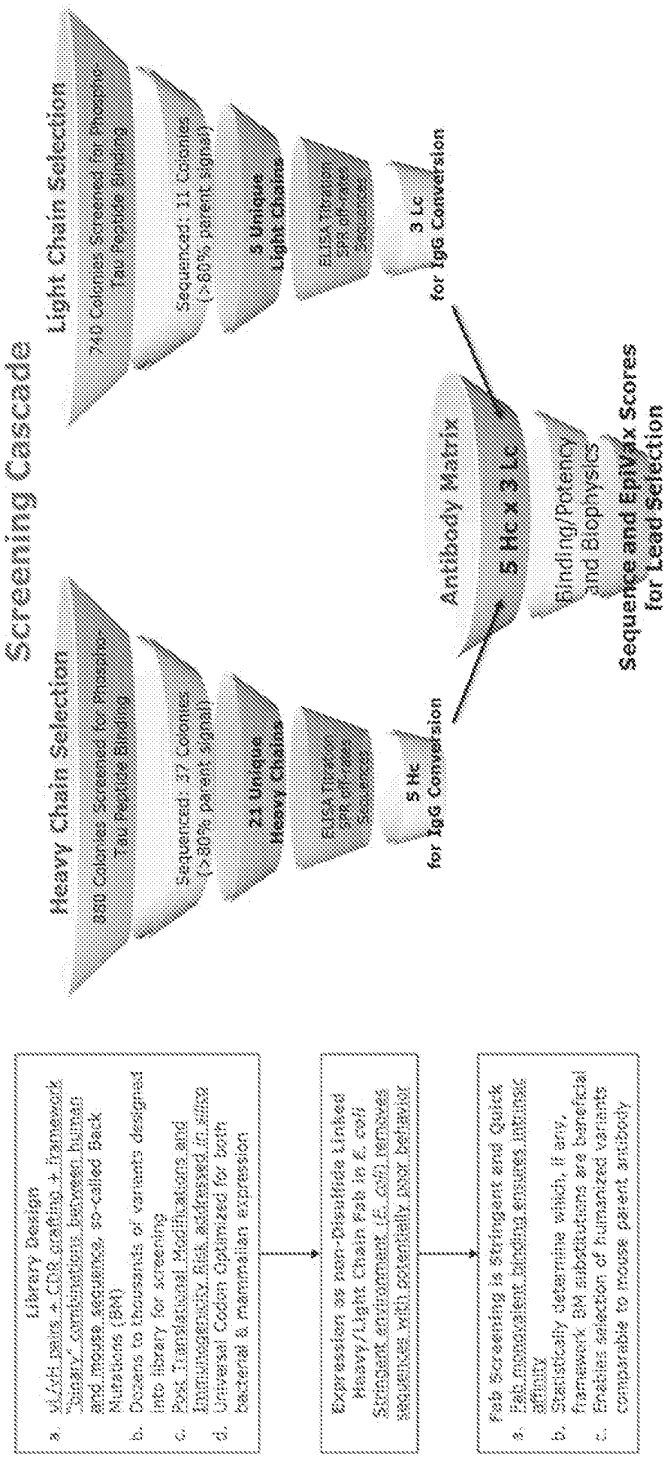

Screening Cascade
Heavy Chain Selection
Light Chain Selection
Antibody Matrix
5 Hc x 3 Lc
Binding/Potency and Biophysics
Sequence and EpiVax Scores for Lead Selection
Library Design
Expression as non-Disulfide Linked Heavy/Light Chain Fab in E. coli
Fab Screening is Stringent and Quick

