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

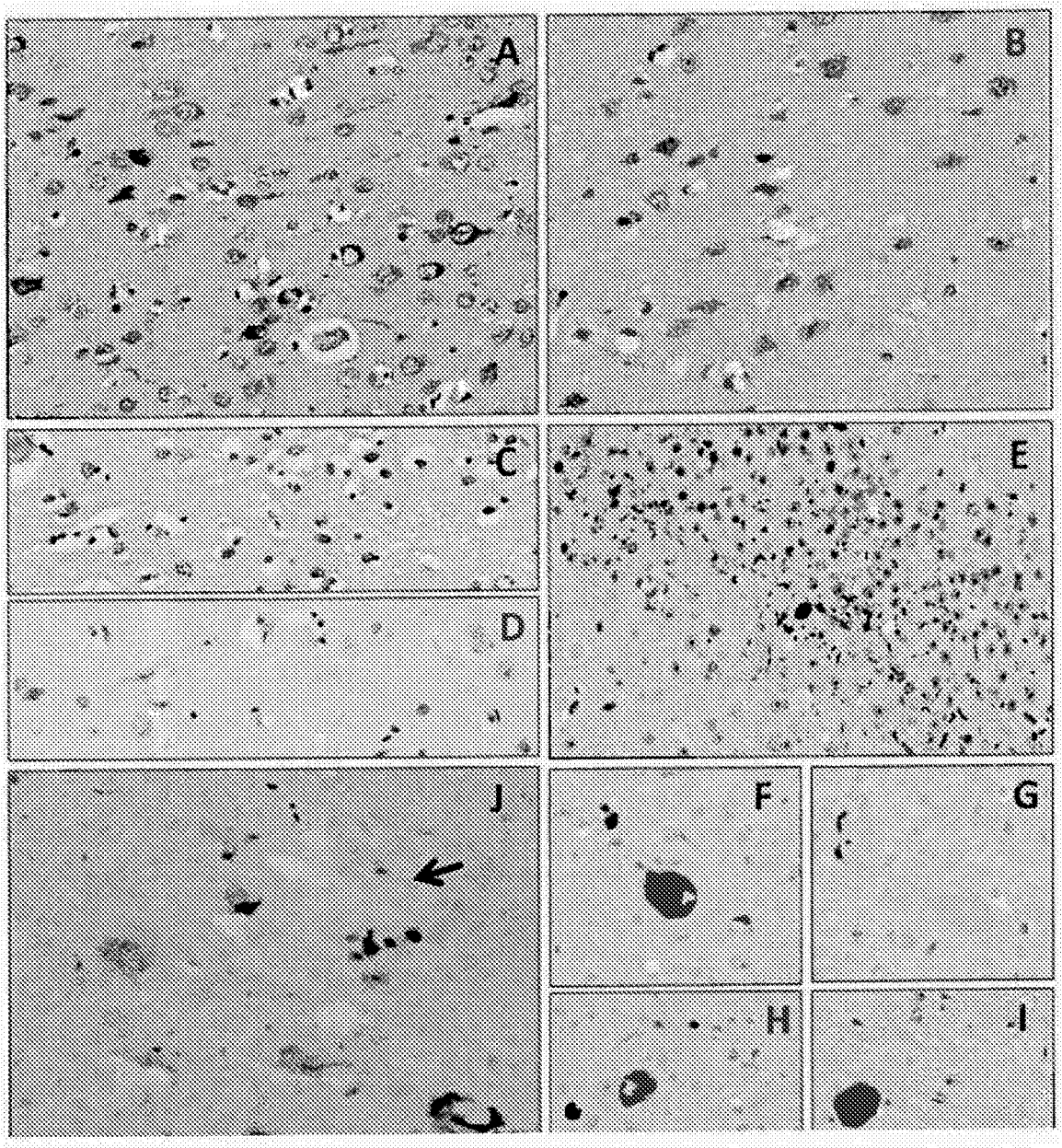


Figure 3

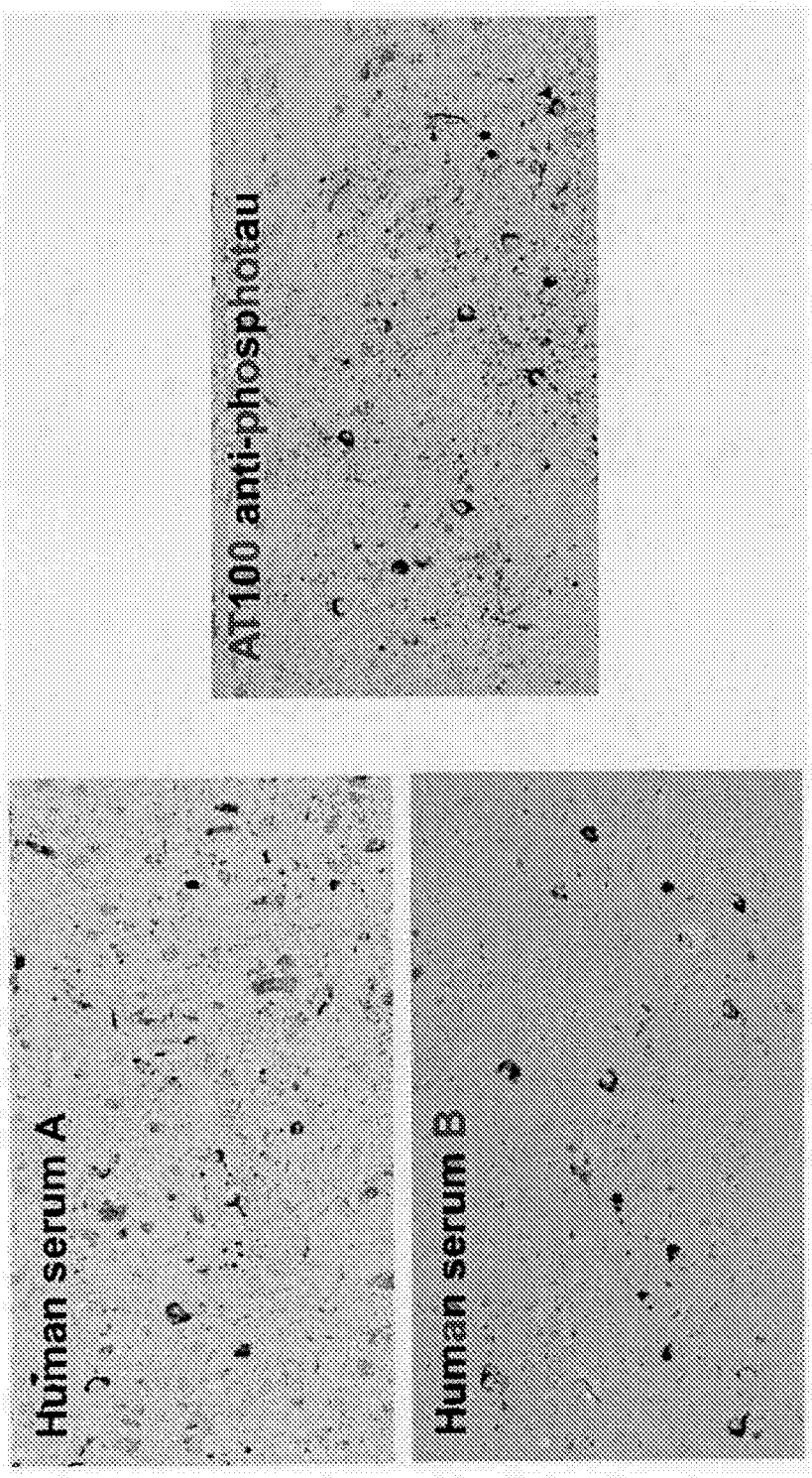


Figure 4

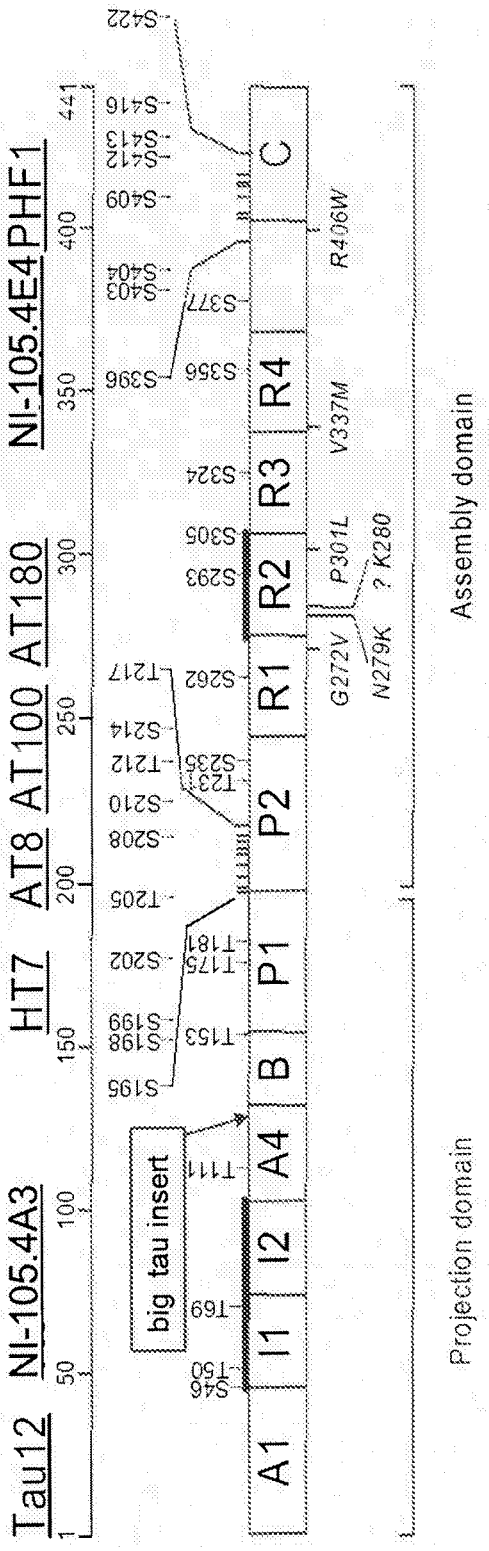

Tau12
NI-105.4A3
HT7
AT8
AT100
AT180
NI-105.4E4
PHF1
A1
I1
I2
A4
B
P1
P2
R1
R2
R3
R4
C
big tau insert
Projection domain
Assembly domain
G272V
P301L
N279K
? K280
V337M
R406W

