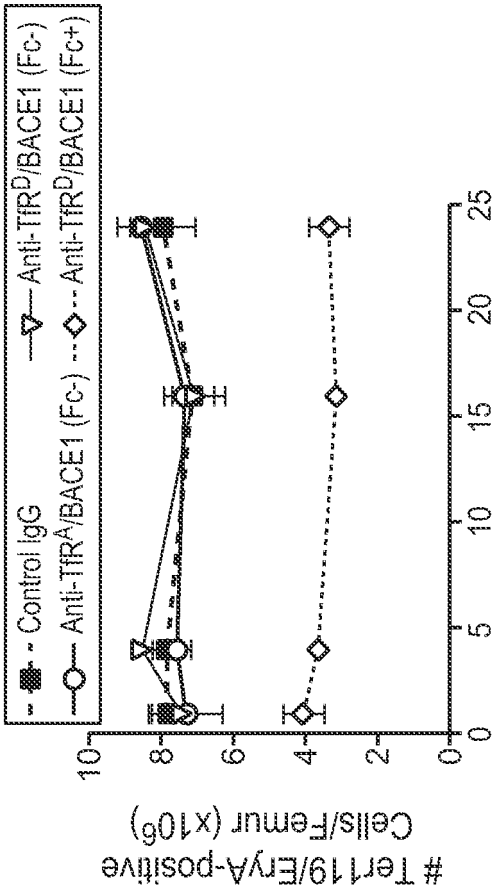


FIG. 12B

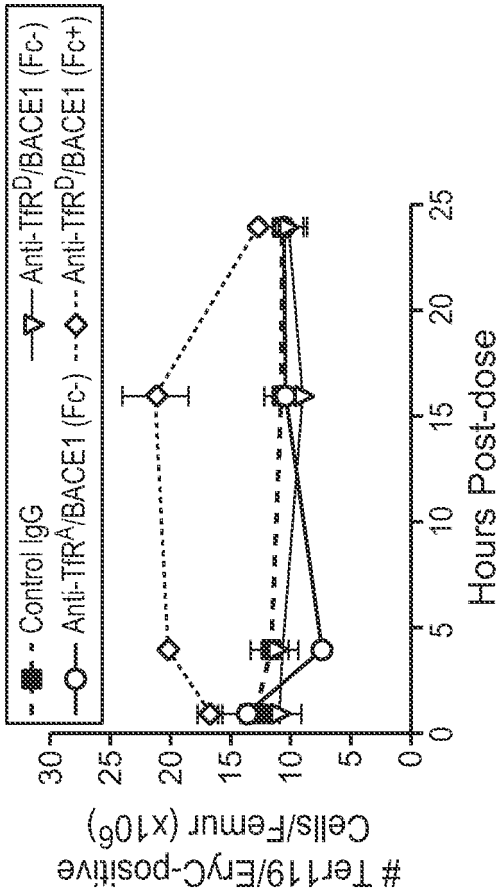


FIG. 12D

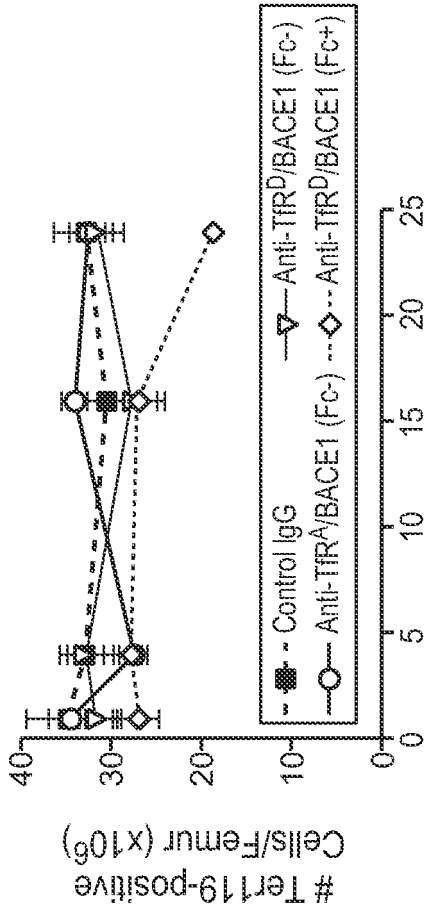


FIG. 12A

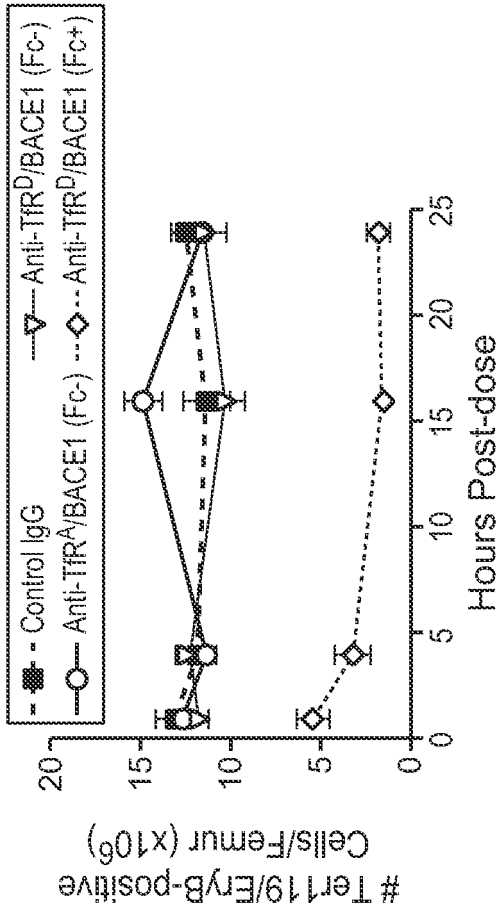


FIG. 12C