FIG. 1

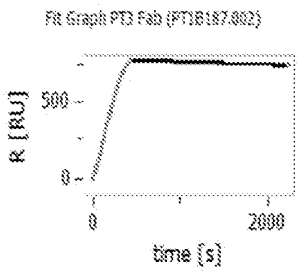



FIG. 2A

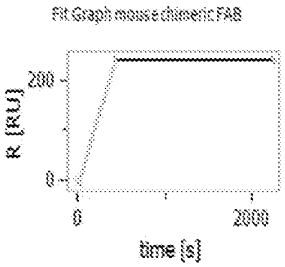



FIG. 2B

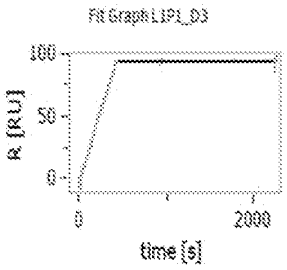



FIG. 2C

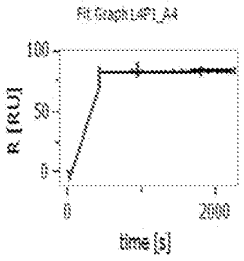



FIG. 2D

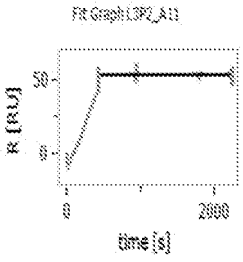



FIG. 2E

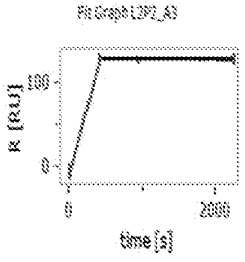



FIG. 2F

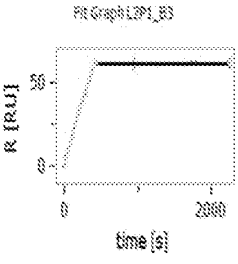



FIG. 2G

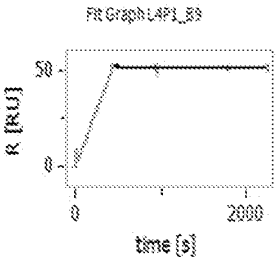



FIG. 2H

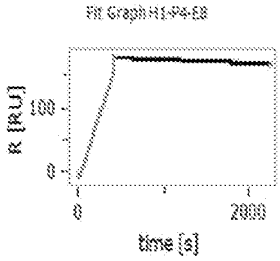



FIG. 2I

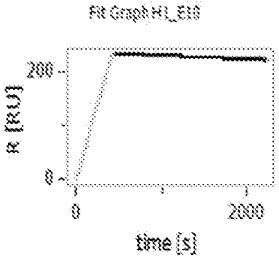



FIG. 2J

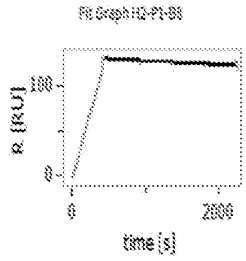



FIG. 2K

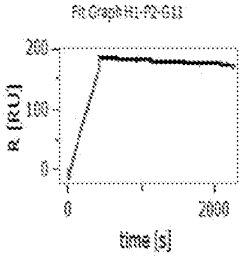



FIG. 2L

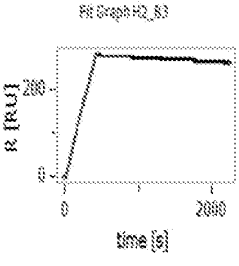



FIG. 2M

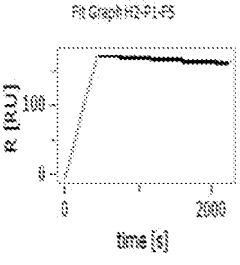



