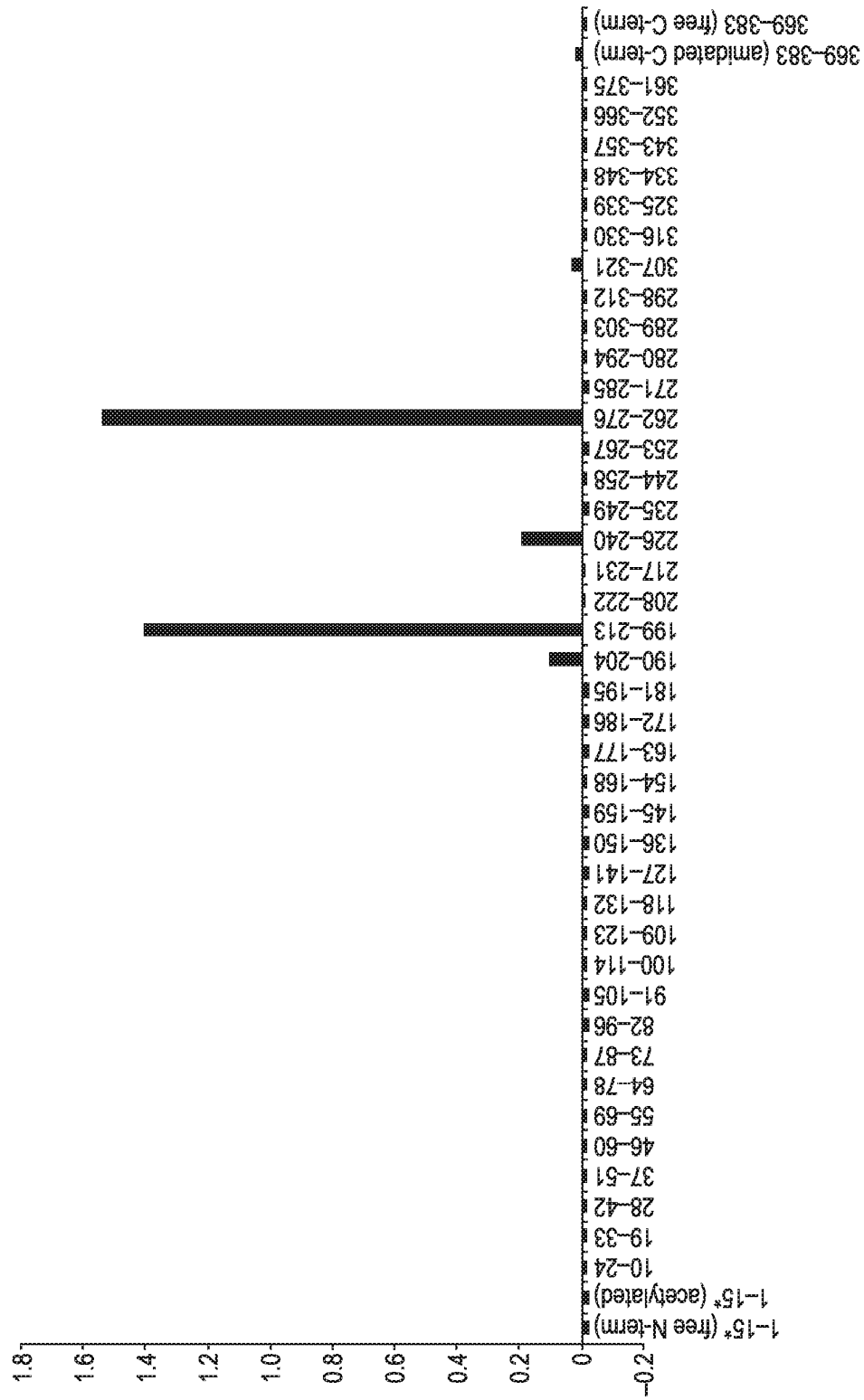
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
−0.2
1–15* (free N-term)
1–15* (acetylated)
10–24
19–33
28–42
37–51
46–60
55–69
64–78
73–87
82–96
91–105
100–114
109–123
118–132
127–141
136–150
145–159
154–168
163–177
172–186
181–195
190–204
199–213
208–222
217–231
226–240
235–249
244–258
253–267
262–276
271–285
280–294
289–303
298–312
307–321
316–330
325–339
334–348
343–357
352–366
361–375
369–383 (amidated C-term)
369–383 (free C-term)