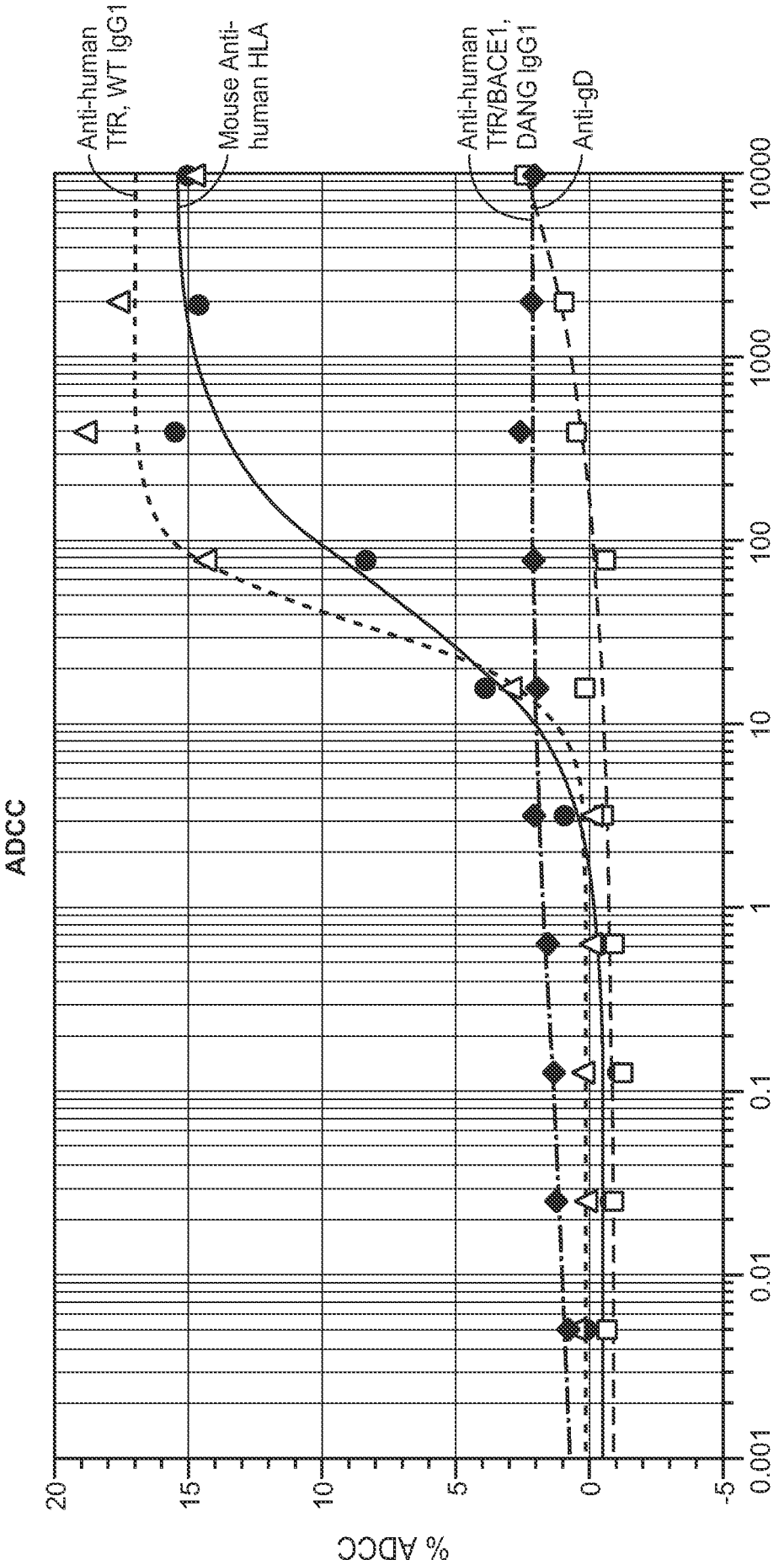

ADCC
% ADCC
20
15
10
5
0
-5
0.001
0.01
0.1
1
10
100
1000
10000
Concentration (ng/mL)
Anti-human TfR, WT IgG1
Mouse Anti-human HLA
Anti-human TfR/BACE1, DANG IgG1
Anti-gD