FIG. 2N

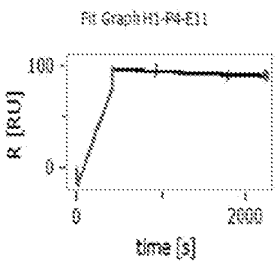



FIG. 2O

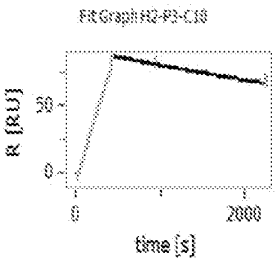



FIG. 2P

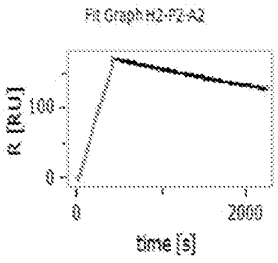



FIG. 2Q

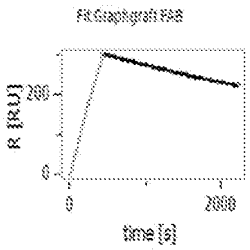



FIG. 2R

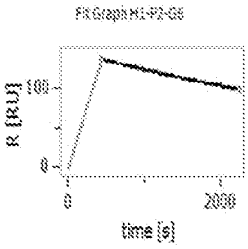



FIG. 2S

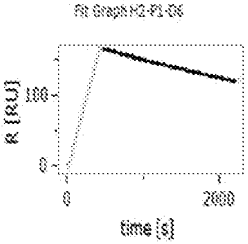



FIG. 2T

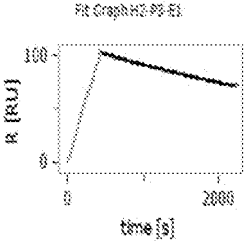



FIG. 2U

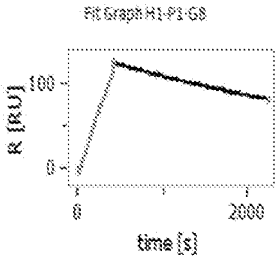



FIG. 2V

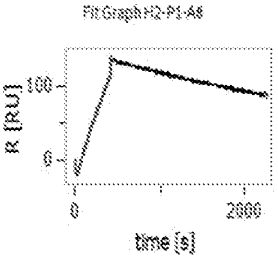



FIG. 2W

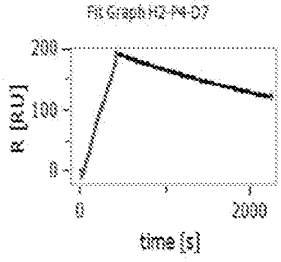



FIG. 2X

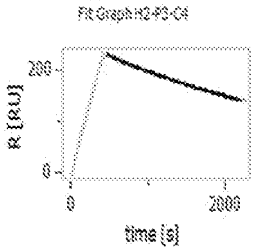



FIG. 2Y

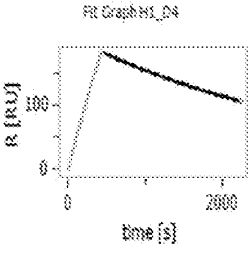



FIG. 2Z

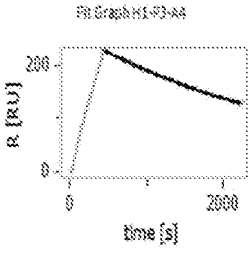



FIG. 2AA