Figure 5

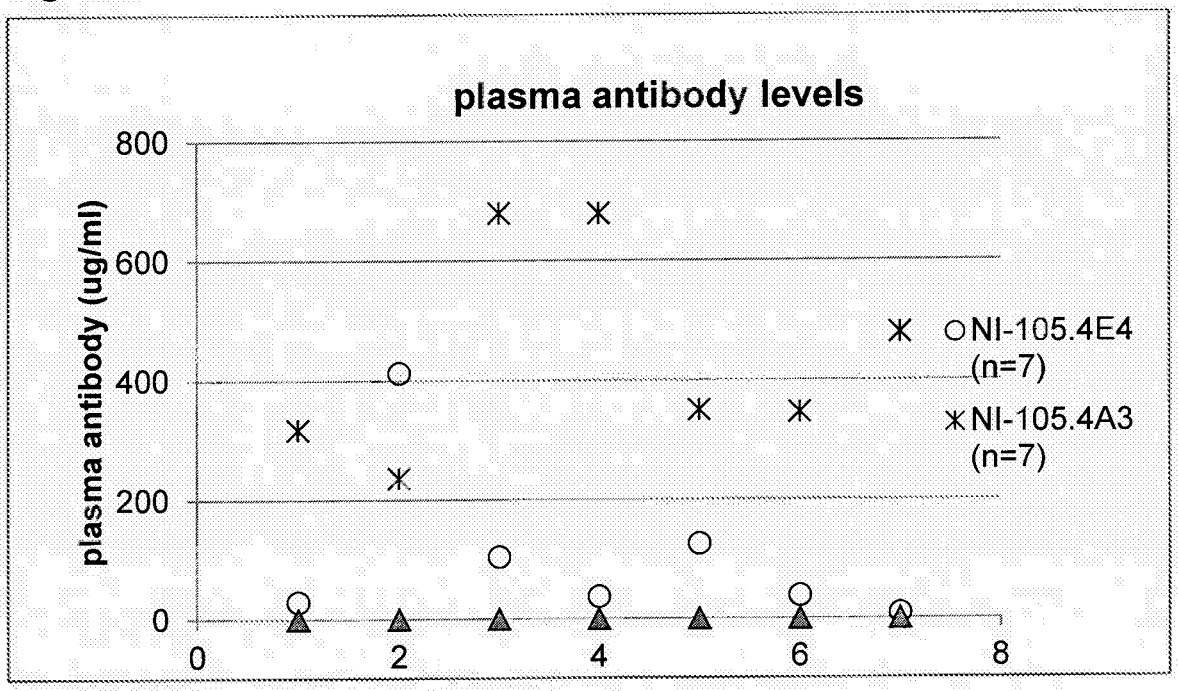


Figure 6

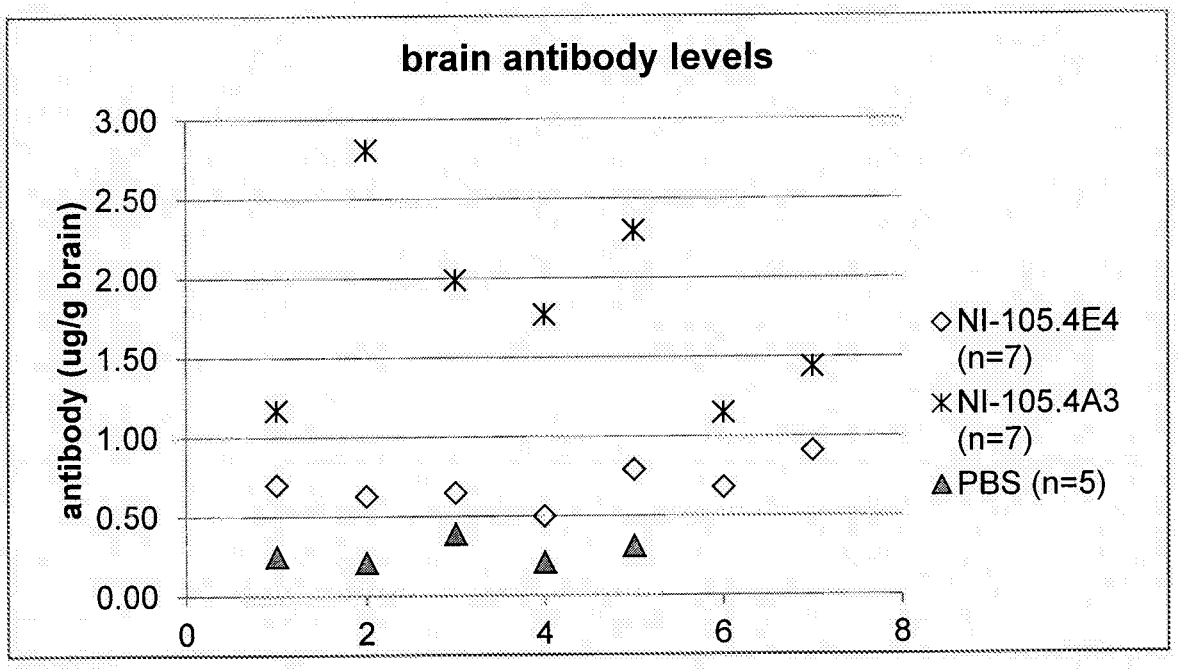


Figure 7A-C