FIG. 13A

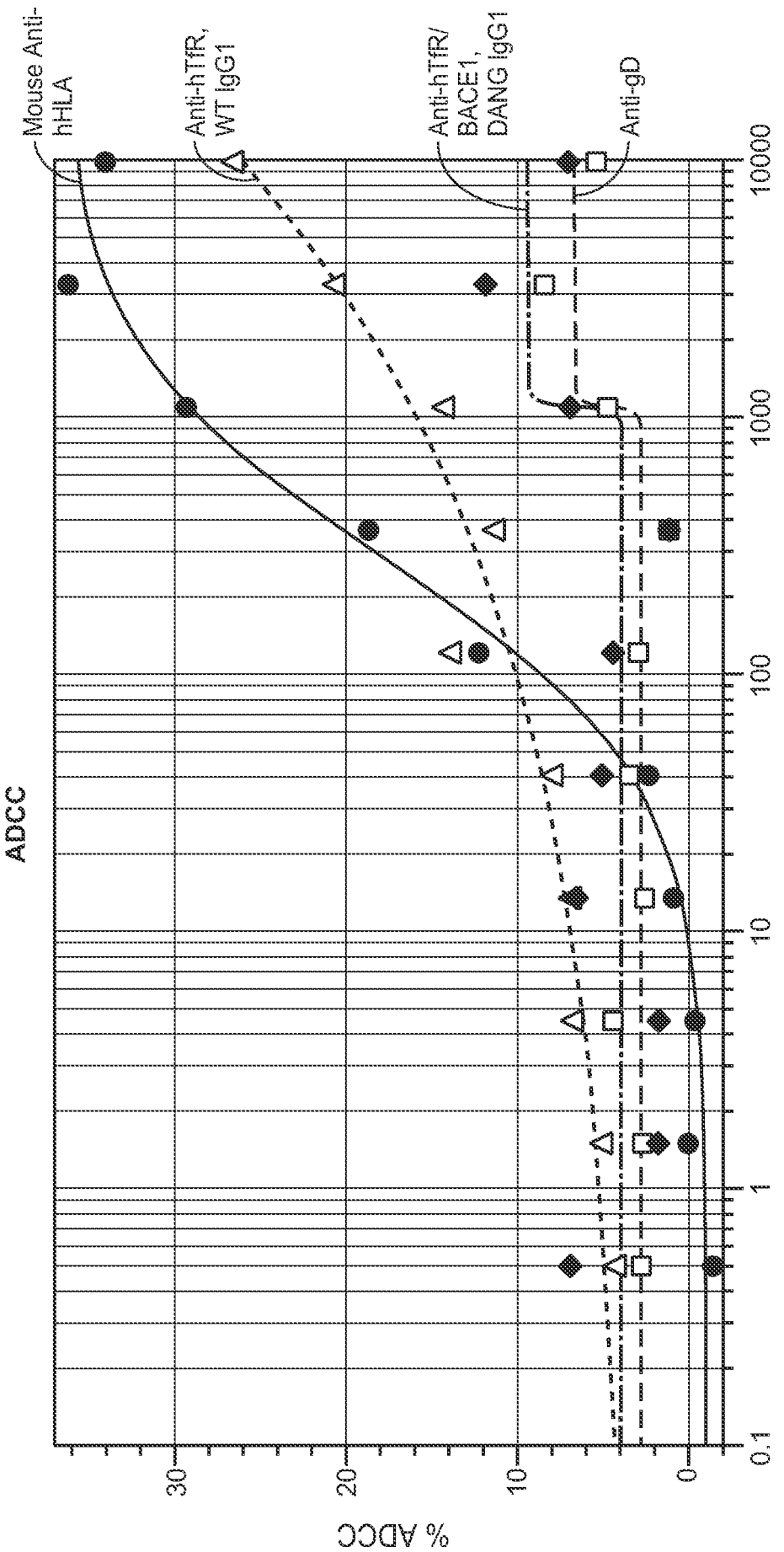

Mouse Anti-hHLA
Anti-hTfR, WT IgG1
Anti-hTfR/ BACE1, DANG IgG1
Anti-gD
ADCC
% ADCC
Concentration (ng/mL)
0.1
1
10
100
1000
10000
0
10
20
30