FIG. 1

VH alignment

```
Majority                EVQLVQSGAEVVXPGALVKISCKASGFNIKDYYLHWVRQRPEQGLEWIGWIDPENG
                        ---------+---------+---------+---------+---------+------
                                 10        20        30        40        50
                        ---------+---------+---------+---------+---------+------
mouse 3D6VH protein     EVQLQQSGADLVRPGALVKLSCKASGFNIKDYYLHWVRQRPEQGLEWIGWIDPENG  56
h3D6VHv1 protein        EVQLVQSGAEVVRPGALVKVSCKASGFNIKDYYLHWVRQAPEQGLEWIGWIDPENG  56
h3D6VHv2 protein        EVQLVQSGAEVKKPGASVKVSCKVSGFNIKDYYLHWVRQAPEQGLEWMGWIDPENG  56
h3D6VHv1b protein       EVQLVQSGAEVVRPGALVKISCKASGFNIKDYYLHWVRQRPEQGLEWIGWIDPENG  56
h3D6VHv1bA11 protein    EVQLVQSGAEVVKPGATVKISCKASGFNIKDYYLHWVRQRPGQGLEWIGWIDPENG  56
h3D6VHv5 protein        EVQLVQSGAEVVKPGATVKISCKASGFTIKDYYLHWVRQRPGQGLEWIGWIDPEDG  56

Majority                DTVYDPKFQGXATITADTSTNTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS        SEQ ID NO:44
                        ---+---------+---------+---------+---------+---------+--
                           60        70        80        90        100       110
                        ---+---------+---------+---------+---------+---------+--
mouse 3D6VH protein     DTVYDPKFQGKATITADTSSNTAYLQLGSLTSEDTAVYFCSTLDFWGQGTTLTVSS  112  SEQ ID NO:7
h3D6VHv1 protein        DTVYDPKFQGKATITADTSTNTAYLQLSSLTSEDTAVYFCSTLDFWGQGTLVTVSS  112  SEQ ID NO:15
h3D6VHv2 protein        DTVYDPKFQGRVTITADTSTNTAYMELSSLTSEDTAVYYCSTLDFWGQGTLVTVSS  112  SEQ ID NO:16
h3D6VHv1b protein       DTVYDPKFQGKATITADTSTNTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS  112  SEQ ID NO:17
h3D6VHv1bA11 protein    DTVYDPKFQGRATITADTSTDTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS  112  SEQ ID NO:18
h3D6VHv5 protein        DTVYAPKFQGRATITADTSTDTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS  112  SEQ ID NO:19
```

FIG. 2

```
VL Alignment

Majority                DVVMTQSPLSLSVTLGQPASISCKSSQSLLDSDGKTYLNWLLQRPGQSPKRLIYLVS
                        ----------+---------+---------+---------+---------+---------
                                  10        20        30        40        50
                        ----------+---------+---------+---------+---------+---------
mouse 3D6VL protein     DVVMTQ□PL□LSVT□GQPASISCKSSQSLLDSDGKTYLNWLLQRPGQSPKRLIYLVS  57
h3D6VLv1 protein        DVVMTQSPLSLSVTLGQPASISCKSSQSLLDSDGKTYLNWLLQRPGQSPKRLIYLVS  57
h3D6VLv2 protein        DVVMTQSPLSL□VTLGQPASISCKSSQSLLDSDGKTYLNWLLQRPGQSP□RLIYLVS  57
h3D6VLv3 protein        DVVMTQSPLSL□VTLGQPASISCKSSQSLLDSDGKTYLNWLLQRPGQSP□RLIYLVS  57
h3D6VLv4 protein        D□VMTQ□PLSLSVT□GQPASISCKSSQSLLDSDGKTYLNWLLQ□PGQSPKRLIYLVS  57

                                                                        SEQ ID NO:45

Majority                KLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPYTFGGGTKLEIKR
                        --+---------+---------+---------+---------+---------+----
                          60        70        80        90        100       110
                        --+---------+---------+---------+---------+---------+----
mouse 3D6VL protein     KLDSGVPDRF□GSGSGTDFTLKISRVEAED□GVYYCWQGTHFPYTFGGGTKLEIKR  113  SEQ ID NO:11
h3D6VLv1 protein        KLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPYTFGGGTKLEIKR  113  SEQ ID NO:20
h3D6VLv2 protein        KLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPYTFGGGTKLEIKR  113  SEQ ID NO:21
h3D6VLv3 protein        KLDSGVP□RFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPYTFGGGTKLEIKR  113  SEQ ID NO:22
h3D6VLv4 protein        KLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPYTFGGGTKLEIKR  113  SEQ ID NO:23
```