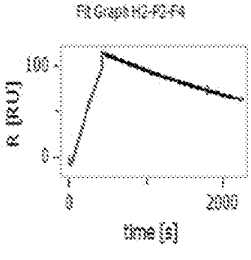



FIG. 2AB

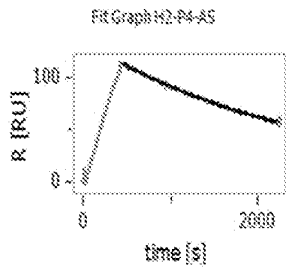



FIG. 2AC

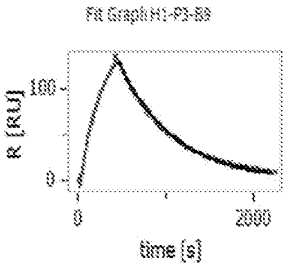



FIG. 2AD

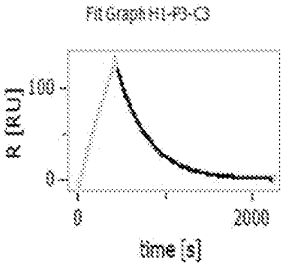



FIG. 2AE

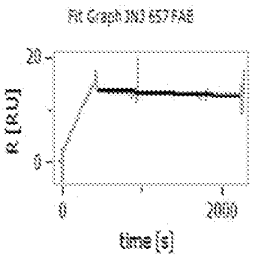



FIG. 2AF

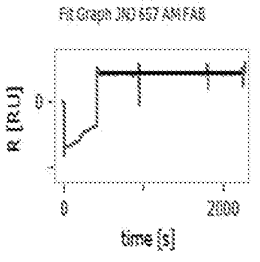



FIG. 2AG

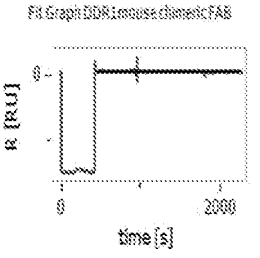



FIG. 2AH

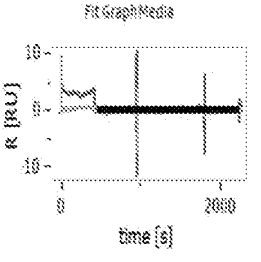



FIG. 2AI

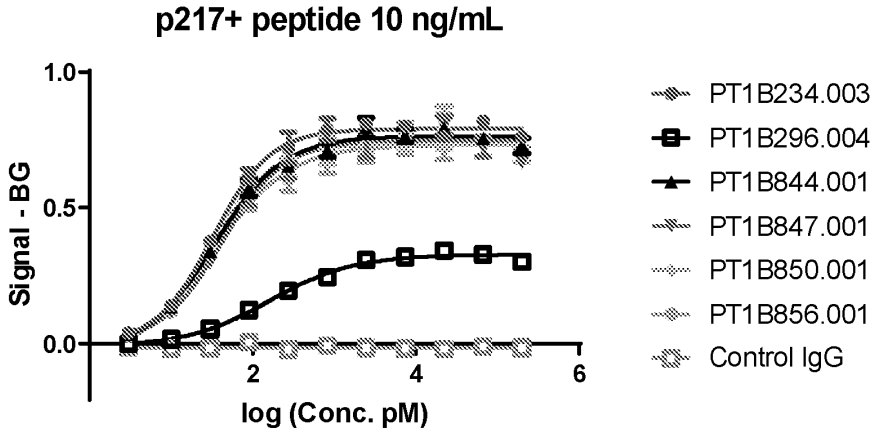



FIG. 3

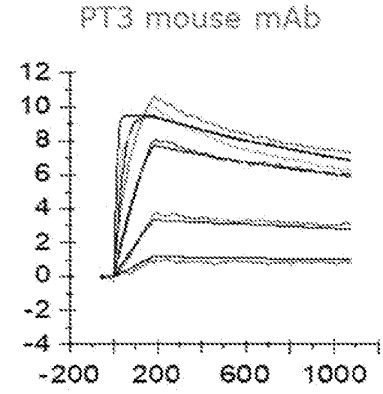



FIG. 4A

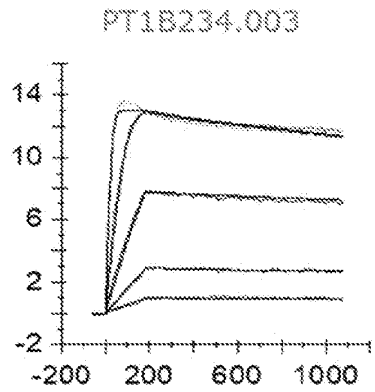



FIG. 4B

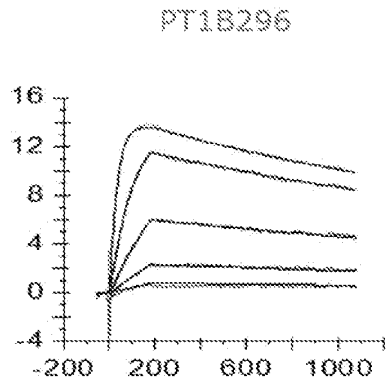



FIG. 4C

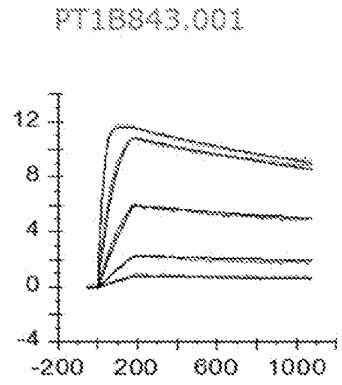



FIG. 4D

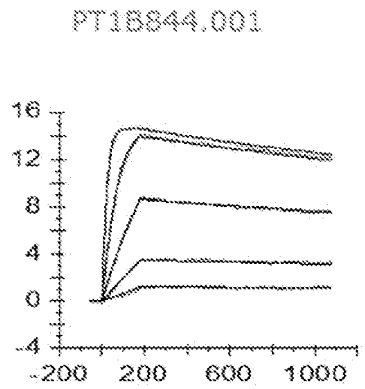



