Figure 1

A) NI-105.4E4-VH (variable heavy chain sequence VH; SEQ ID NO:9)

```
 --FR1-------------------------CDR1----FR2---------CDR2-------
 EVQLVESGGGLVQPGGSLKLSCAASGFNFNISAIHWVRQASGKGLEWVGRIRSKSHNYATLY

--------FR3-----------------------------CDR3------JH-------
AASLKGRFTLSRDDSRNTAYLQMSSLQTEDMAVYYCTVLSANYDTFDYWGQGTLVTVSS
```

NI-105.4E4-VL (variable light chain sequence VL; SEQ ID NO:11)

```
--FR1-------------------CDR1-------FR2------------CDR2---FR3--
SYELTQPPSVSVSPGQTARISCFGDTLPKQYTYWYQQKPGQAPVLVIYKDTERPSGIPERFS
LPV
------------------------CDR3------JK--------
GSSSGTTVTLTISGVQAEDEADYYCLSADNSATWVFGGGTKVTVL
```

B) NI-105.24B2-VH (variable heavy chain sequence VH; SEQ ID NO:13)

```
FR1--------------------------CDR1-FR2-----------CDR2---------
QVQLVQSGAEVKKPGASVKVSCKASGYTFVNYIIHWVRQAPGQGLEWMGIINPNGGNTSYAE
E
----FR3-------------------------------CDR3--JH---------
KFQARVTLTSDTSTSTVYMDLSSLTSEDTAVYYCAVLSPSNPWGQGTTVTVSS
```

NI-105.4E4-VL (variable light chain sequence VL; SEQ ID NO:15)

```
FR1-------------------CDR1-------FR2------------CDR2---FR3----
SYELTQPPSVSVSPGQTAGITCSGDALPKQFVYWYQKKPGQAPVLLIYKDTERPSRIPERFS
V
------------------------CDR3-------JK--------
GSTSGTTVALTINGVQAEDEADYYCQSADRSGALWVFGGGTKLTVL
```

C) NI-105.4A3-VH (variable heavy chain sequence VH; SEQ ID NO:17)

```
FR1--------------------------CDR1-FR2-----------CDR2---------
QVQLVESGGGAVQPGGSLRLSCAASGFTFSDYAMHWVRQAPGKGLQWVAVISYEGTYKYYAD
E     T
----FR3-------------------------------CDR3-------------JH-------
SVKGRFTISRDNSKNTLNLQMSSLRVEDTAVYFCVKARAFASGQRSTSTVPDYWGQGTLVTV

SS
```

NI-105.4A3-VL (variable light chain sequence VL; SEQ ID NO:19)

```
FR1-------------------CDR1-------FR2------------CDR2---FR3----
SYELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDNKRPSGIPERFS

------------------------CDR3-------JK--------
GSSSGTVATLTISGAQVDDEADYYCYSTDISGDLRVFGGGTKLTVL
```