FIG. 3

VH Alignment
Majority
EVQLVQSGAEVVKPGALVKISCKASGFNIKDYYLHWVRQRPGQGLEWIGWIDPENG
10 20 30 40 50
h3D6VHv1 protein EVQLVQSGAEVVRPGALVKMSCKASGFNIKDYYLHWVRQAPEDGLEWIGWIDPENG 56
h3D6VHv1b protein EVQLVQSGAEVVRPGALVKISCKASGFNIKDYYLHWVRQRPEDGLEWIGWIDPENG 56
h3D6VHv1bA11 protein EVQLVQSGAEVVKPGATVKISCKASGFNIKDYYLHWVRQRPGQGLEWIGWIDPENG 56
h3D6VHv1bA11B6G2 protein EVQLVQSGAEVVKPGATVKISCKASGFTIKDYYLHWVRQRPGKGLEWIGWVDPEDG 56
h3D6VHv1bA11B6H3 protein EVQLVQSGAEVVKPGATVKISCKASGFTIKDYYLHWVRQRPGKGLEWIGWIDPEDG 56
h3D6VHv1c protein EVQLVQSGAEVKRPGALVKISCKASGFNFKDYYLHWVRQRPEQGLEWMGWIDPENG 56
h3D6VHv1d protein EVQLVQSGAEVKRPGALVKISCKASGYTFTDYYLHWVRQRPEQGLEWMGWVDPEDG 56
h3D6VHv1e protein EVQLVQSGADVVKPGALVKISCKASGFTIKDYYLHWVRQRPEQGLEWIGWIDPENG 56
h3D6VHv1f protein EVQLVQSGADVVKPGALVKISCKASGFTIKDYYLHWVRQRPGQGLEWIGWVDPEDG 56
h3D6VHv2 protein EVQLVQSGAEVKKPGASVKMSCKMSGFNIKDYYLHWVRQAPEQGLEWMGWIDPENG 56
h3D6VHv3 protein EVQLVQSGAEVKKPGALVKISCKMSGFNIKDYYLHWVRQAPGKGLEWMGWIDPENG 56
h3D6VHv3b protein EVQLVQSGAEVKKPGALVKISCKMSGYNFKDYYLHWVRQAPGKGLEWMGWIDPENG 56
h3D6VHv3c protein EVQLVQSGAEVKKPGALVKISCKMSGYTFTDYYLHWVRQAPGKGLEWMGWVDPEDG 56
h3D6VHv4 protein EVQLVQSGAEVVKPGALVKISCKMSGFNIKDYYLHWVRQRPGKGLEWIGWIDPENG 56
h3D6VHv4b protein EVQLVQSGAEVVKPGALVKISCKMSGYNFKDYYLHWVRQRPGKGLEWMGWIDPENG 56
h3D6VHv4c protein EVQLVQSGAEVVKPGALVKISCKMSGYTFTDYYLHWVRQRPGKGLEWMGWVDPEDG 56
h3D6VHv5 protein EVQLVQSGAEVVKPGATVKISCKASGFTIKDYYLHWVRQRPGQGLEWIGWIDPEDG 56