FIG. 4E

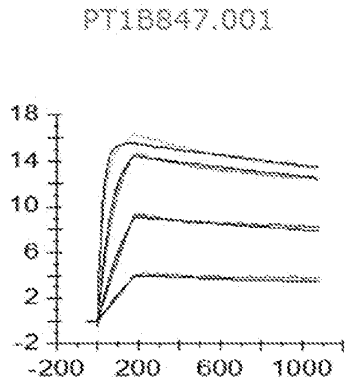



FIG. 4F

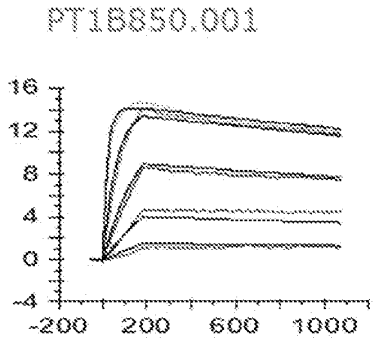



FIG. 4G

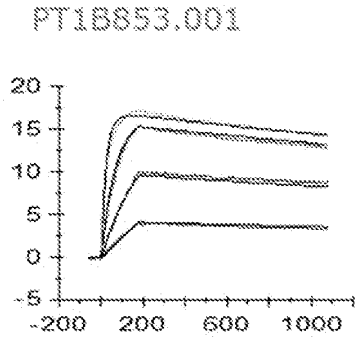



FIG. 4H

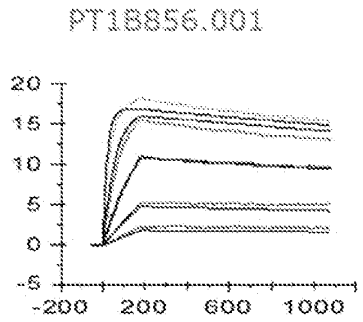



FIG. 4I

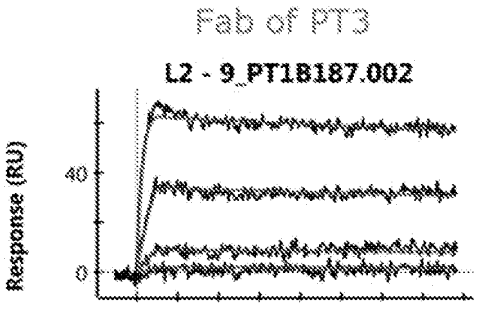



FIG. 5A

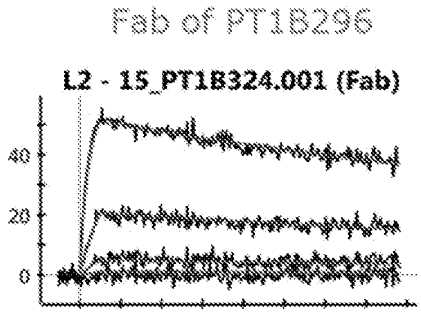



FIG. 5B

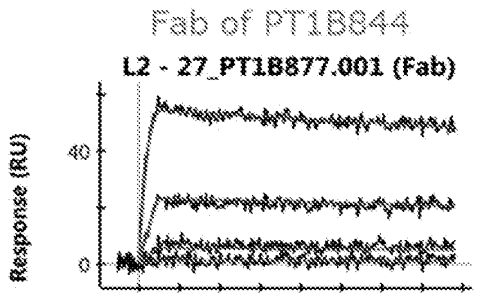



FIG. 5C

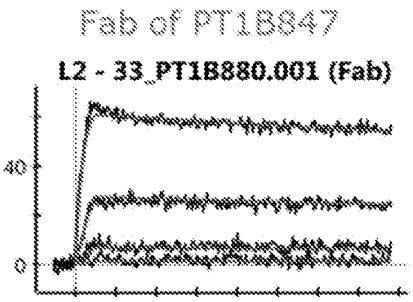



FIG. 5D

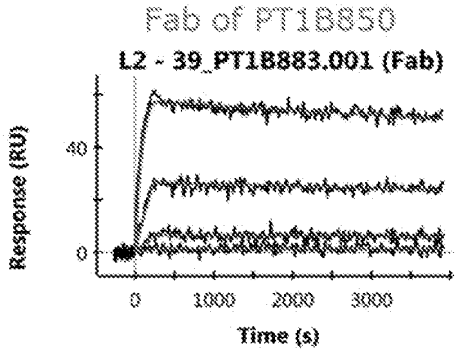



FIG. 5E

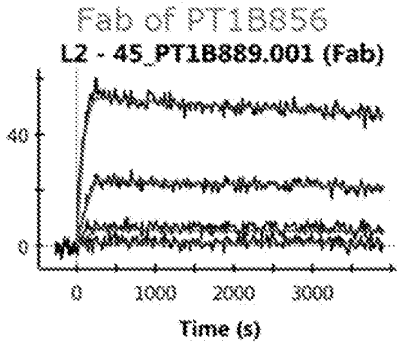



FIG. 5F

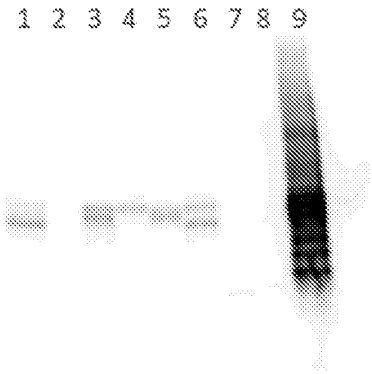



FIG. 6A

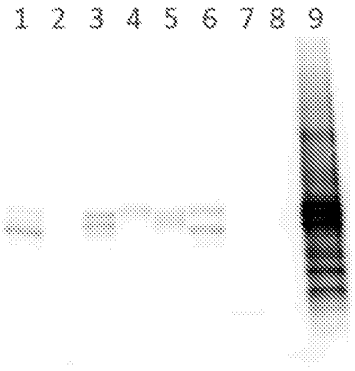



FIG. 6B

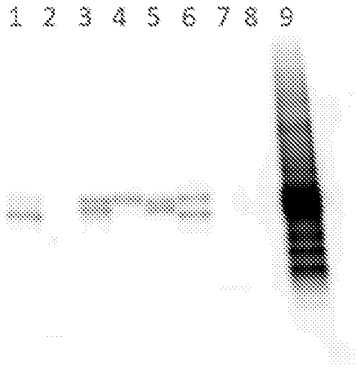



FIG. 6C

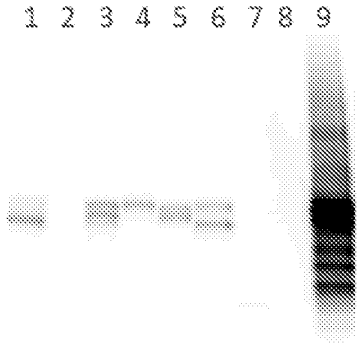