FIG. 13B

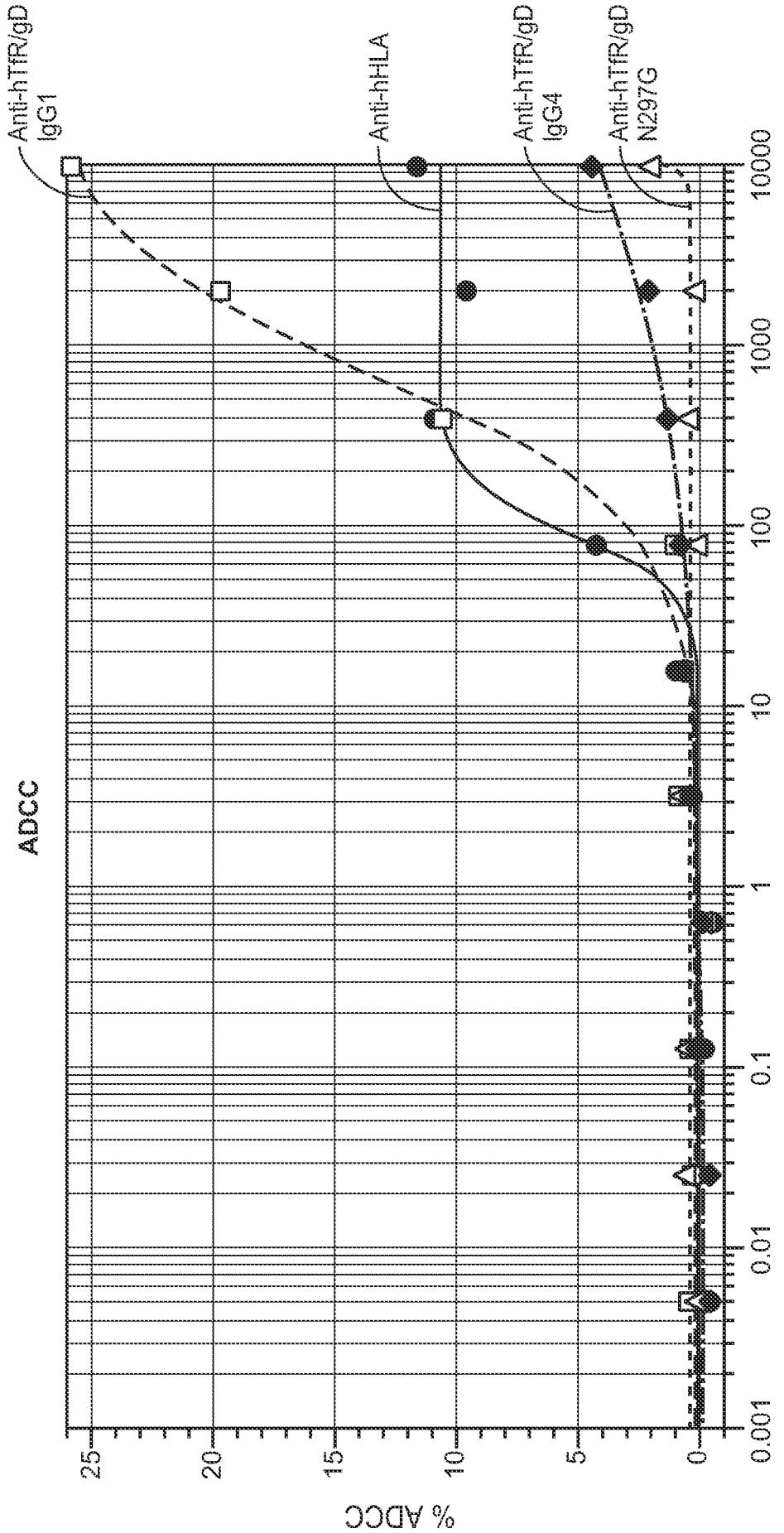

Anti-hTfR/gD IgG1
Anti-hHLA
Anti-hTfR/gD IgG4
Anti-hTfR/gD N297G
ADCC
% ADCC
0
5
10
15
20
25
0.001
0.01
0.1
1
10
100
1000
10000
Concentration (ng/mL)

FIG. 14A

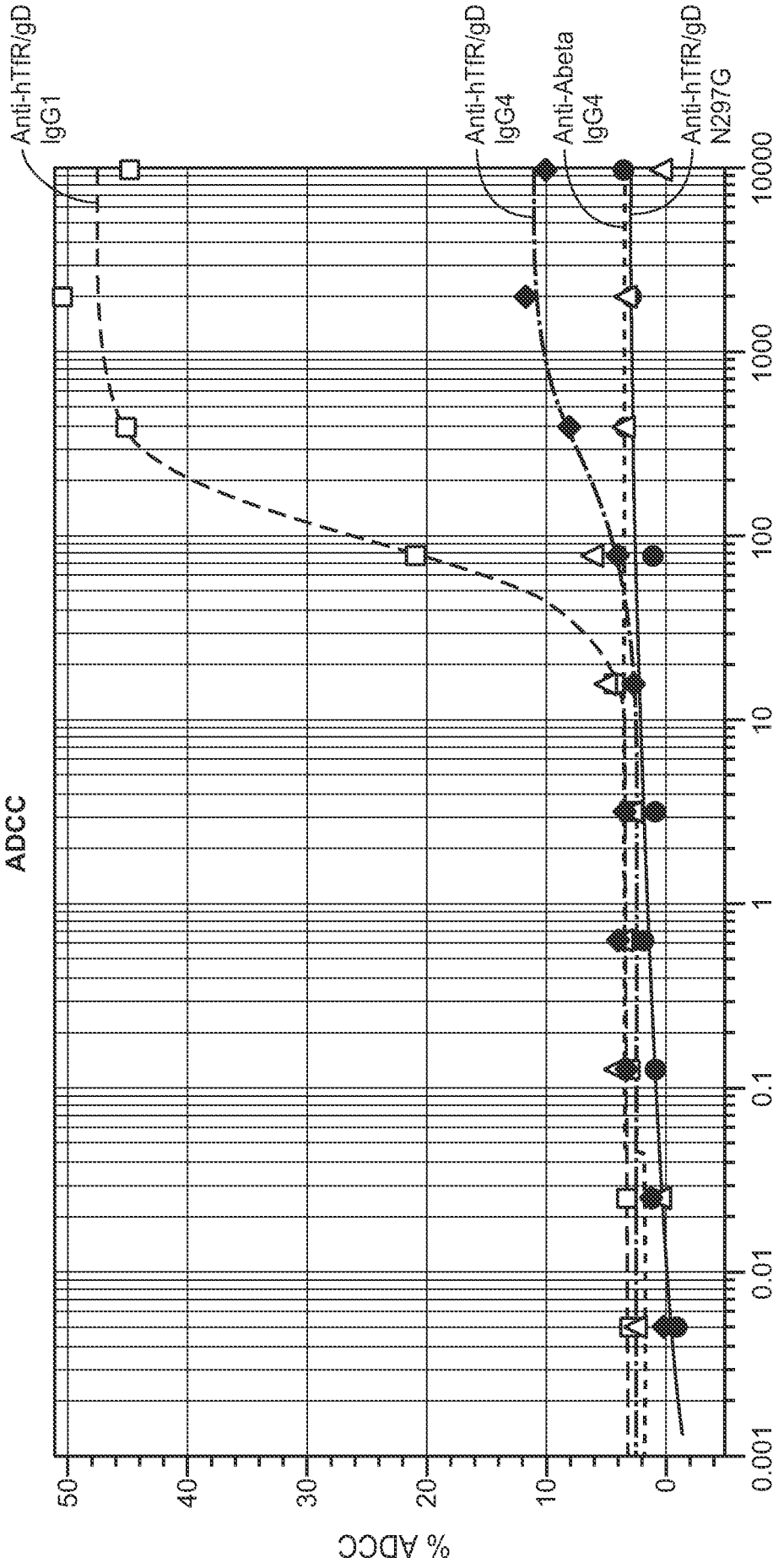

Anti-hTfR/gD IgG1
Anti-hTfR/gD IgG4
Anti-Abeta IgG4
Anti-hTfR/gD N297G
ADCC
% ADCC
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
10000
Concentration (ng/mL)