Figure 2

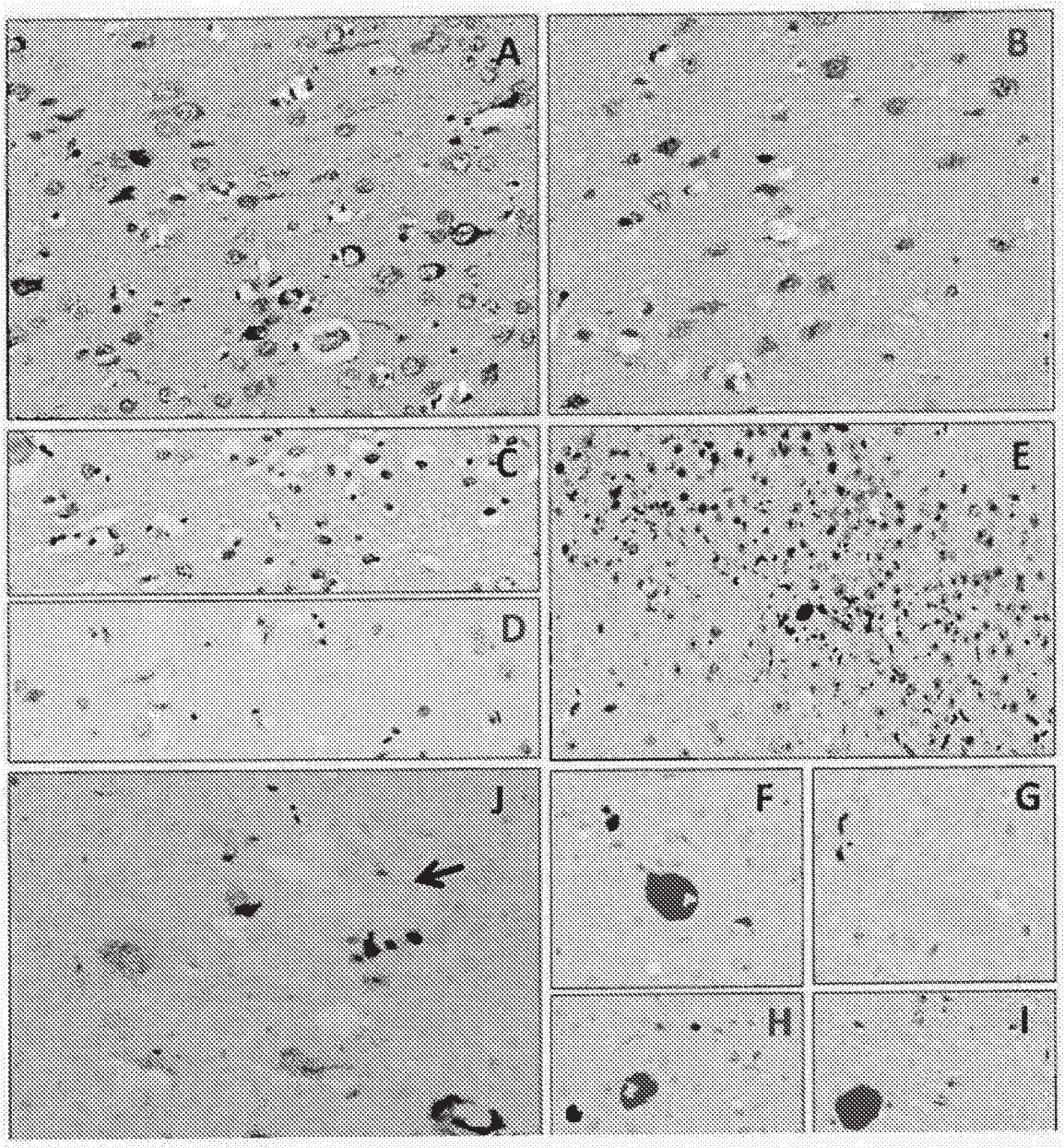


Figure 3

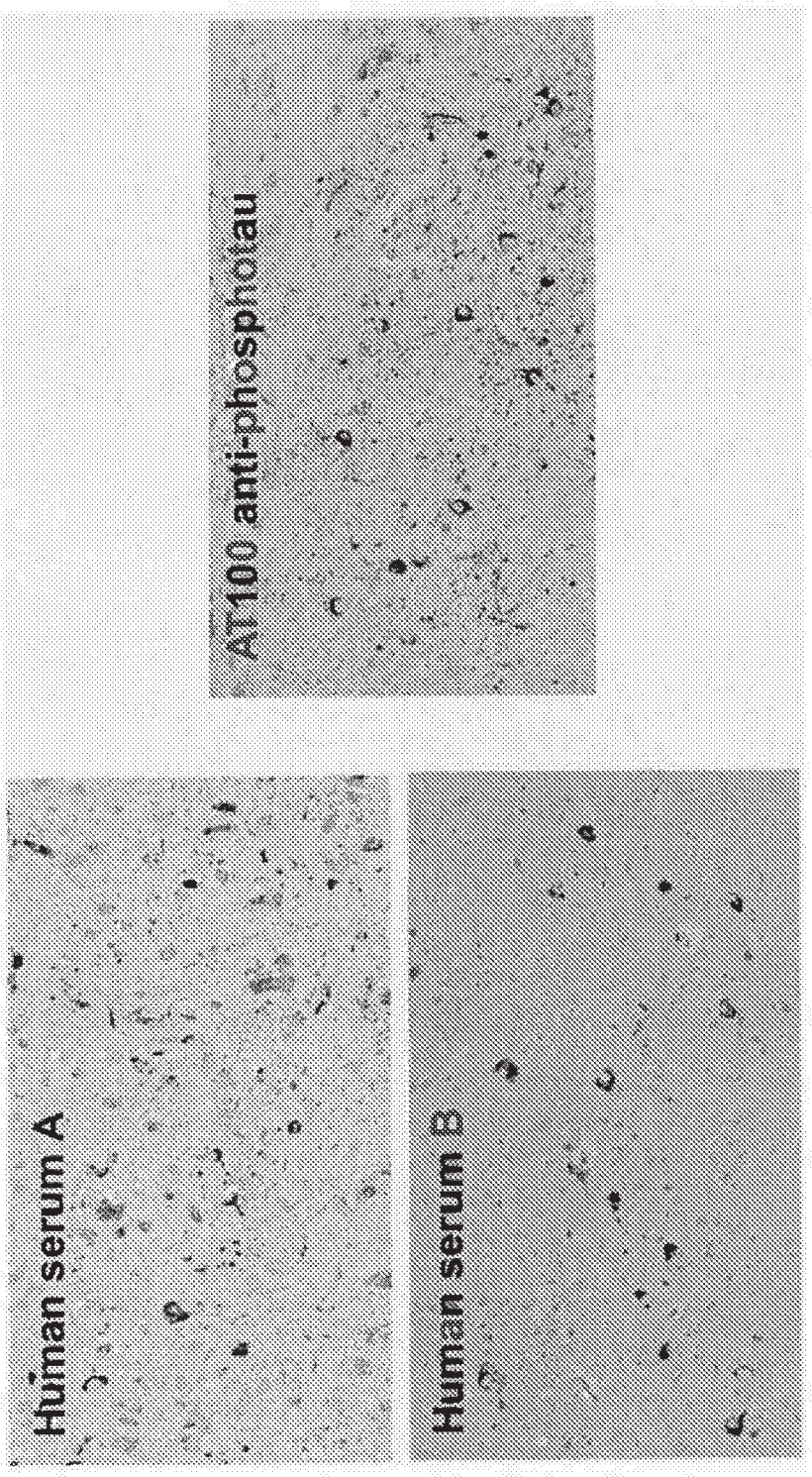


Figure 4

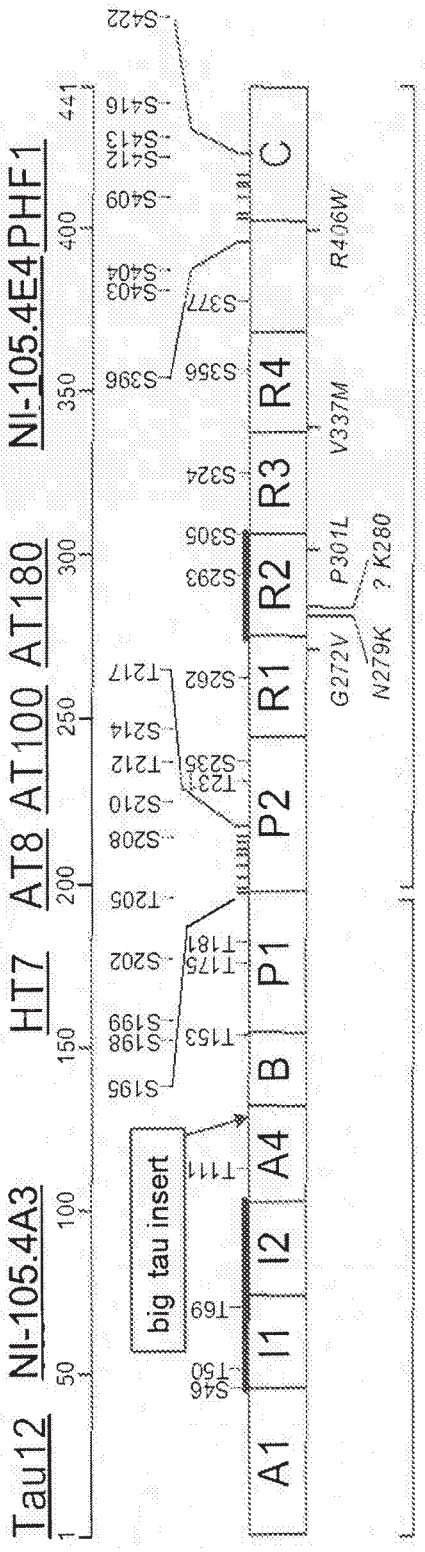

Tau12
NI-105.4A3
HT7
AT8
AT100
AT180
NI-105.4E4PHF1
1
50
100
150
200
250
300
350
400
441
A1
I1
I2
A4
B
P1
P2
R1
R2
R3
R4
C
big tau insert
S46
T69
T111
S195
S198
S199
T153
T175
T181
S202
T205
S208
S210
T212
T217
S214
S235
S262
S293
S305
S324
S356
S377
S396
S403
S404
S409
S412
S413
S416
S422
G272V
P301L
? K280
N279K
V337M
R406W
Projection domain
Assembly domain