FIG. 6D

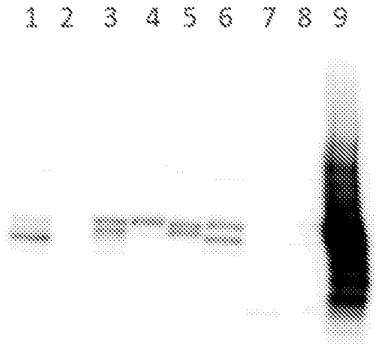



FIG. 6E

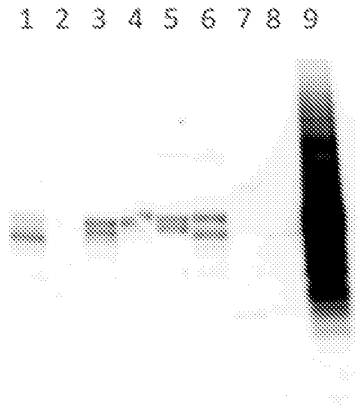



FIG. 6F

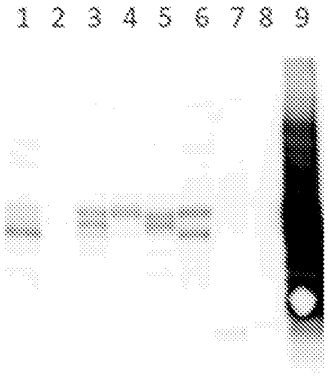



FIG. 6G

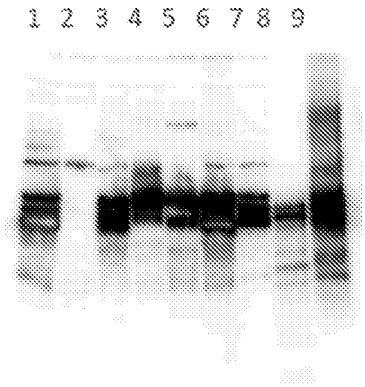



FIG. 6H

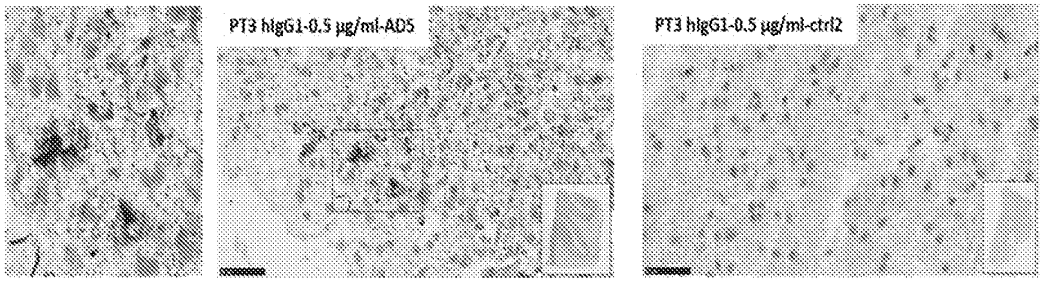



FIG. 7A

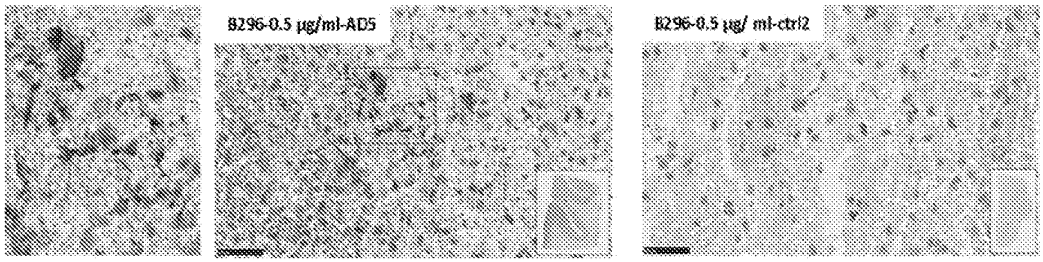



FIG. 7B

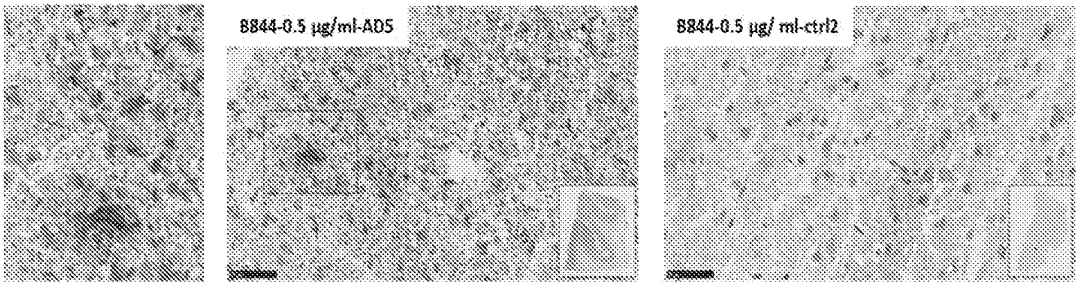



FIG. 7C

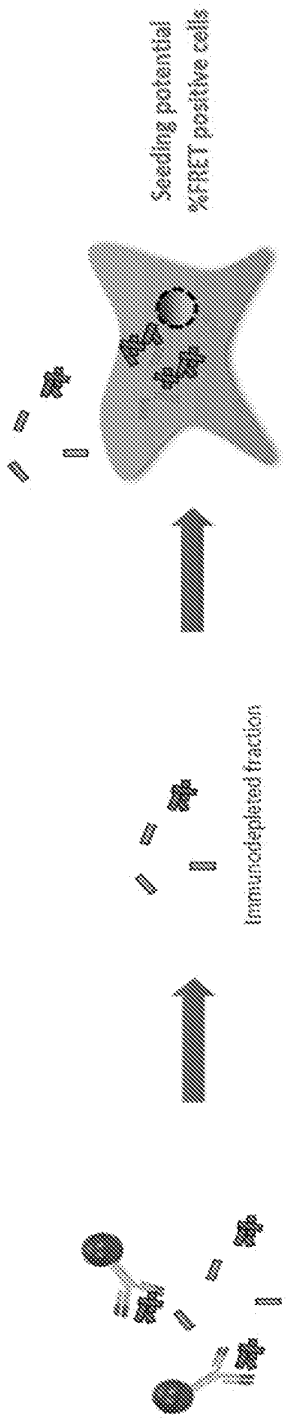

Seeding potential
%RET positive cells
Immunodepleted fraction

FIG. 8A

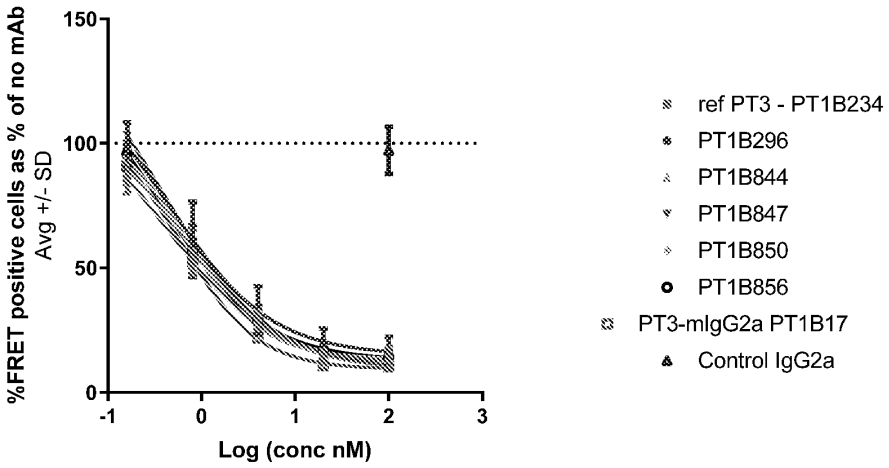

%FRET positive cells as % of no mAb
Avg +/- SD
150
100
50
0
-1
0
1
2
3
Log (conc nM)
ref PT3 - PT1B234
PT1B296
PT1B844
PT1B847
PT1B850
PT1B856
PT3-mIgG2a PT1B17
Control IgG2a