FIG. 4A

```
                                                                                                                    SEQ ID NO:71
Majority          DTVYDPKFQGRVTITADTSTNTAYLELGSLTSEDTAVYFCSTLDFWGQGTLVTVSS
                  ---+----------+----------+----------+----------+----------+--
                     60         70         80         90         100        110

h3D6VHv1 protein  DTVYDPKFQGKATITADTSTNTAYLQLSSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:15
h3D6VHv1b protein DTVYDPKFQGKATITADTSTNTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:17
h3D6VHv1bA11 protein
                  DTVYDPKFQGRATITADTSTDTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:18
h3D6VHv1bA11B6G2 protein
                  DTVYAPKFQGRATITADTSTDTAYLELGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:46
h3D6VHv1bA11B6H3 protein
                  DTVYAPKFQGRATITADTSTDTAYLELGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:47
h3D6VHv1c protein DTVYDEKFQGRVTITADTSTNTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:48
h3D6VHv1d protein DTVYAEKFQGRVTITADTSTNTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:49
h3D6VHv1e protein DTVYAEKFQGRVTITADTSTNTAYLELGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:50
h3D6VHv1f protein DTVYAEKFQGRVTITADTSTDTAYMELGSLTSEDTAVYFCSTLDYWGQGTLVTVSS 112  SEQ ID NO:51
h3D6VHv2 protein  DTVYDPKFQGRVTITADTSTNTAYMELSSLTSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:16
h3D6VHv3 protein  DTVYDPKFQGRVTITADTSTDTAYMELSSLRSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:52
h3D6VHv3b protein DTVYDEKFQGRVTITADTSTNTAYMELGSLRSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:53
h3D6VHv3c protein DTVYAEKFQGRVTITADTSTNTAYMELGSLRSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:54
h3D6VHv4 protein  DTVYDPKFQGKATITADTSTNTAYLELGSLTSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:55
h3D6VHv4b protein DTVYDEKFQGRVTITADTSTDTAYLELGSLTSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:56
h3D6VHv4c protein DTVYAEKFQGRVTITADTSTDTAYLELGSLTSEDTAVYMCSTLDFWGQGTLVTVSS 112  SEQ ID NO:57
h3D6VHv5 protein  DTVYAPKFQGRATITADTSTDTAYLQLGSLTSEDTAVYFCSTLDFWGQGTLVTVSS 112  SEQ ID NO:19
```