Figure 5

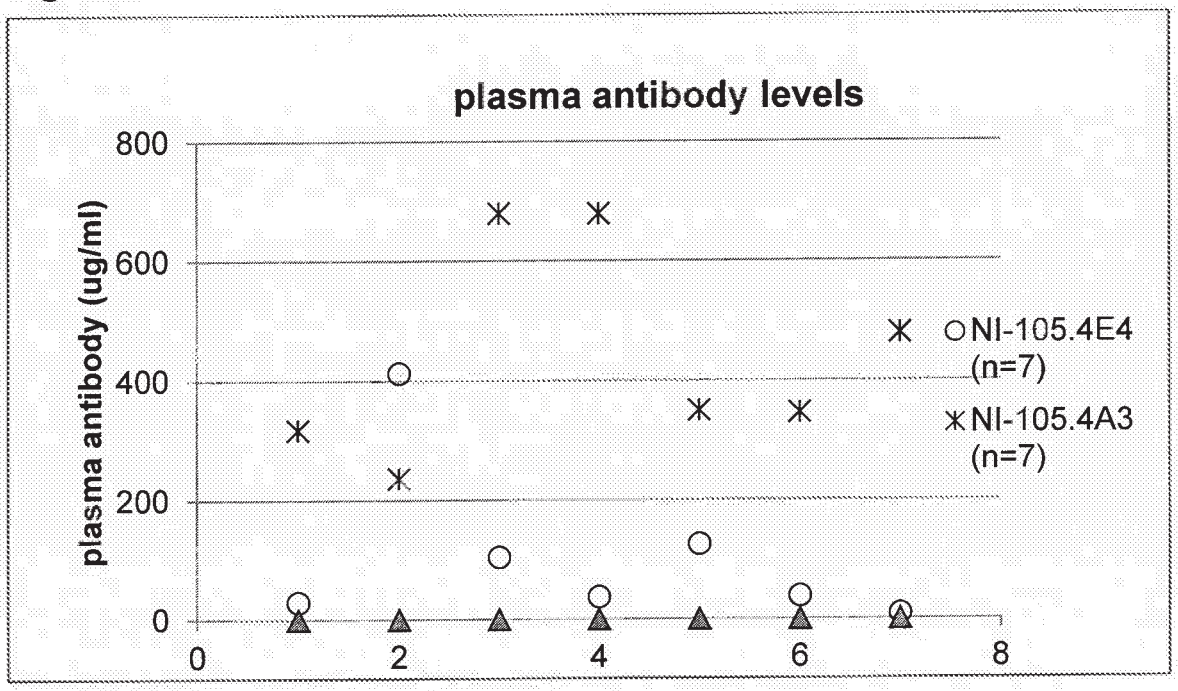


Figure 6

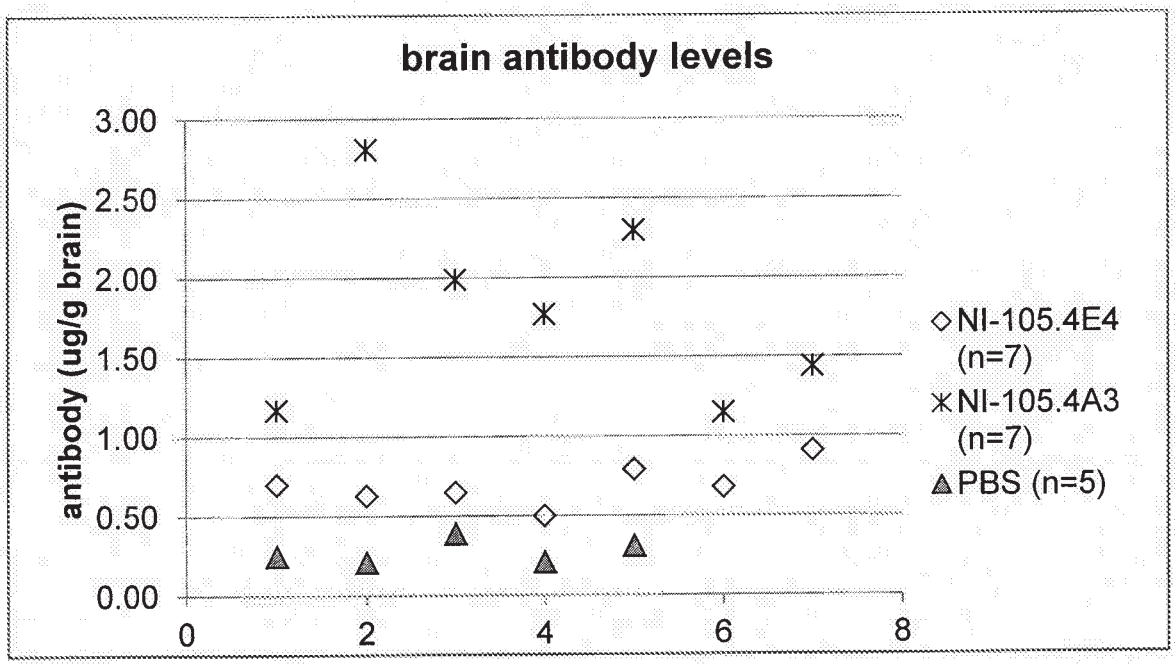


Figure 7A-C

Fig. 7A

NI-105.17C1 VH (SEQ ID NO:44)
EVQLVQSGAEVKKPGESLKISCKAFGYSFTNFWIGWVRQVPGKGLEWVGIIYPGDSD
TRYSPSFQGQVTISADKSIDTAYLQWGHLKASDSAMYFCARRGFWTGSQIEYWGQG
TQVTVSS

NI-105.17C1 VL (SEQ ID NO:46)
QSALTQPPSASGSPGHSVTISCTGTSSDVGNYSFVSWYQQYPGKAPKVIIYDVSKRS
SGVPDRFFGSKSANTASLTVSGVQEEDEADYFCSSYGGSKYPWVFGGGTKLTVL

