

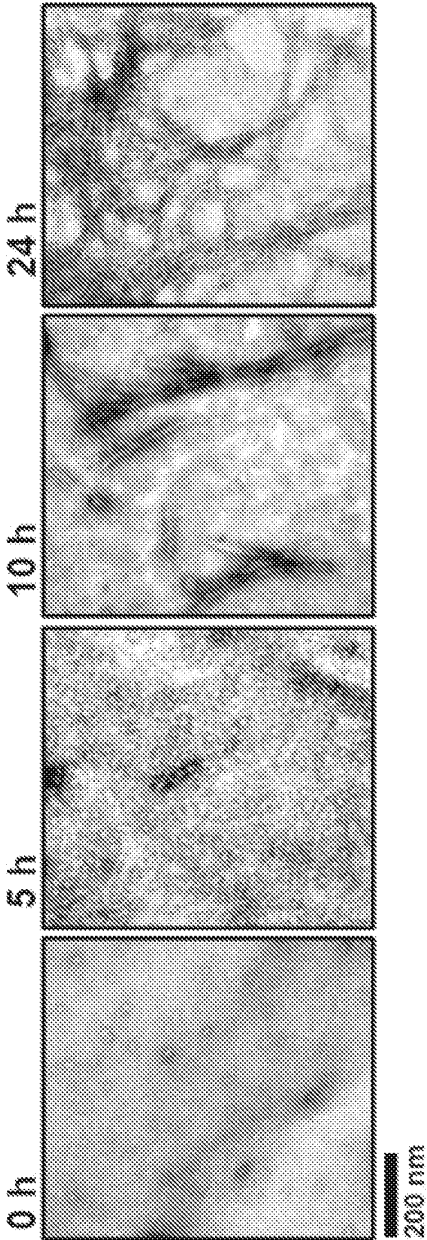


FIG. 1A

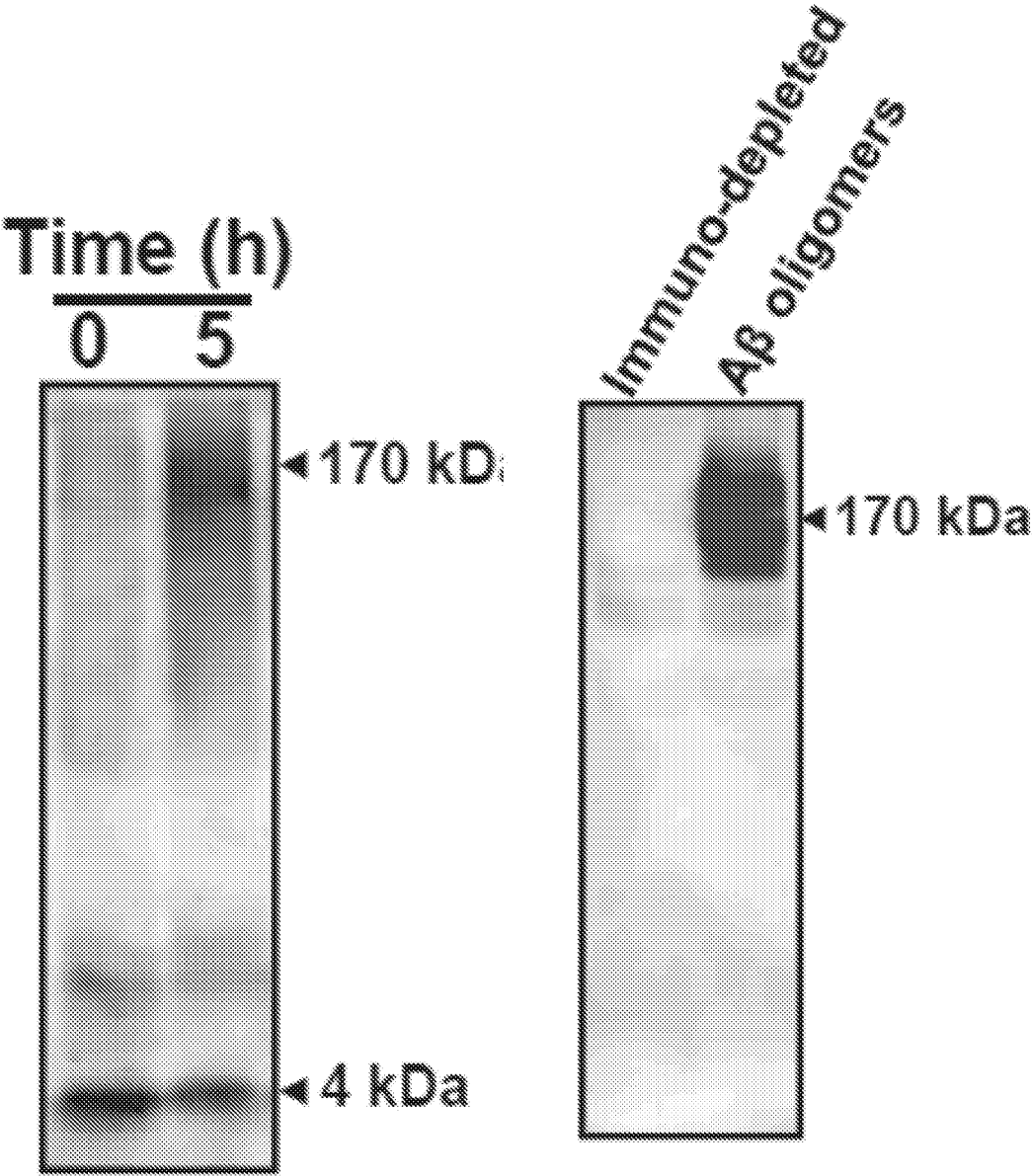


FIG. 1B

FIG. 7A

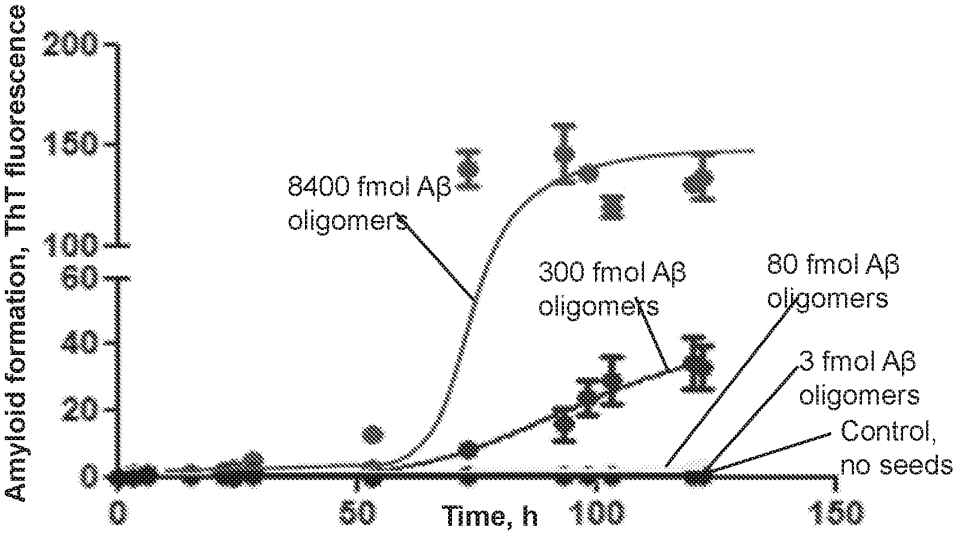


FIG. 2A

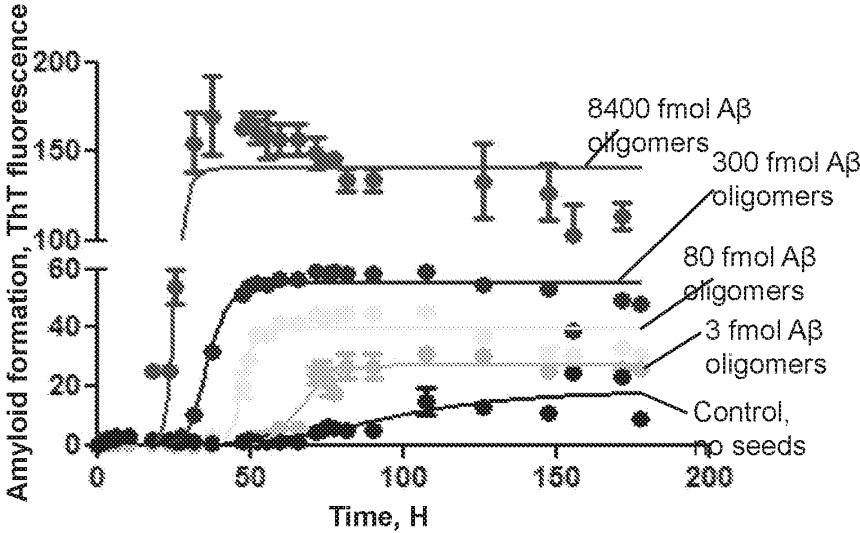


FIG. 2B

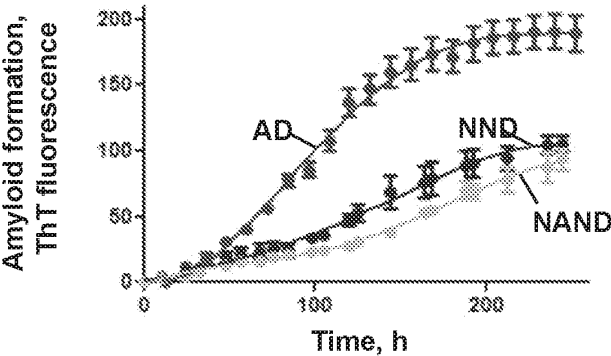


FIG. 3A

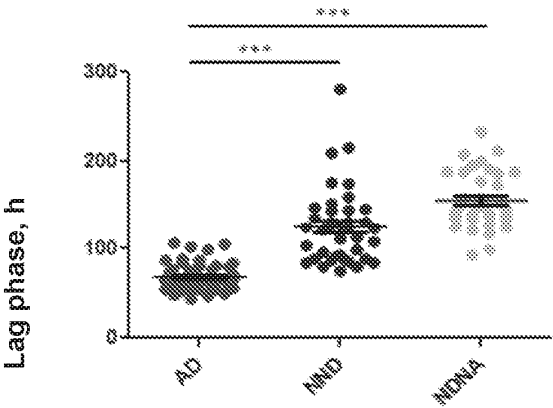


FIG. 3B

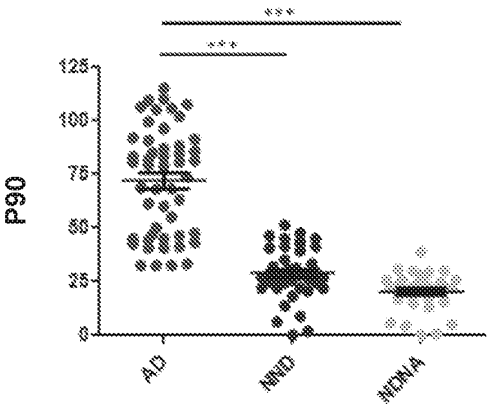


FIG. 3C

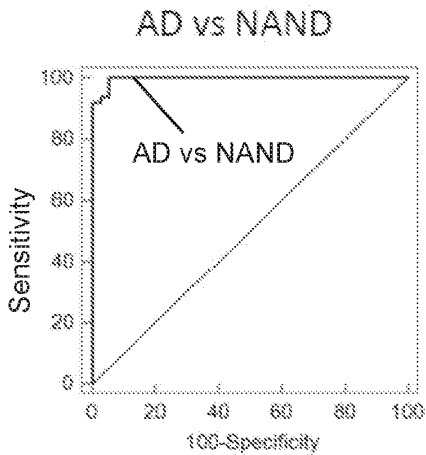