FIG. 4B

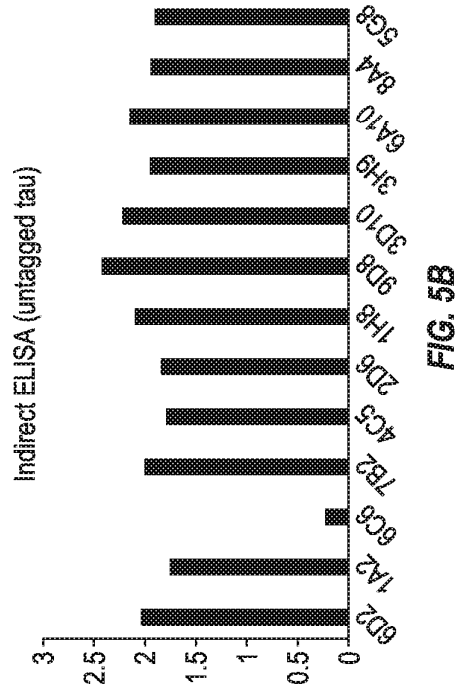

FIG. 5B

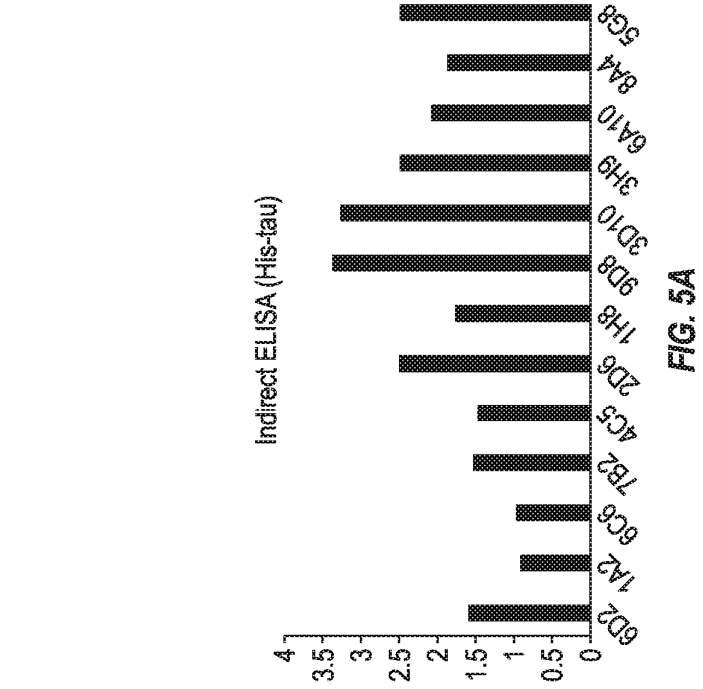

FIG. 5A

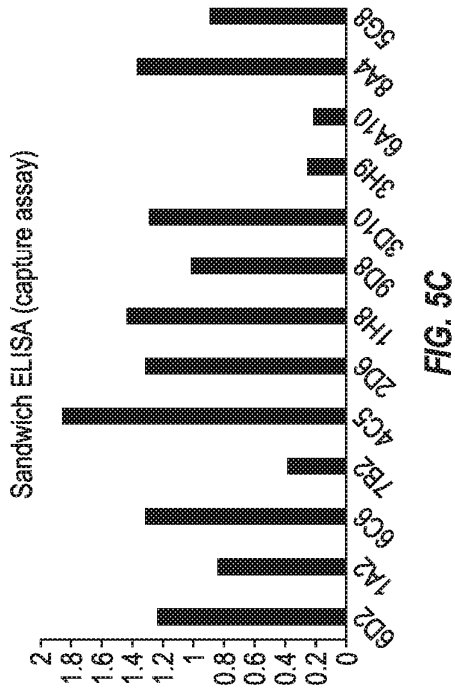

FIG. 5C

Name	k_a ($M^{-1}s^{-1}$)	k_d (s^{-1})	k_D (nM)
3D6	2.58×10^6	1.19×10^{-3}	0.46
1H8	5.07×10^5	5.61×10^{-3}	11.1
3H9	4.71×10^5	1.41×10^{-3}	3.0
5G8	3.75×10^5	2.54×10^{-3}	6.78
6D2	3.83×10^5	3.18×10^{-3}	8.29
7G6	5.76×10^5	3.32×10^{-3}	5.77
8A4	5.99×10^5	2.27×10^{-3}	3.8