Fig. 7B

NI-105.6C5 VH (SEQ ID NO:48)
QVQLVESGGGVVQPGRSLRVSCAASGFTFSSYDMHWVRQAPGKGLEWVAVIWFD
GSNEFYADSVKGRFTISRDNSKNTLFLQMNSLRAEDTAVYYCARDLGASVTTSNAEN
FHHWGQGTLVTVSS

NI-105.6C5 VL (SEQ ID NO:49)
SYELTQPPSVSVSPGQTARITCSGDALPKRYVYWYQQKSGQAPVLVIYEDSKRPSGI
PETFSGSSSGTMATLTISGAQVEDEADYYCYSTDSNGHHWVFGGGTKLTVL

Fig. 7C

NI-105.29G10 VH (SEQ ID NO:50)
EVQLVESGGDLVQPGGSLRLSCAASGFDFSGYSMAWVRQAPGKGLEWVSYISGTY
VSGGTGTMYYLDSVKGRFFISRDDATSSLYLQMDSLRDEDTAVYYCARVYDYGEDW
GQGTLVTVSS

NI-105.29G10 VK (SEQ ID NO:51)
DIVMTQSPDSLAVSLGERATINCKSSRSVLYSSNSKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTEFTLTISSLQAEDVAVYYCQQYYGTPRTFGQGTKVEIK

Figure 7D-F

Fig. 7D

NI-105.6L9 VH (SEQ ID NO:52)
EVQLVESGGGLVQPGGSLRLSCAGTRFTFSTYAMGWVRQAPGRGLEWVSAIGGSG
DSTSYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGVYDYLWGSYRLF
DYWGQGTLVTVSS

NI-105.6L9 VL (SEQ ID NO:53)
SYVLTQPPSVSVAPGQTARFTCGGNNIASKSVHWYQQKPGQAPVLVVYDDSDRPS
RIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDSTSDHVVFGGGTKLTVL

Fig. 7E

NI-105.40E8 VH (SEQ ID NO:54)
EVQLVESGGGLVQPGGSLRLSCAASGFTFPNYVMTWVRQAPGKGLEWVSGISGSG
GSTDYADSVKGRFTISRDNSKNTLYLQMNSLRVEDTALYYCAKGSGGIRGQGTMVT
VSS

NI-105.40E8 VL (SEQ ID NO:55)
QSALTQPRSVSGSPGQSVTISCTGTSSDVGGYNYVSWHQQHPGKAPKLLIYDVTKR
PSGVPDRFSGSKSGNTAALTISGLQAEDEADYYCHSYVGSYTLVFGGGTKLTVL

Fig. 7F

NI-105.48E5 VH (SEQ ID NO:56)
EVQLVESGGGLVQPGGSLKLSCAASGFTFSGSAMHWVRQASGKGLEWVGRIRSKA
NSYATAYAASVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCTSPTVTTEVWGQG
TLVTVSS

NI-105.48E5 VK (SEQ ID NO:57)
DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKDYLAWYQQKPGQPPKLLIYWA
STRESGVSDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSTPITFGQGTRLEIK

Figure 7G-I

Fig. 7G

NI-105.6E3 VH (SEQ ID NO:58)
EVQLVESGGGLVQPGGSLRLSCIGSSGMTFSSYAFNWVRQTPGKGLEWVSSISRFG
STVDYTDSVRGRFTISRDDGQRSLYLQMNSLRVEDTAVYYCVRSTASGSRSPGIIWG
QGTTVTVSS

NI-105.6E3 VK (SEQ ID NO:59)
DIQMTQSPSSLSASVGDRVTITCRASQGIVNNLAWFQQKPGKAPKSLIYAASSLQGG
VPSKFSGSASGTDFSLTISNLQPEDFATYFCQQYNSYPWTFGQGTKVEIK

Fig. 7H

NI-105.22E1 VH (SEQ ID NO:60)
EVQLVQSGAEVKKPGESLKISCKGSGYRFTTYWIGWVRQMPGKGLEWMGIIYPGDS
DTRYSPSYQGQVTISADKSISTAYLQWSSLKASDTGMYYCARVAGDIGYENYYYYG
MDVWGQGTTVTVSS

NI-105.22E1 VK (SEQ ID NO:61)
DIVMTQSPDSLAVSLGERATINCKSSQSVLYGSNNKNYLAWYQQKLGQSPKLLIYWA
SARESGVPDRFGGSGSGTDFTLTISSLQAEDVAVYYCQQYYSTPWTFGQGTKVEIK

Fig. 7I

NI-105.26B12 VH (SEQ ID NO:62)
QVQLVESGGGVVQPGRSLRLSCAASGFTFTRYGMHWVRQAPGKGLEWVAVIWYD
GTNKYYADSLQGRFTISRDTSTNTLYLQMNGLRVEDRAVYYCAREGFQGAIDYWGQ
GTLVTVSS

NI-105.26B12 VK (SEQ ID NO:64)
DIVMTQSPDSLAVSLGERATINCKSSQNILYSSDNKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSIPRTFGQGTKVEIK

Figure 7J-L

Fig. 7J

NI-105.12E12 VH (SEQ ID NO:65)
EVQLVESGGGLVQPGGSLKLSCAASGFSFSDSAFHWARQASGKGLEWVGRIRSKG
NNYATAYAASVKGRFTVSRDDSKNTTYLQMNSLKTDDTAIYYCTRQGPSYGGINWG
LGTLVTVSS

NI-105.12E12 VK (SEQ ID NO:66)
DIVMTQSPDSLAVSLGERATINCKSSQTILYSSNNKNYLAWYQQKPGQPPKLLIYWAS
TRESGVPDRFSGSGSGTDFTLTISSLRAEDVAVYYCQQYYSSPQTFGQGTKVEIK

Fig. 7K

NI-105.60E7 VH (SEQ ID NO:67)
EVQLVESGGGFVRPGGSITLSCATSGFTFTKAWMTWVRQAPVKGLEWIGHIKTRIEG
ATTDYAAPVEGRFTISRDDSKNMVYLQMNSLKTEDSGIYYCSTDFDYWGQGTLVTV
SS

NI-105.60E7 VK (SEQ ID NO:68)
DVVMTQSPLSLPVTLGQPASISCTSSQSLLYSDGNTYLNWFQQRPGQSPRRLMYKV
SKRDPGVPDRFSGSGSGTDFTLSISRVEAEDVGVYYCMQGSLWPRYTFGQGTKVEI
K