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

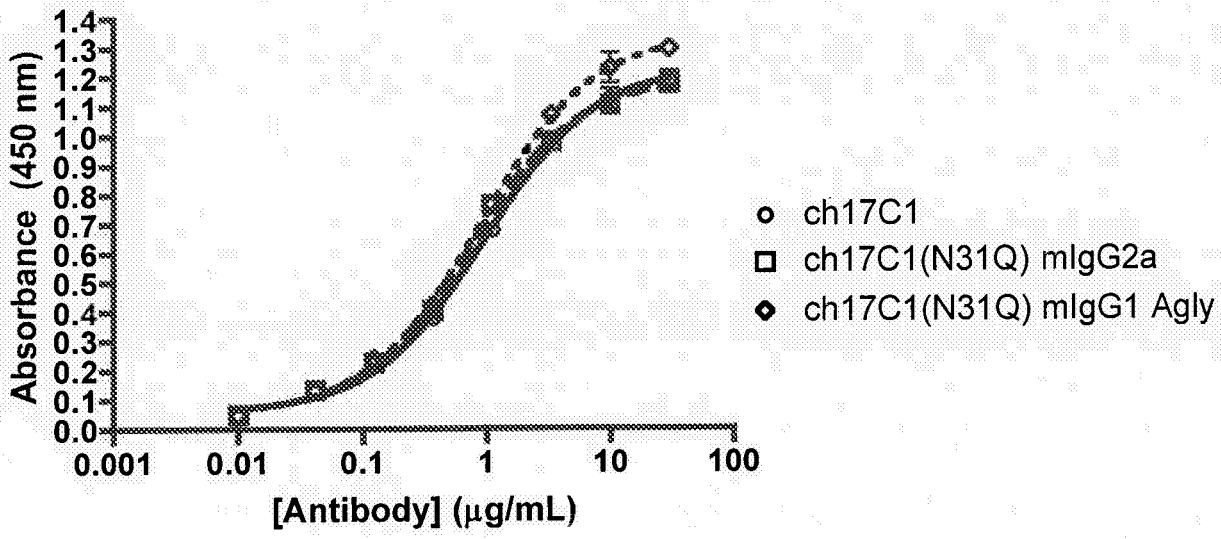
Fig. 7O

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)