FIG. 14B

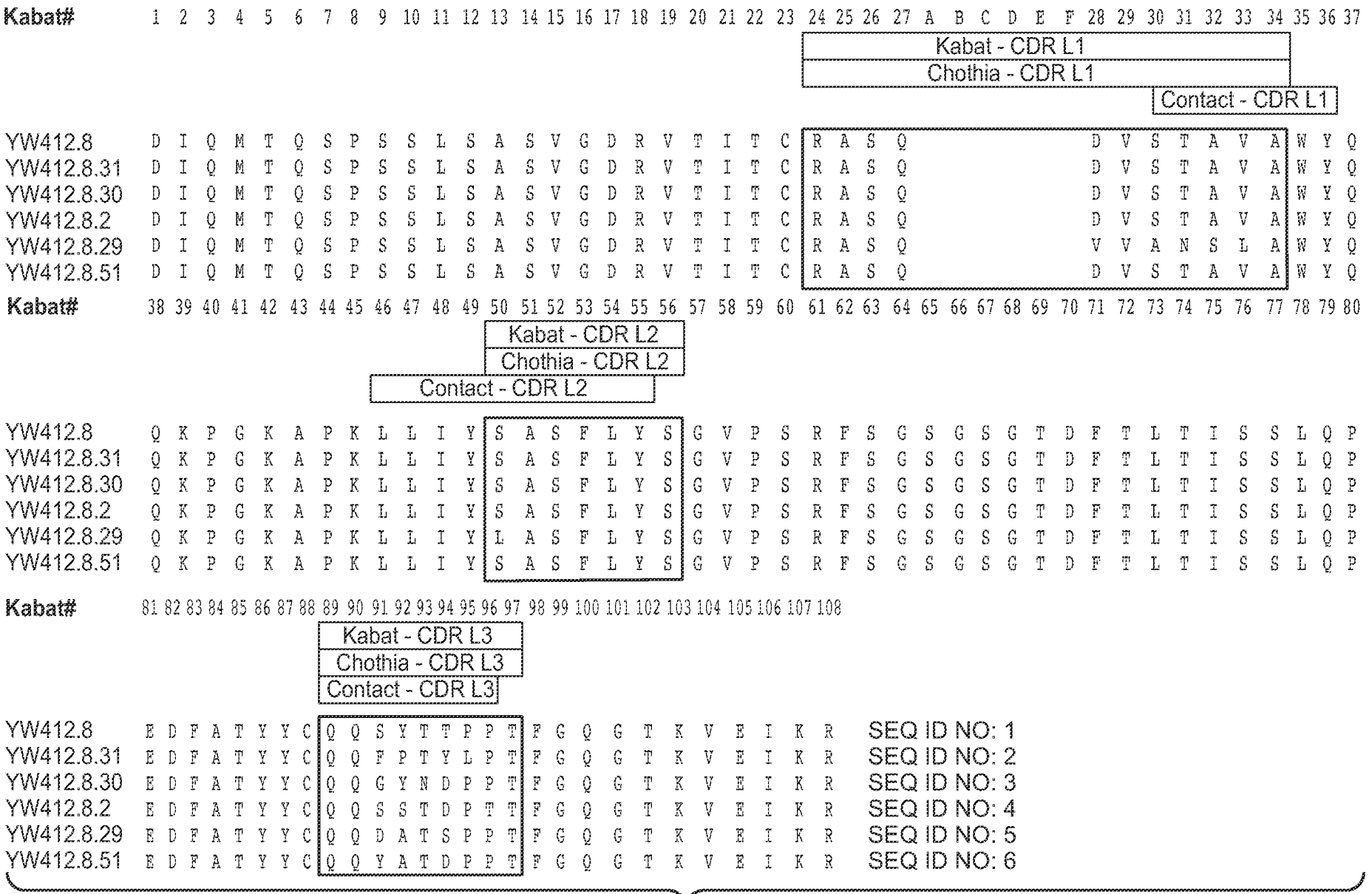

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Chothia - CDR L1
Contact - CDR L1
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YW412.8.30 D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q D V S T A V A W Y Q
YW412.8.2 D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q D V S T A V A W Y Q
YW412.8.29 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 V V A N S L A W Y Q
YW412.8.51 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 D V S T A V A W Y Q
Kabat#
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
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YW412.8.31 Q K P G K A P K L L I Y S A S F L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
YW412.8.30 Q K P G K A P K L L I Y S A S F L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
YW412.8.2 Q K P G K A P K L L I Y S A S F L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
YW412.8.29 Q K P G K A P K L L I Y L A S F L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
YW412.8.51 Q K P G K A P K L L I Y S A S F L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
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Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
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YW412.8.30 E D F A T Y Y C Q Q G Y N D P P T F G Q G T K V E I K R SEQ ID NO: 3
YW412.8.2 E D F A T Y Y C Q Q S S T D P T T F G Q G T K V E I K R SEQ ID NO: 4
YW412.8.29 E D F A T Y Y C Q Q D A T S P P T F G Q G T K V E I K R SEQ ID NO: 5
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FIG. 15A