Fig. 7L

NI-105.14E2 VH (SEQ ID NO:69)
EVQLVQSGAEVKKPGDSLRISCKASGYNFPNYWIGWVRQMPGKGLEWMGIIYPGDS
DIRYSPSFQGHVTISSDKSITTAYLQWTSLKVADSAMYYCARVERPDKGGWFGPWG
QGTLVTVSS

NI-105.14E2 VK (SEQ ID NO:70)
DIVMTQSPDSLAVSLGERATINCKSSQTLLYTSNNQNYLAWYQHKPGQPPKVLIYWA
STREYGVPDRFSGSGSGTDFTLTISSLQPEDVAVYYCQQYYNSPYTFGQGTKLEIK

Figure 7M-O

Fig. 7M

NI-105.39E2 VH (SEQ ID NO:71)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSAYGMNWVRQAPGKGLEWVAHITGSG
TPIFYADSVKGRFTISRDNAKSSLYLQMNSLRNDDTALYFCVRGTVDYWGQGTLVTV
SS

NI-105.39E2 VL (SEQ ID NO:72)
QAGLTQPPSVSKDLRQTATLTCSGNSNNVGNQGAAWLQQFPGHPPKLLFYENINRP
SGISERFSASRSGNTASLTITGLQPEDEADYYCSAWDGHLNAWVFGGGTKLTVL

Fig. 7N

NI-105.19C6 VH (SEQ ID NO:73)
EVQLVQSGAEVKKPGESLKISCKASGYSFISYWVGWVRQMPGKGLEWMGIIYPGDS
DTRYSPSFEGQVSISADKSISTAYLQWTSLKASDTAMYYCARHWGPAAVTDSPWFG
PWGQGTLVTVSS

NI-105.19C6 VK (SEQ ID NO:74)
DIVMTQSPDSLAVSLGERATINCKSSQTVLYTSNNKNYLAWYQQKPGQPPKLLIYWA
STRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHYYSTPFTFGPGTKVDIK

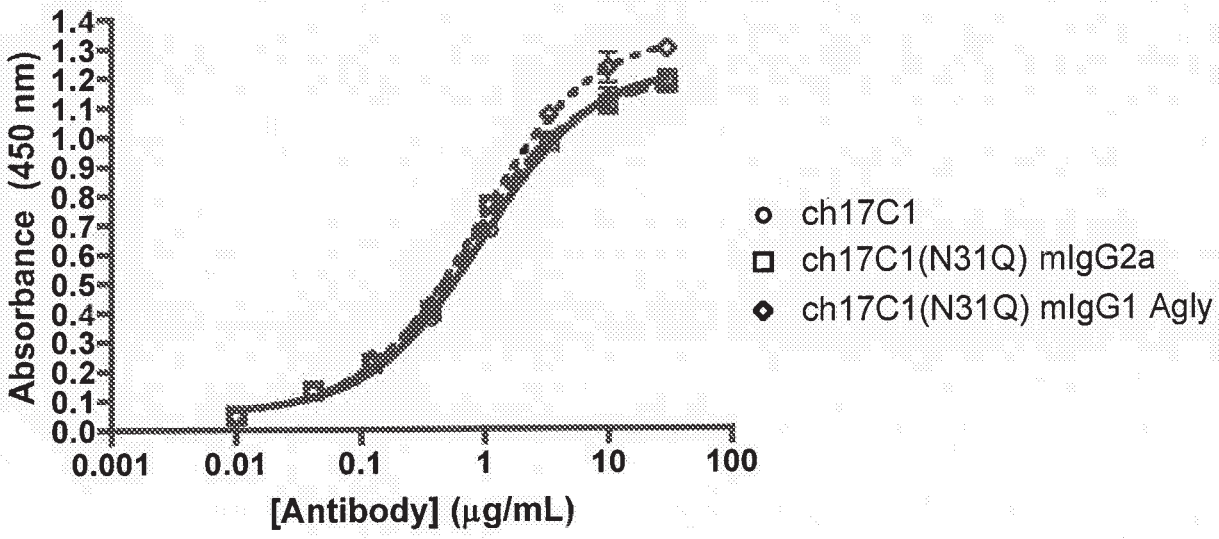
Fig. 7O

NI-105.9C4 VH (after primer-induced mutation corrections) (SEQ ID NO:76)
QVQLVQSGAEVKKPGASVKVSCKASGYIFTAFFMHWVRQAPGQGLEWMGWINPDS
GATKYAHNFQGRVTMTRDTSISTAFMELSGLKSDDTGVYYCATGMAVTGNFWGQG
TLVTVSS

NI-105.9C4 VL (after primer-induced mutation corrections) (SEQ ID NO:78)
SYELTQPPSVSVSPGQTARITCSGDVLAETYARWFQQKPGQAPVLVMYRDRERPAG
IPERFSGSSSGNTVTLTISGAQAEDEAVYHCHSVADNNLDWVFGGGTKLTVL

Figure 8A-B

A)



B)