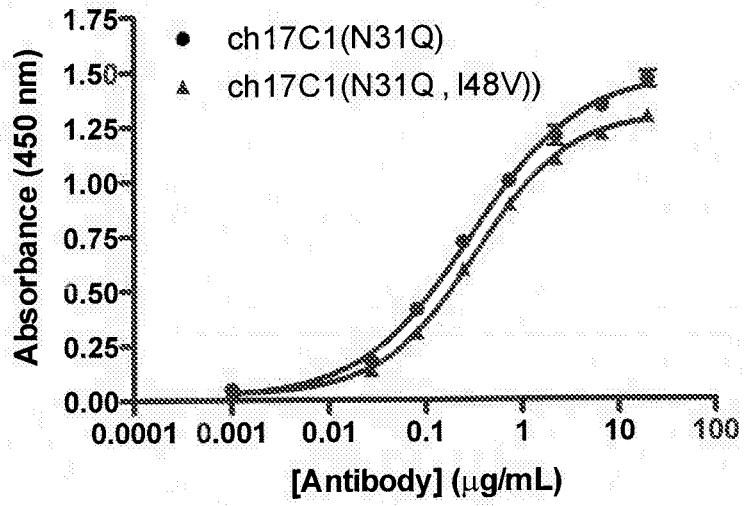


Figure 9

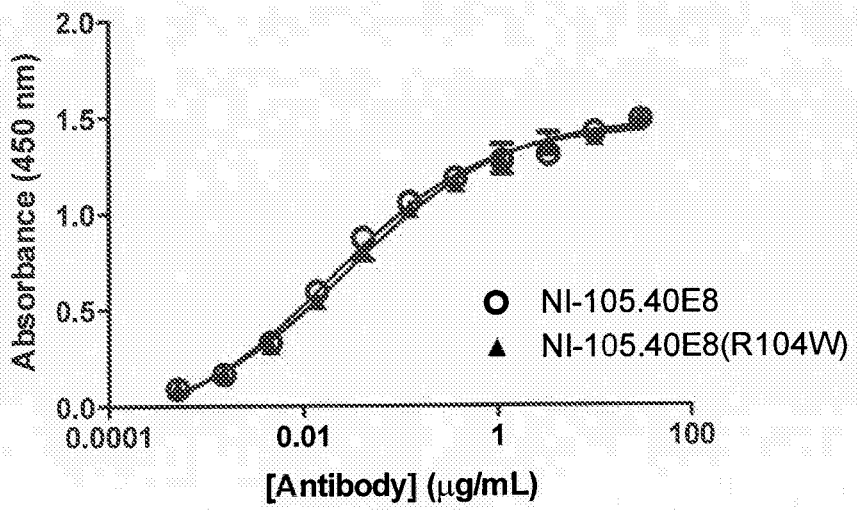

2.0
1.5
1.0
0.5
0.0
Absorbance (450 nm)
0.0001
0.01
1
100
[Antibody] (μg/mL)
NI-105.40E8
NI-105.40E8(R104W)