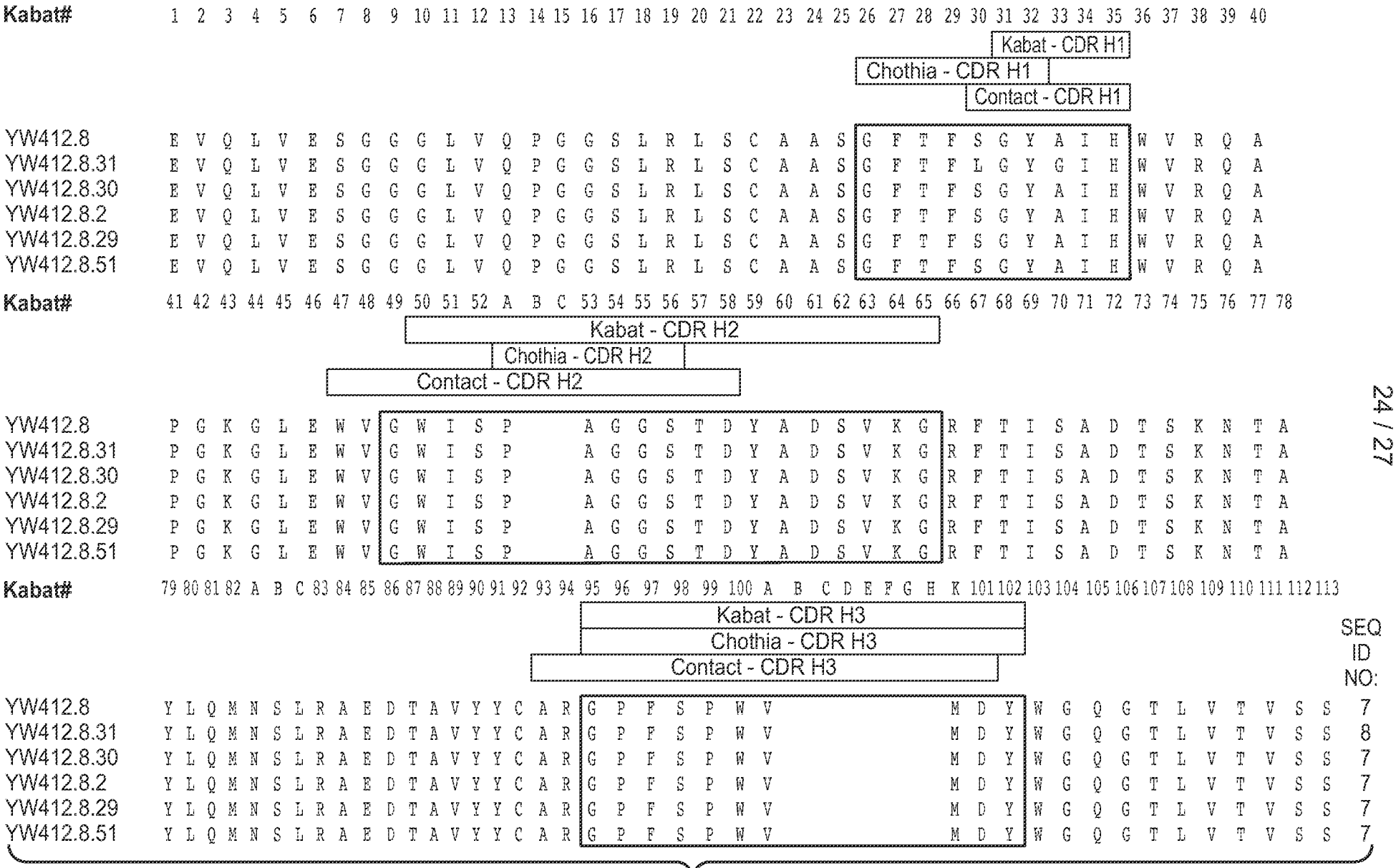

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Kabat - CDR H1
Chothia - CDR H1
Contact - CDR H1
YW412.8 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S G Y A I H W V R Q A
YW412.8.31 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F L G Y G I H W V R Q A
YW412.8.30 E V Q L V 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 G Y A I H W V R Q A
YW412.8.2 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 G Y A I H W V R Q A
YW412.8.29 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 G Y A I H W V R Q A
YW412.8.51 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 G Y A I H W V R Q A
Kabat#
41 42 43 44 45 46 47 48 49 50 51 52 A B C 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
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
YW412.8 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.31 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.30 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.2 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.29 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
YW412.8.51 P G K G L E W V G W I S P A G G S T D Y A D S V K G R F T I S A D T S K N T A
Kabat#
79 80 81 82 A B C 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 A B C D E F G H K 101 102 103 104 105 106 107 108 109 110 111 112 113
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3
SEQ ID NO:
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YW412.8.31 Y L Q M N S L R A E D T A V Y Y C A R G P F S P W V M D Y W G Q G T L V T V S S 8
YW412.8.30 Y L Q M N S L R A E D T A V Y Y C A R G P F S P W V M D Y W G Q G T L V T V S S 7
YW412.8.2 Y L Q M N S L R A E D T A V Y Y C A R G P F S P W V M D Y W G Q G T L V T V S S 7
YW412.8.29 Y L Q M N S L R A E D T A V Y Y C A R G P F S P W V M D Y W G Q G T L V T V S S 7
YW412.8.51 Y L Q M N S L R A E D T A V Y Y C A R G P F S P W V M D Y W G Q G T L V T V S S 7