FIG. 6

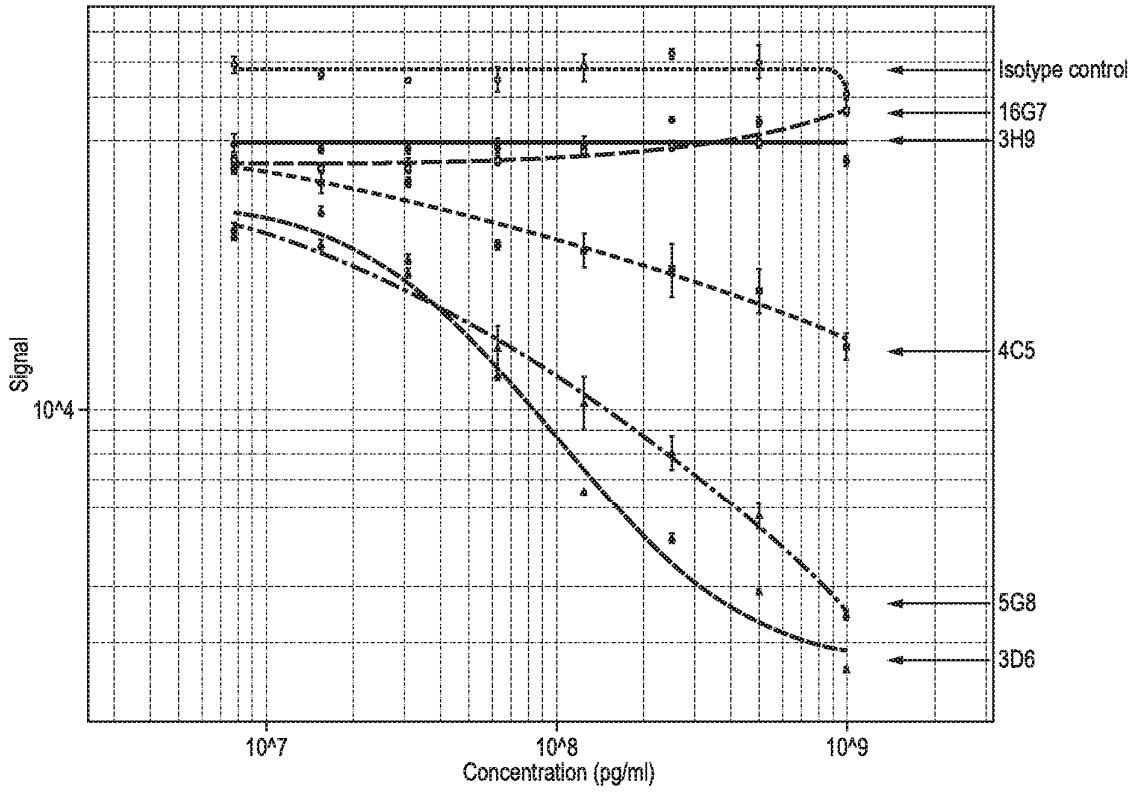

FIG. 7

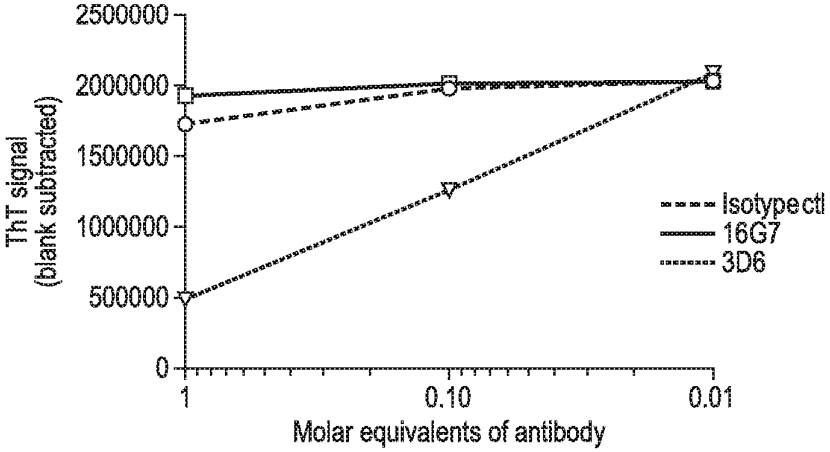
2500000
2000000
1500000
1000000
500000
0
ThT signal
(blank subtracted)
1
0.10
0.01
Molar equivalents of antibody
Isotype ctl
16G7
3D6