Figure 10

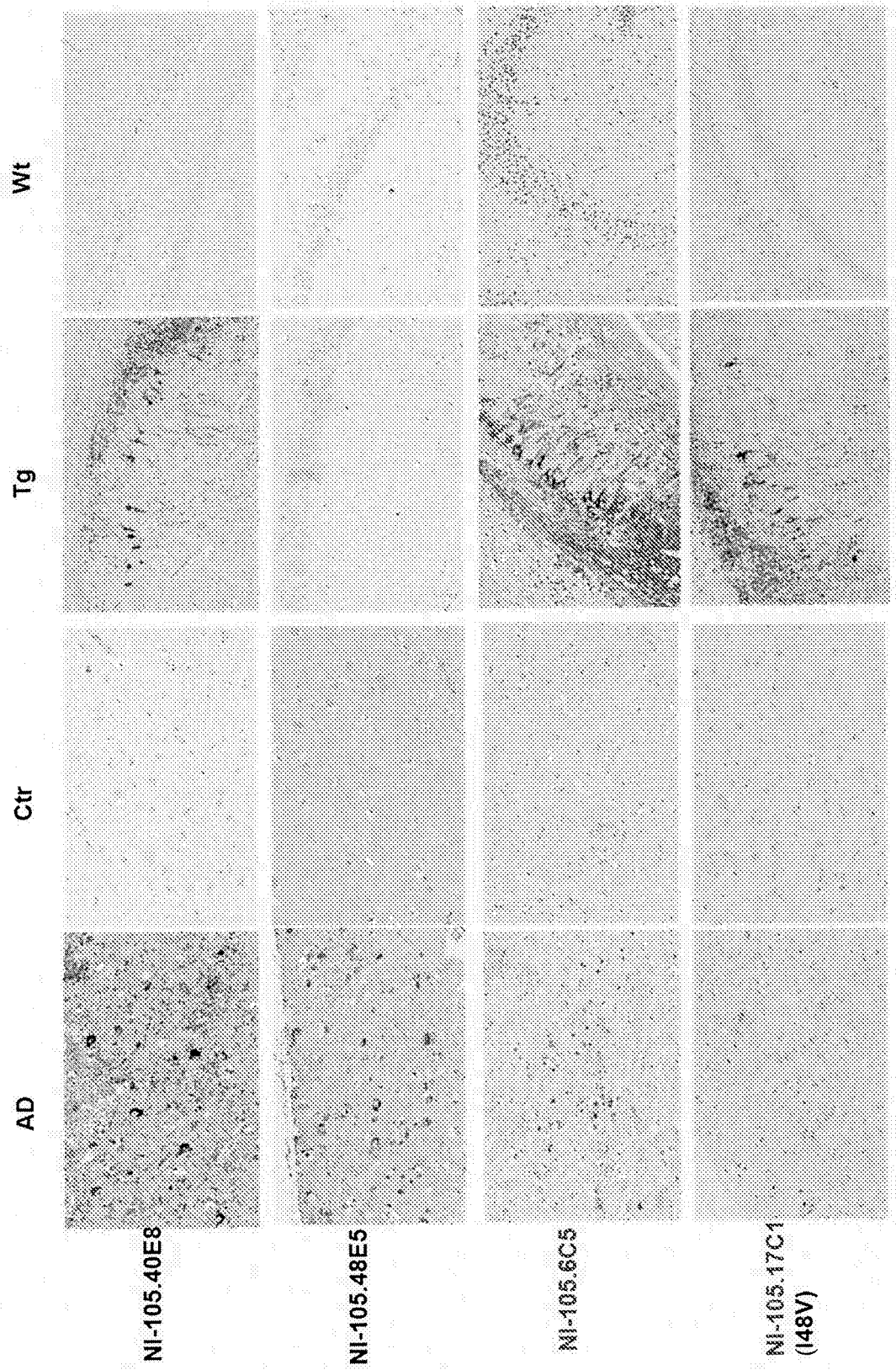


Figure 11

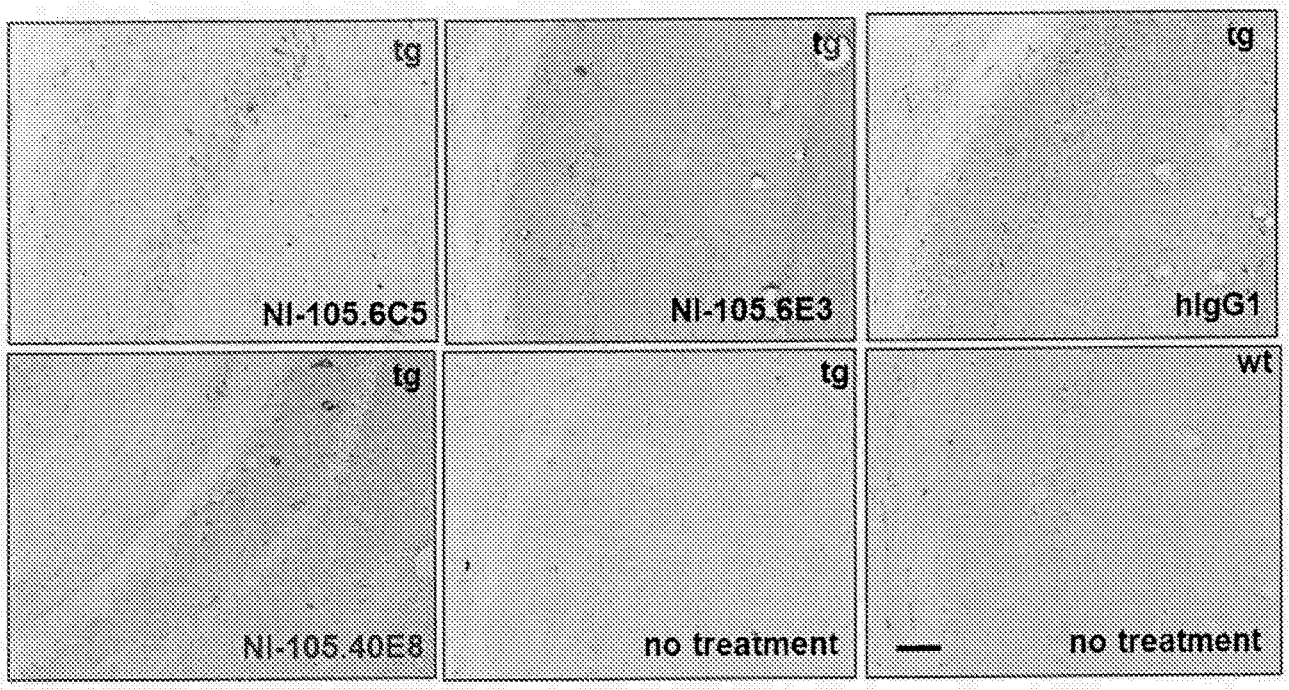

tg
NI-105.6C5
tg
NI-105.6E3
tg
hIgG1
tg
NI-105.40E8
tg
no treatment
wt
no treatment