FIG. 15B

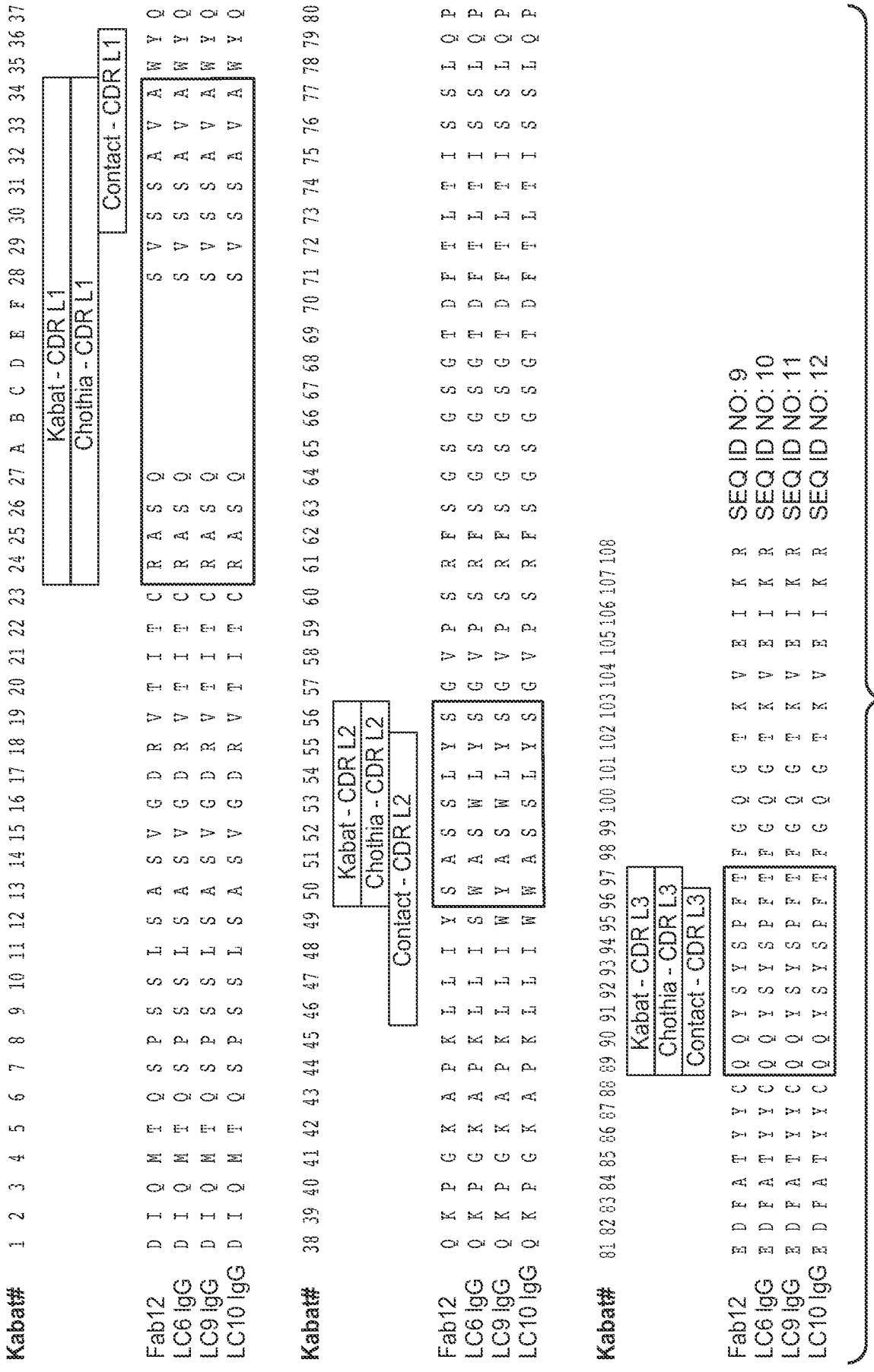

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Chothia - CDR L1
Contact - CDR L1
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LC6 IgG D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q S V S S A V A W Y Q
LC9 IgG D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q S V S S A V A W Y Q
LC10 IgG 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 V S S A V A W Y Q
Kabat#
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
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LC6 IgG Q K P G K A P K L L I S W A S W L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
LC9 IgG Q K P G K A P K L L I W Y A S W L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
LC10 IgG Q K P G K A P K L L I W W A S S L Y S G V P S R F S G S G S G T D F T L T I S S L Q P
Kabat#
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
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LC6 IgG E D F A T Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 10
LC9 IgG E D F A T Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 11
LC10 IgG E D F A T Y Y C Q Q Y S Y S P F T F G Q G T K V E I K R SEQ ID NO: 12