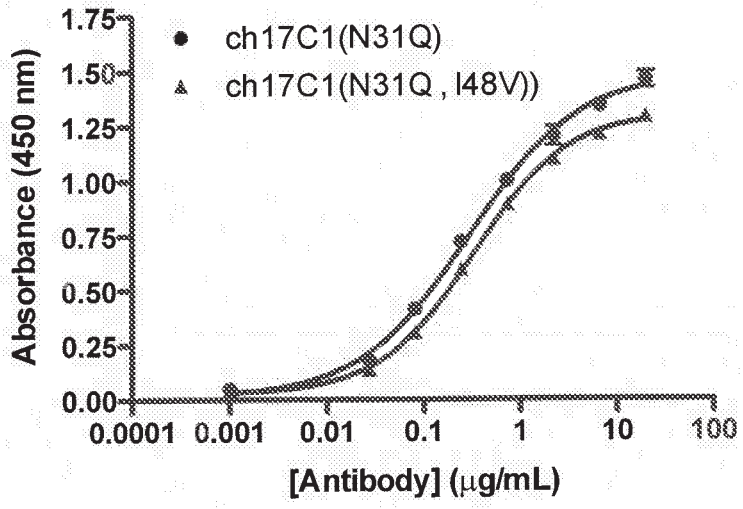


Figure 9

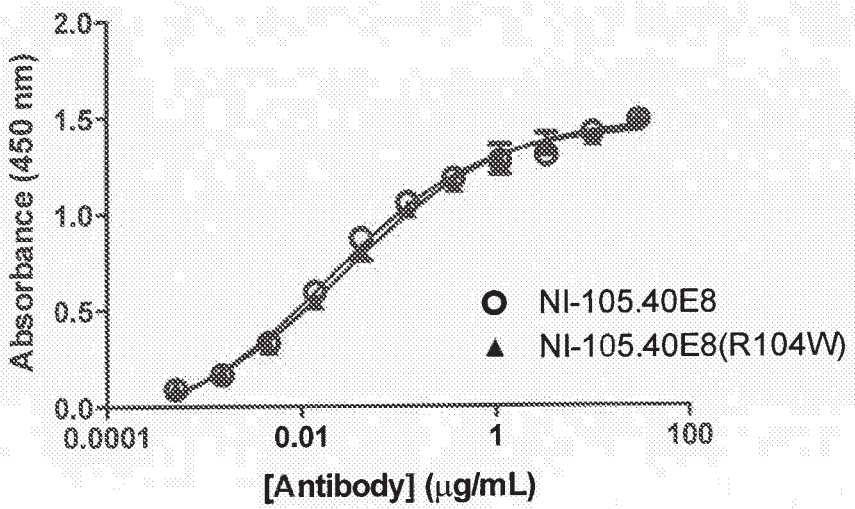

2.0
1.5
1.0
0.5
0.0
Absorbance (450 nm)
0.0001
0.01
1
100
[Antibody] (μg/mL)
NI-105.40E8
NI-105.40E8(R104W)