Figure 12A-C

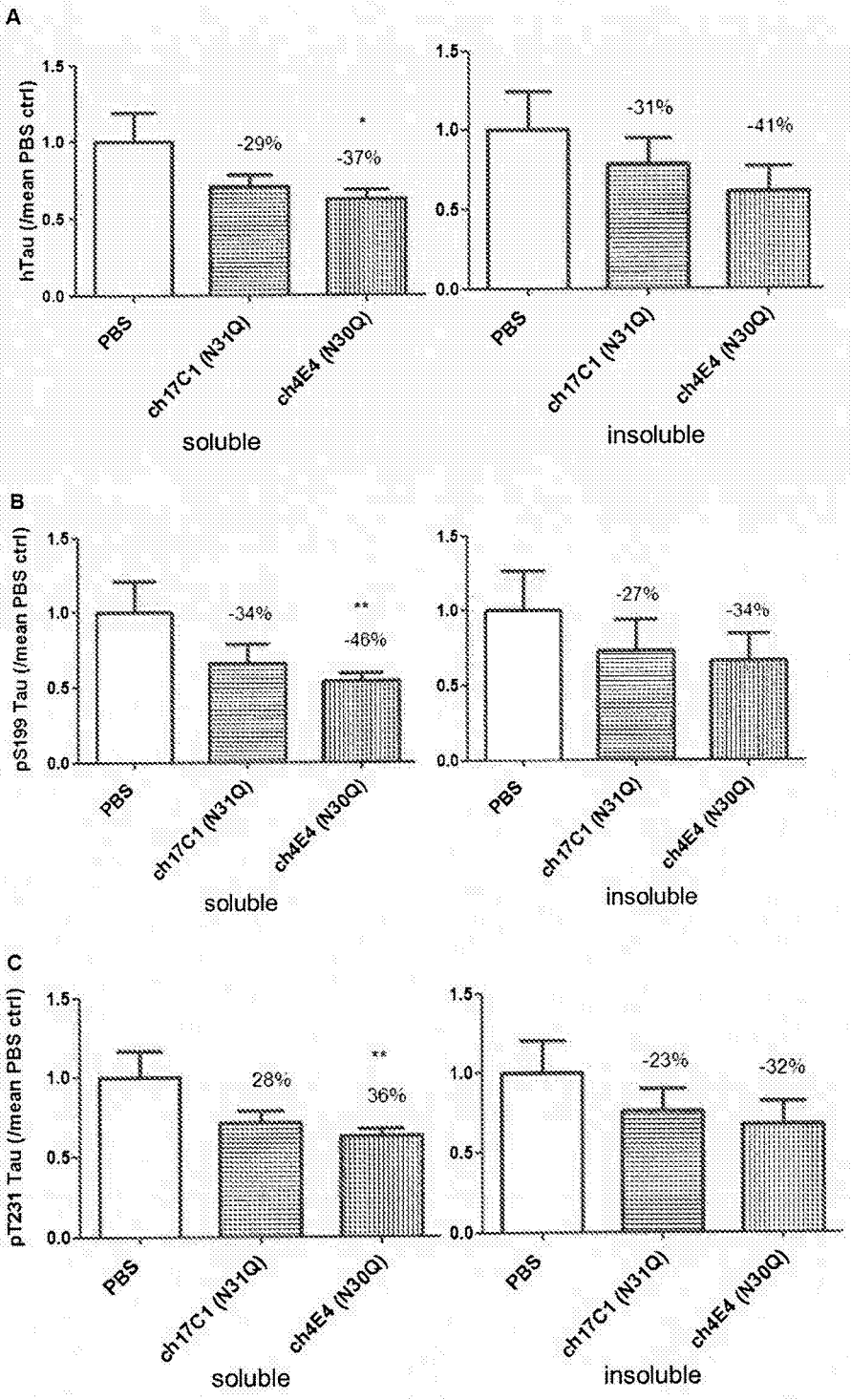

A
hTau (/mean PBS ctrl)
1.5
1.0
0.5
0.0
-29%
*
-37%
-31%
-41%
PBS
ch17C1 (N31Q)
ch4E4 (N30Q)
soluble
insoluble
B
pS199 Tau (/mean PBS ctrl)
-34%
**
-46%
-27%
-34%
C
pT231 Tau (/mean PBS ctrl)
28%
**
36%
-23%
-32%

Figure 12D

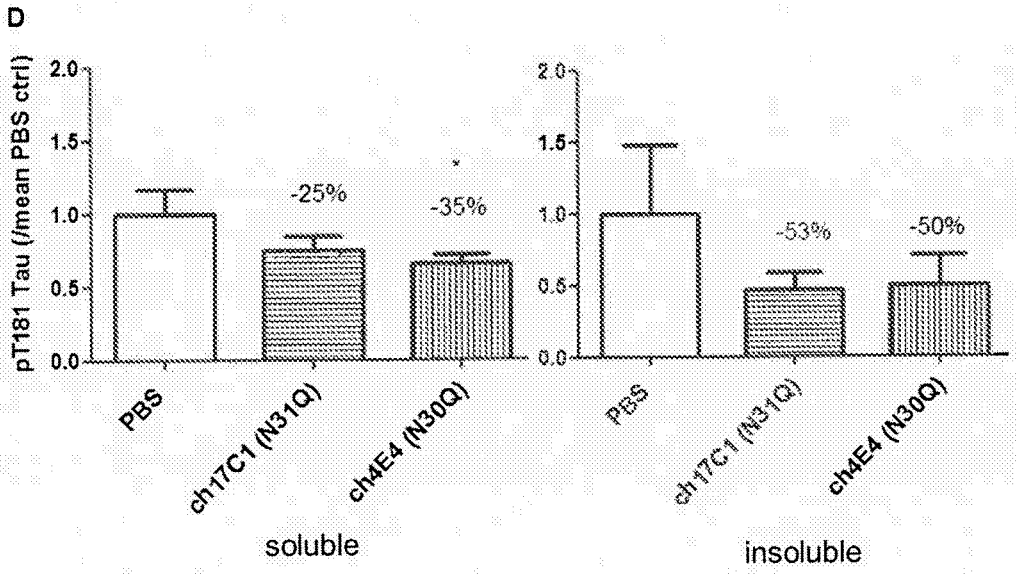

D
pT181 Tau (/mean PBS ctrl)
2.0
1.5
1.0
0.5
0.0
-25%
-35%
*
-53%
-50%
PBS
ch17C1 (N31Q)
ch4E4 (N30Q)
soluble
insoluble