FIG. 8B

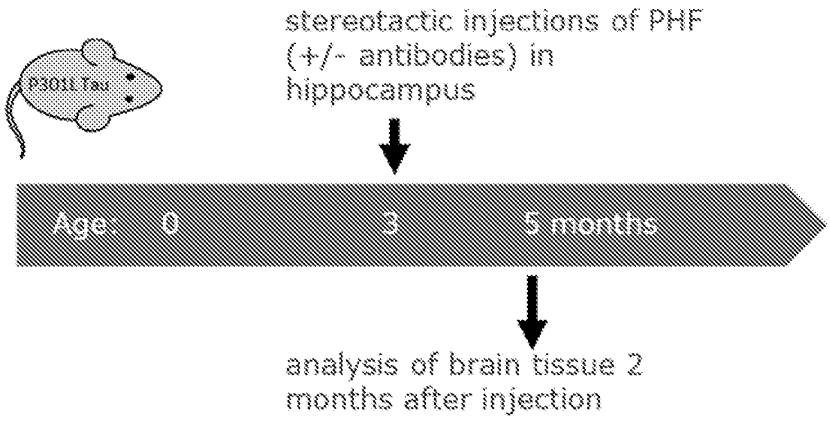

P301L Tau
stereotactic injections of PHF
(+/- antibodies) in
hippocampus
Age: 0
3
5 months
analysis of brain tissue 2
months after injection

FIG. 9A

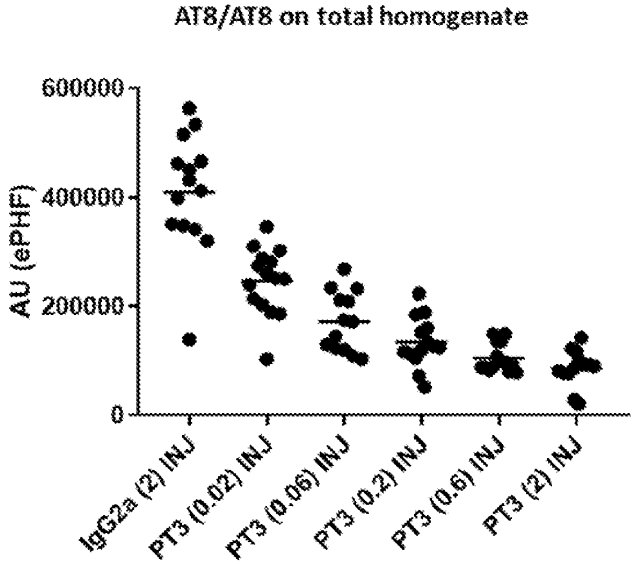

AT8/AT8 on total homogenate
AU (ePHF)
600000
400000
200000
0
IgG2a (2) INJ
PT3 (0.02) INJ
PT3 (0.06) INJ
PT3 (0.2) INJ
PT3 (0.6) INJ
PT3 (2) INJ

FIG. 9B

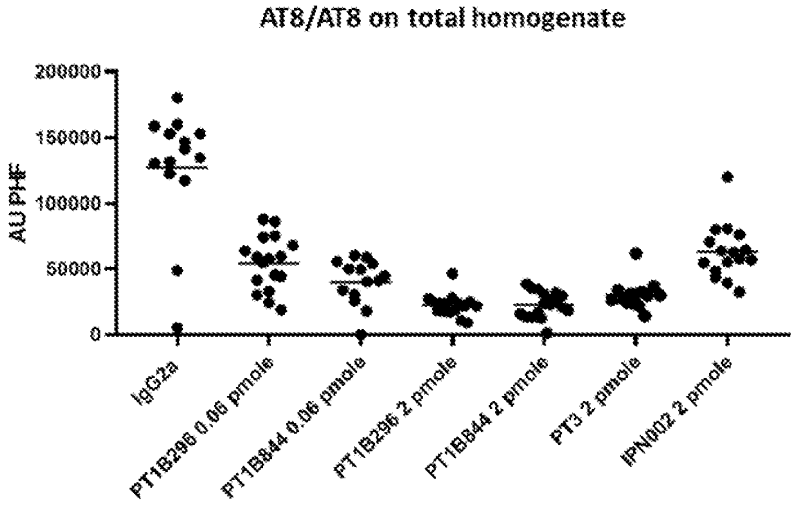

AT8/AT8 on total homogenate
AU PHF
200000
150000
100000
50000
0
IgG2a
PT1B296 0.06 pmole
PT1B844 0.06 pmole
PT1B296 2 pmole
PT1B844 2 pmole
PT3 2 pmole
IPN002 2 pmole