FIG. 16A

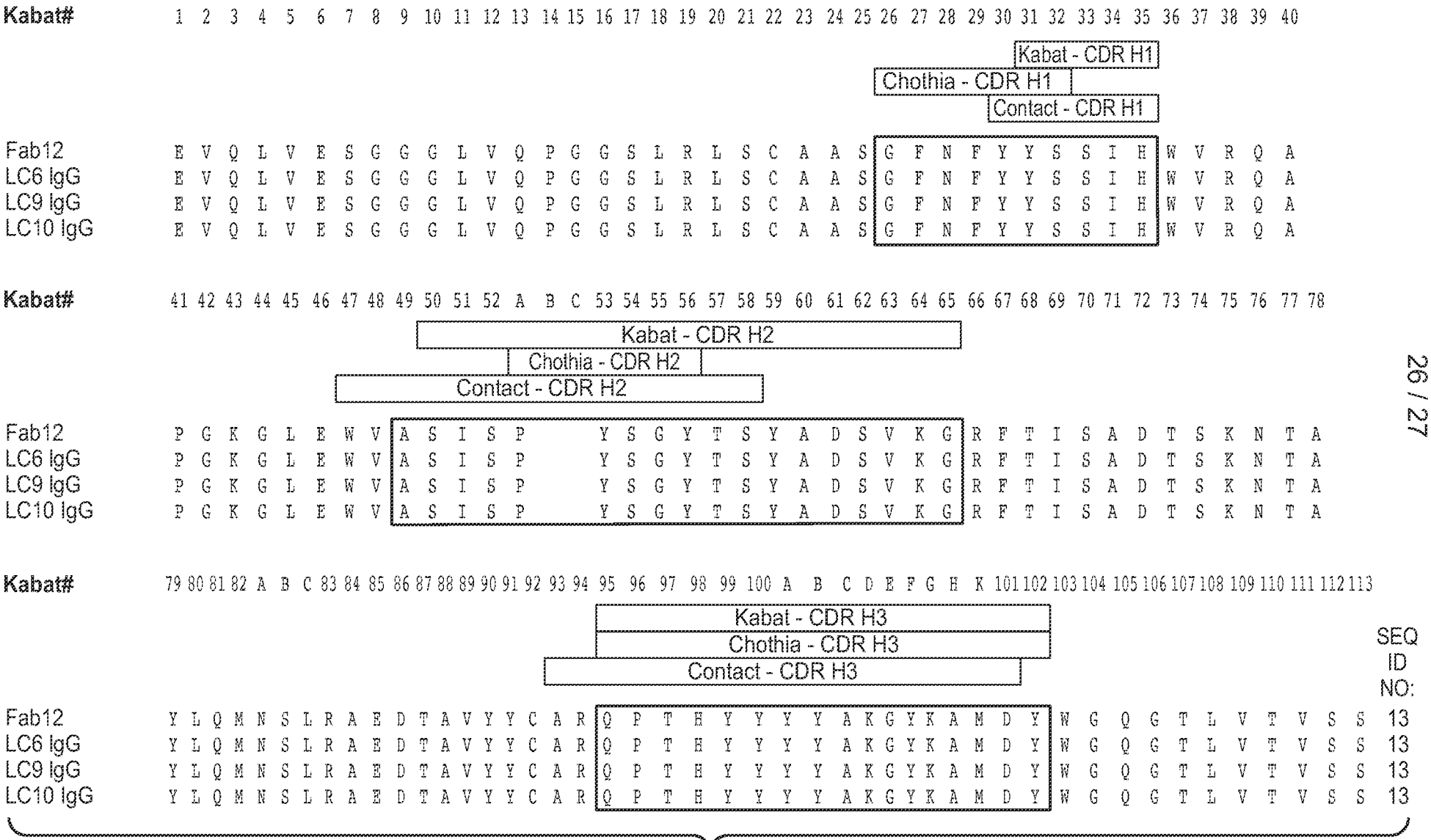

Kabat#
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Kabat - CDR H1
Chothia - CDR H1
Contact - CDR H1
Fab12 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
LC6 IgG E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
LC9 IgG E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N F Y Y S S I H W V R Q A
LC10 IgG 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 N F Y Y S S I H W V R Q A
Kabat#
41 42 43 44 45 46 47 48 49 50 51 52 A B C 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
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
Fab12 P G K G L E W V A S I S P Y S G Y T S Y A D S V K G R F T I S A D T S K N T A
LC6 IgG P G K G L E W V A S I S P Y S G Y T S Y A D S V K G R F T I S A D T S K N T A
LC9 IgG P G K G L E W V A S I S P Y S G Y T S Y A D S V K G R F T I S A D T S K N T A
LC10 IgG P G K G L E W V A S I S P Y S G Y T S Y A D S V K G R F T I S A D T S K N T A
Kabat#
79 80 81 82 A B C 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 A B C D E F G H K 101 102 103 104 105 106 107 108 109 110 111 112 113
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3
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LC6 IgG Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S 13
LC9 IgG Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S 13
LC10 IgG Y L Q M N S L R A E D T A V Y Y C A R Q P T H Y Y Y Y A K G Y K A M D Y W G Q G T L V T V S S 13

FIG. 16B

```
  1 EVQLVESGGG LVQPGGSLRL SCAASGFTFS SYGMSWVRQA PGKGLELVAS
 51 INSNGGSTYY PDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCASGD
101 YWGQGTTVTV SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT
151 VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT KTYTCNVDHK
201 PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP SVFLFPPKPK DTLMISRTPE
251 VTCVVVDVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVVSVLTV
301 LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM
351 TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS
401 RLTVDKSRWQ EGNVFSCSVM HEALHNHYTQ KSLSLSLG (SEQ ID NO: 14)
```

FIG. 17A

```
  1 DIVMTQSPLS LPVTPGEPAS ISCRSSQSLV YSNGDTYLHW YLQKPGQSPQ
 51 LLIYKVSNRF SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCSQSTHVP
101 WTFGQGTKVE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK
151 VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE
201 VTHQGLSSPV TKSFNRGEC (SEQ ID NO: 15)
```

FIG. 17B