Figure 13

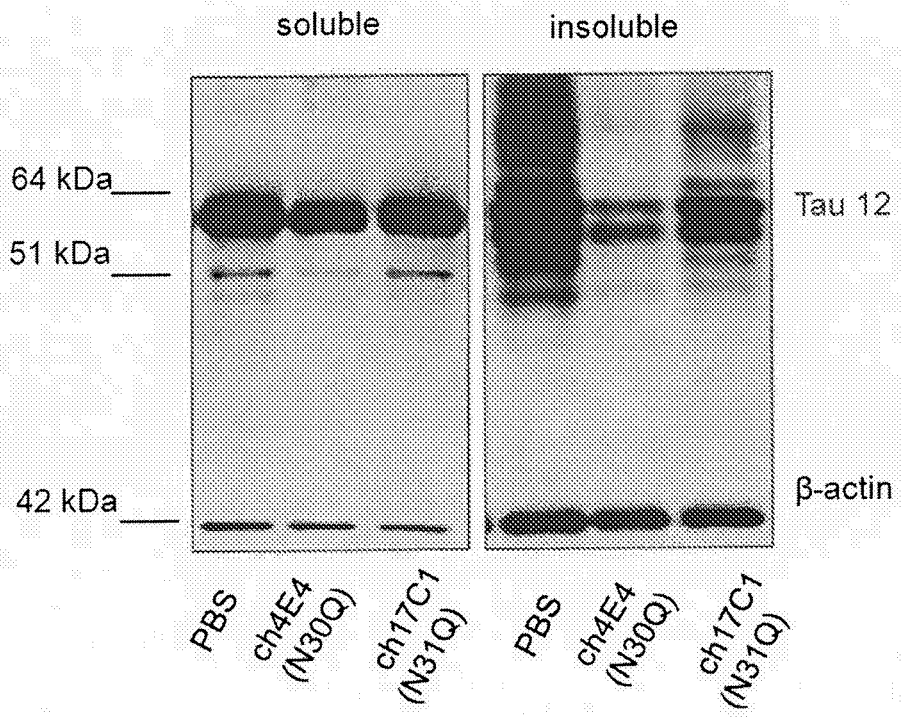

soluble
insoluble
64 kDa
51 kDa
42 kDa
Tau 12
β-actin
PBS
ch4E4 (N30Q)
ch17C1 (N31Q)
PBS
ch4E4 (N30Q)
ch17C1 (N31Q)

Figure 14

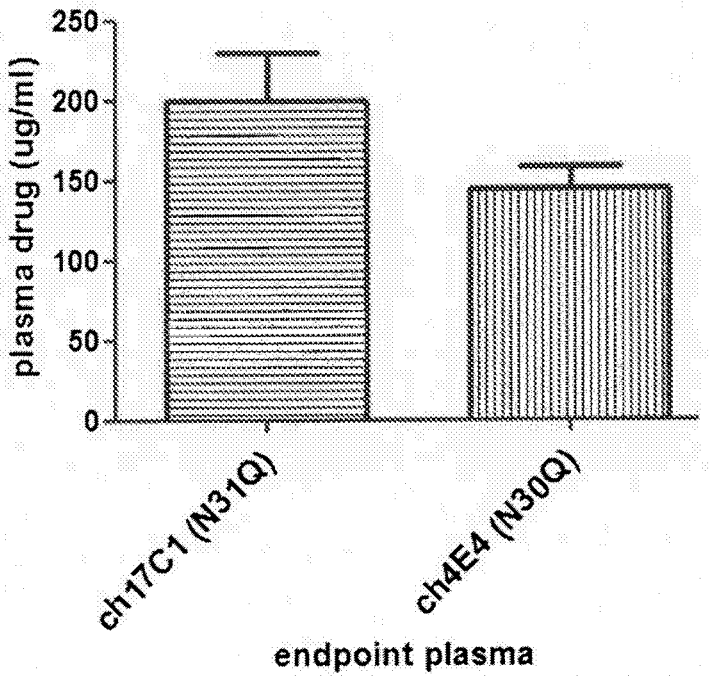

250
200
150
100
50
0
plasma drug (ug/ml)
ch17C1 (N31Q)
ch4E4 (N30Q)
endpoint plasma

Figure 15