FIG. 8

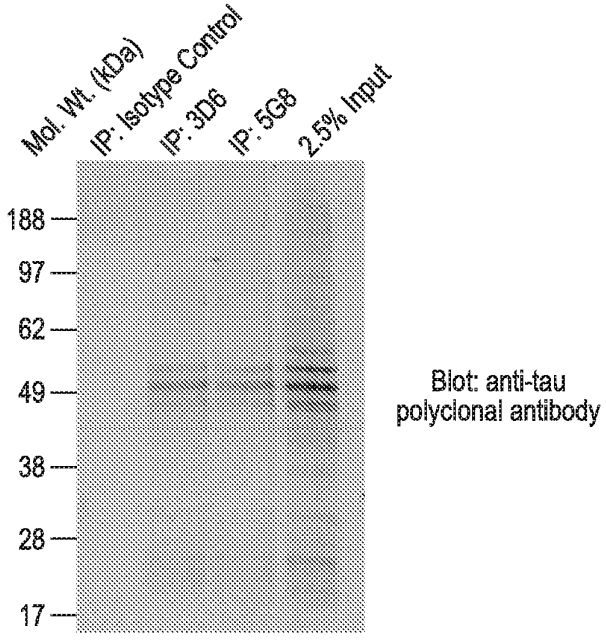
Mol. Wt. (kDa)
IP: Isotype Control
IP: 3D6
IP: 5G8
2.5% Input
188
97
62
49
38
28
17
Blot: anti-tau
polyclonal antibody

FIG. 9

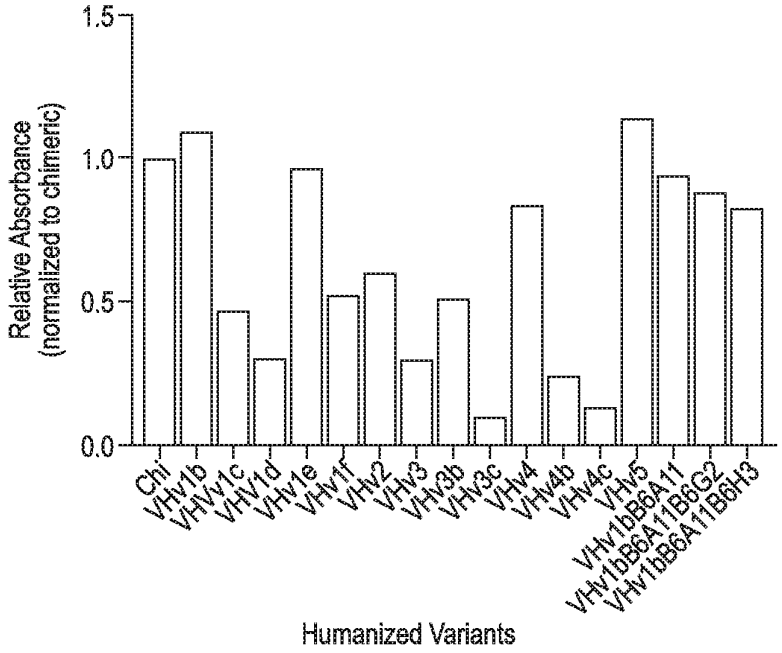

FIG. 10A

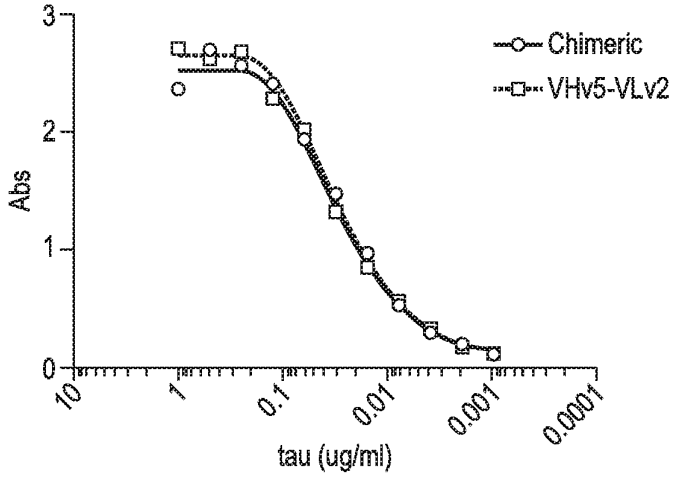

FIG. 10B

Name	k_a ($M^{-1}s^{-1}$)	k_d (s^{-1})	k_D (nM)
h3D6-VHv5VLv2	9.03×10^6	9.14×10^{-4}	0.10

FIG. 10C