Figure 10

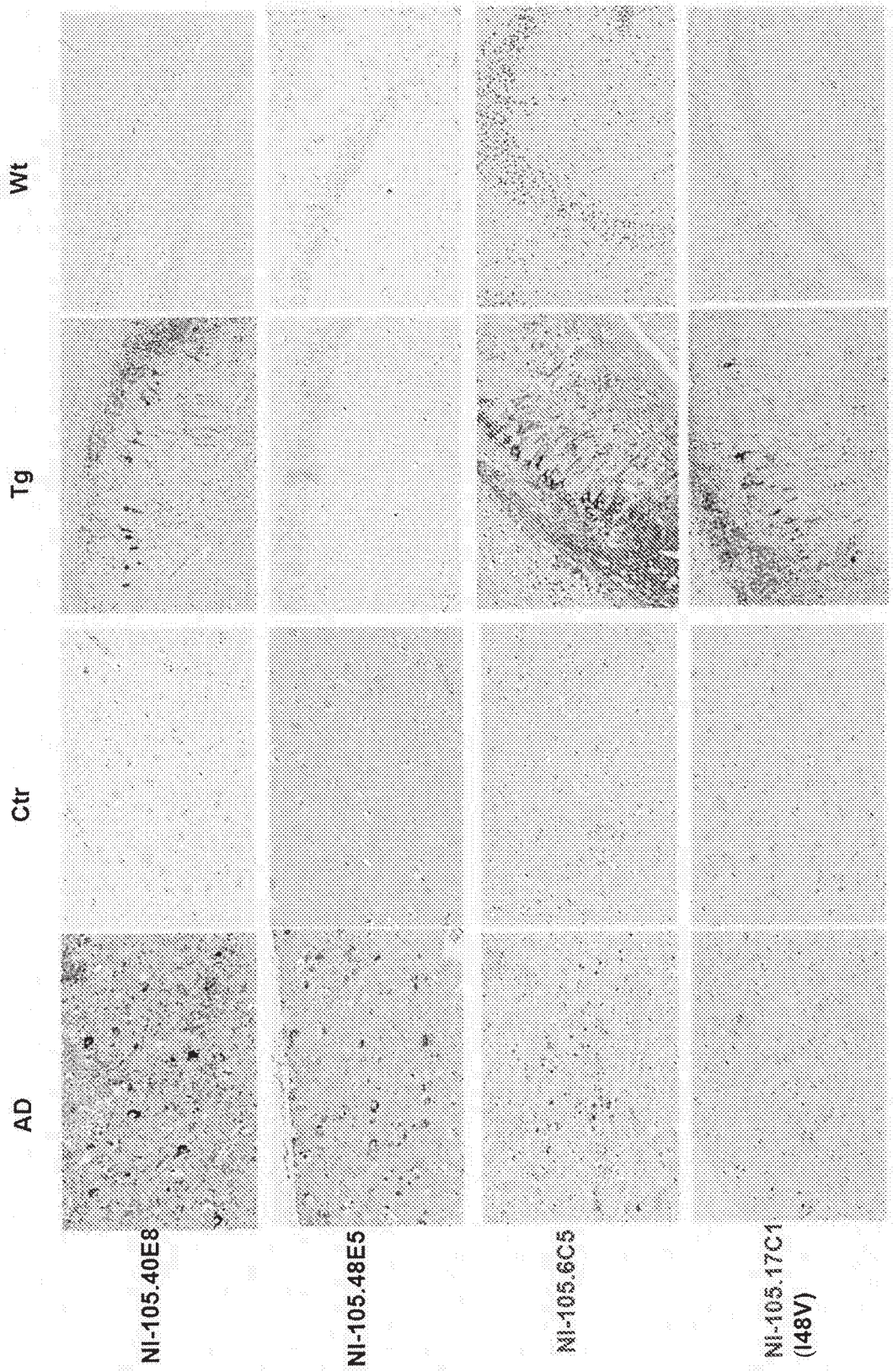


Figure 11

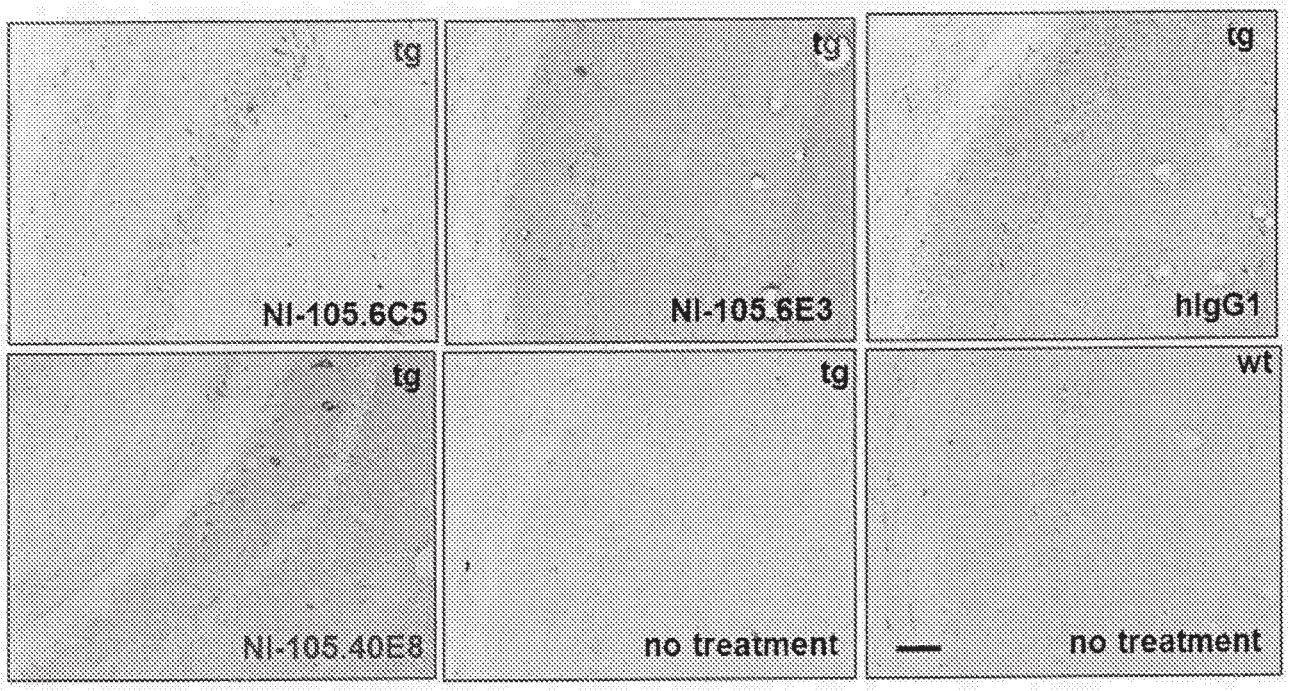

tg
NI-105.6C5
tg
NI-105.6E3
tg
hIgG1
tg
NI-105.40E8
tg
no treatment
wt
no treatment

Figure 12A-C

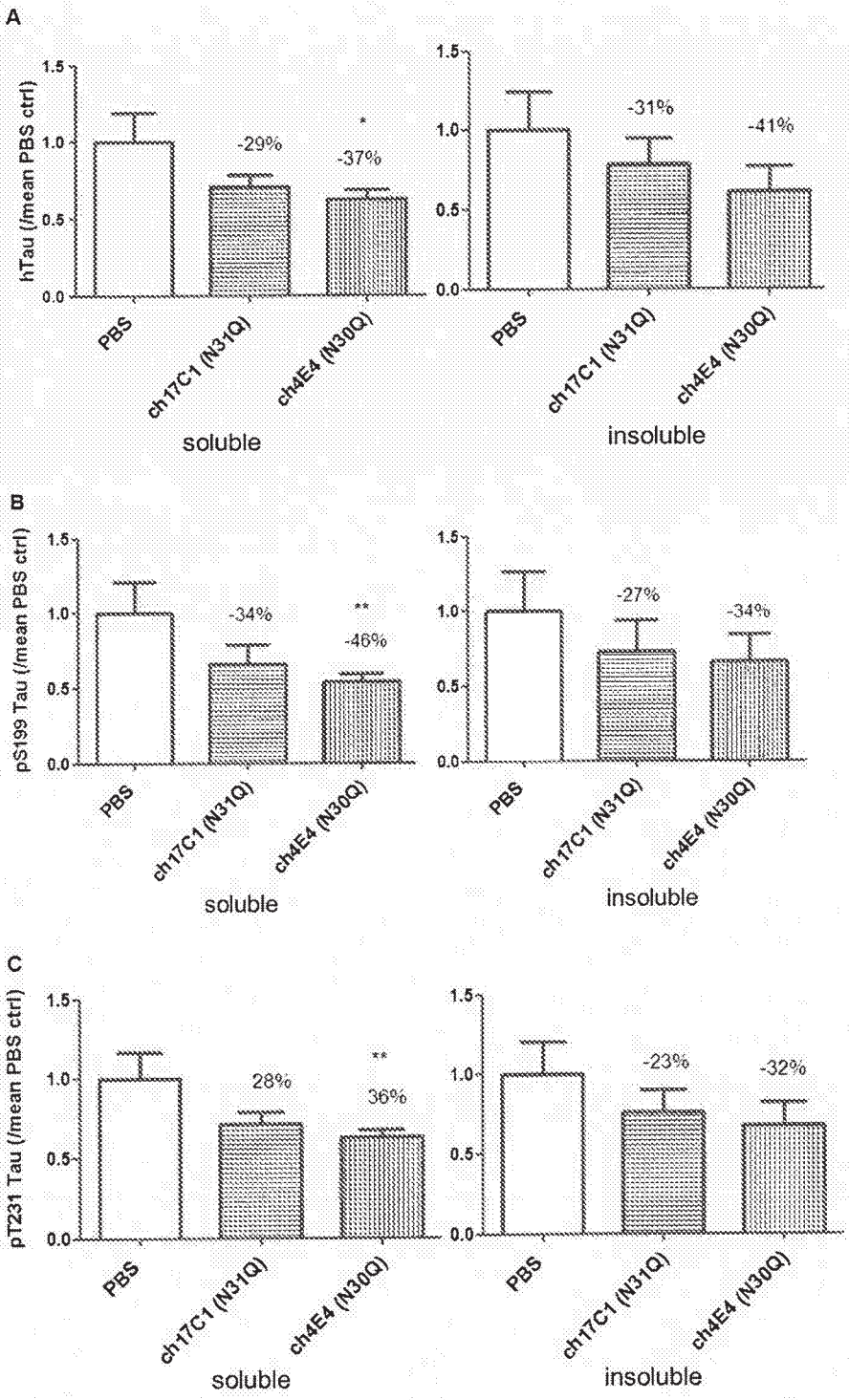

A
hTau (/mean PBS ctrl)
1.5
1.0
0.5
0.0
-29%
*
-37%
-31%
-41%
PBS
ch17C1 (N31Q)
ch4E4 (N30Q)
soluble
insoluble
B
pS199 Tau (/mean PBS ctrl)
-34%
**
-46%
-27%
-34%
C
pT231 Tau (/mean PBS ctrl)
28%
**
36%
-23%
-32%