FIG. 9C

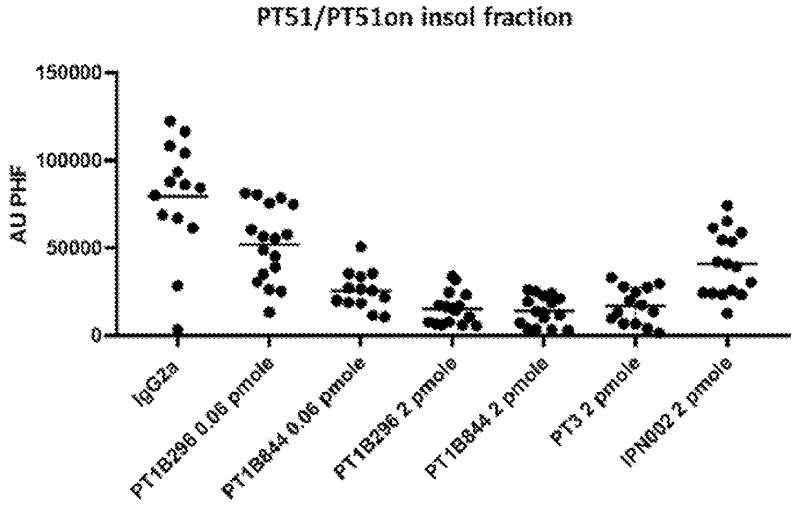



FIG. 9D

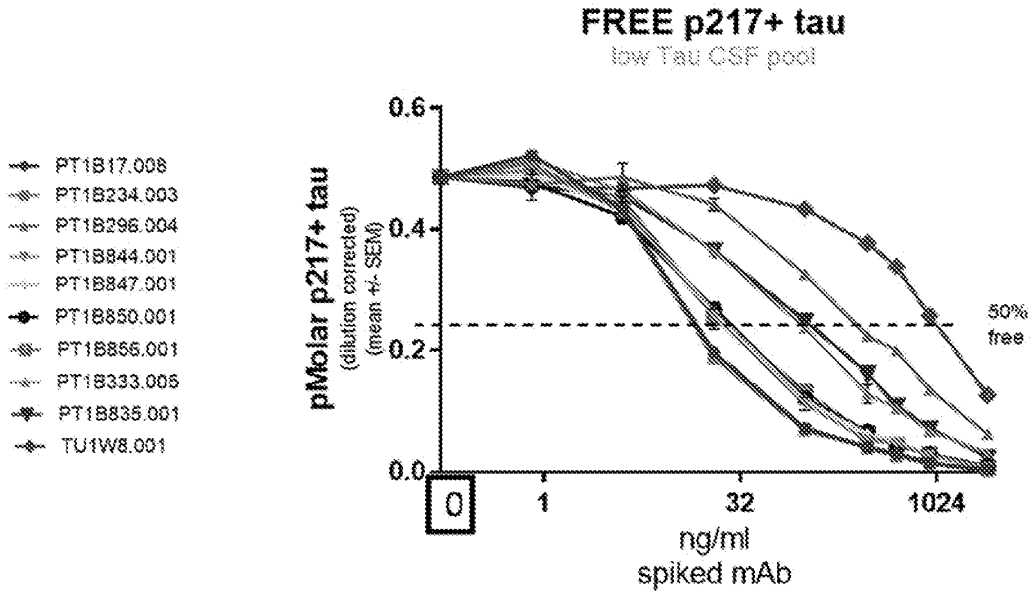



FIG. 10A

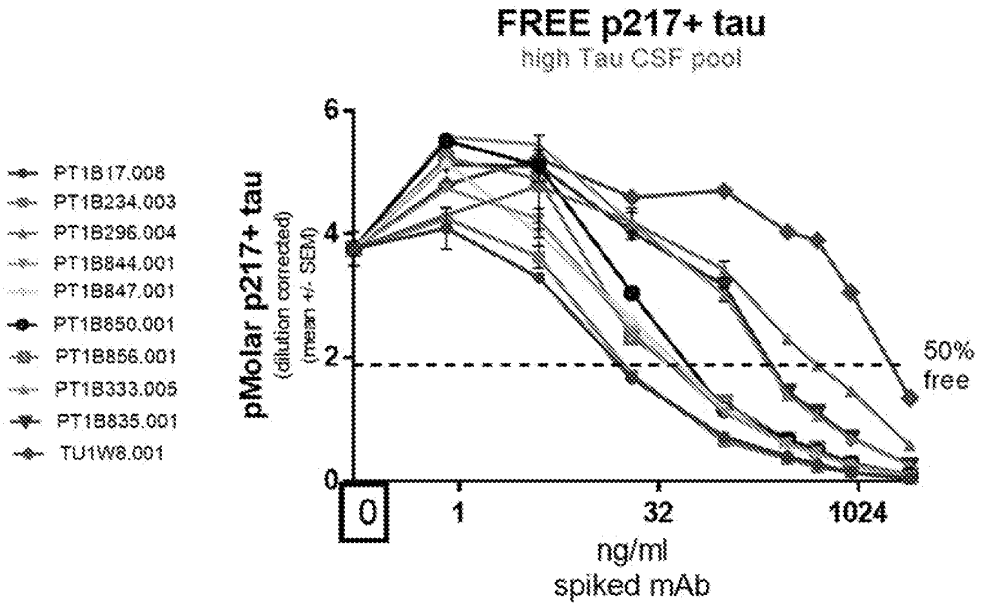
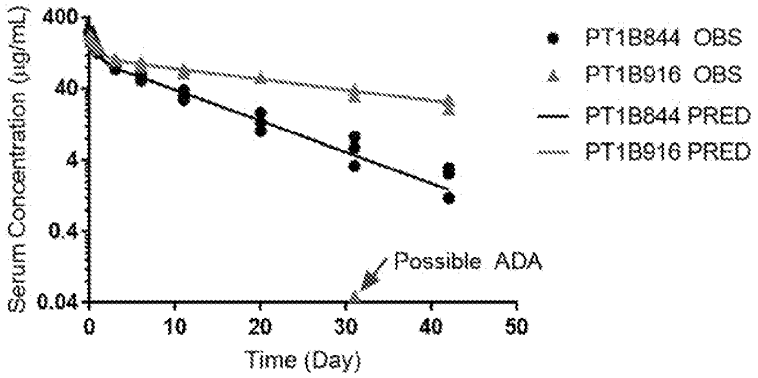



FIG. 10B




| Compound | β $T_{1/2}$ (days) | |
|---|---|---|
| | WT | YTE |
| PT1B844 | 6.91 | 20.05 |

FIG. 11