Figure 12D

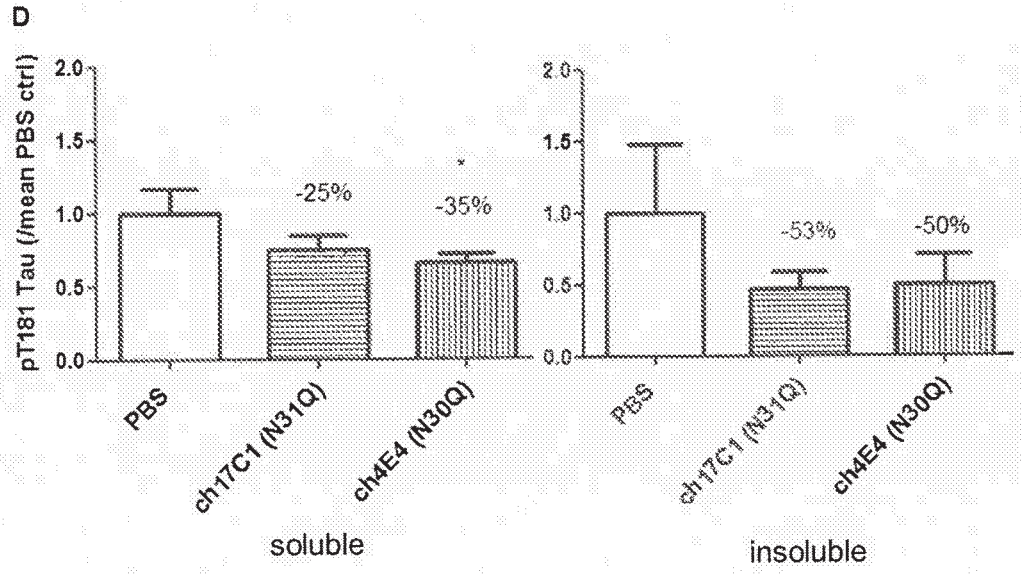

D
pT181 Tau (/mean PBS ctrl)
2.0
1.5
1.0
0.5
0.0
-25%
-35%
-53%
-50%
*
PBS
ch17C1 (N31Q)
ch4E4 (N30Q)
soluble
insoluble

Figure 13

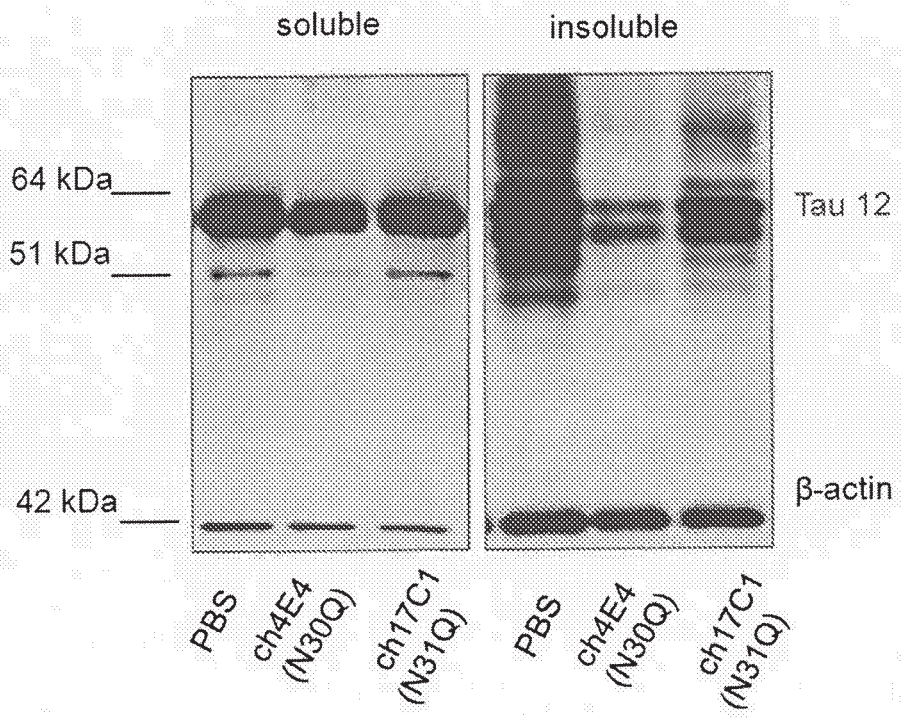

soluble
insoluble
64 kDa
51 kDa
42 kDa
Tau 12
β-actin
PBS
ch4E4 (N30Q)
ch17C1 (N31Q)
PBS
ch4E4 (N30Q)
ch17C1 (N31Q)

Figure 14

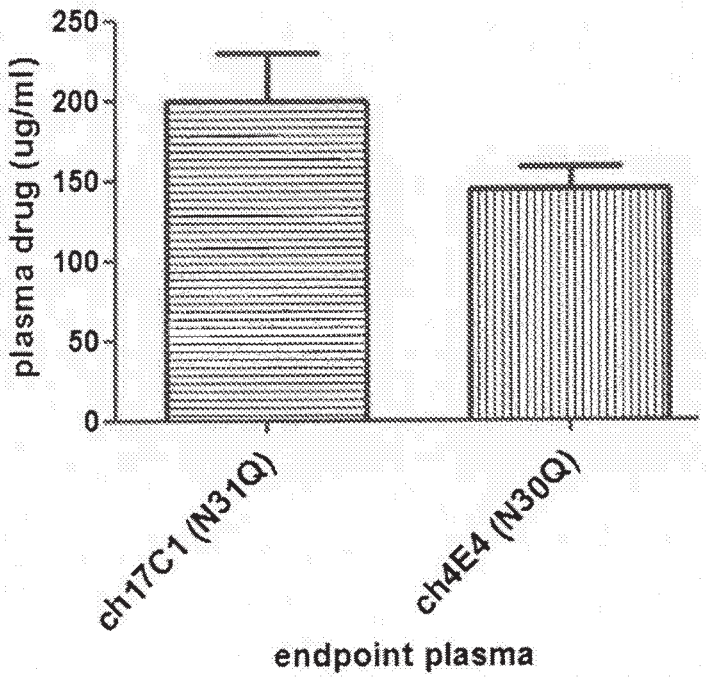

250
200
150
100
50
0
plasma drug (ug/ml)
ch17C1 (N31Q)
ch4E4 (N30Q)
endpoint plasma

Figure 15