FIG. 4A

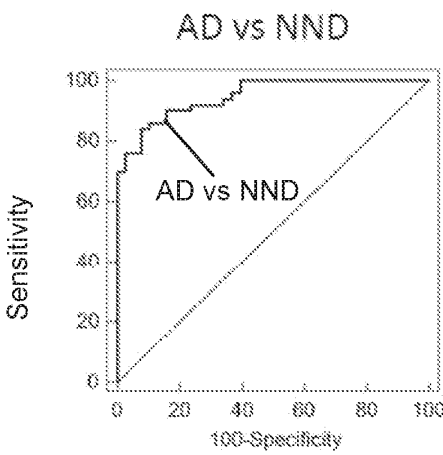


FIG. 4B

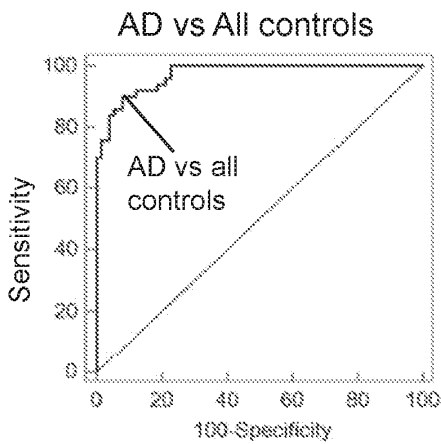


FIG. 4C

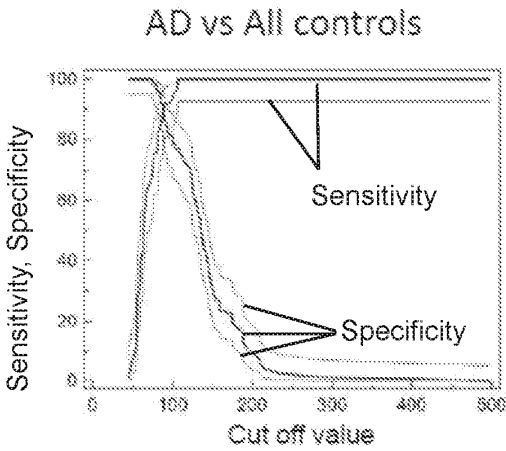


FIG. 4D

FIGS. 4A-D

Table 1: Estimation of sensitivity, specificity, and predictive value for Aβ-PCMA in CSF¹

GROUPS	SENSITIVITY ²	SPECIFICITY ²	POSITIVE PREDICTIVE VALUE ²	NEGATIVE PREDICTIVE VALUE ²
AD vs NAND	100.0%	94.6%	96.2%	100.0%
AD vs NND	90.0%	84.2%	88.2%	86.5%
AD vs controls ³	90.0%	92.0%	88.2%	93.2%

1. For estimation of sensitivity, specificity and predictive value the results of the lag phase as shown in FIG. 9B were used. Cutoffs were estimated by Receiver Operating Characteristics (ROC) curve analysis using the MedCalc software.
2. Sensitivity was estimated by the formula: $[\text{True positives}/(\text{True positives} + \text{False negatives})] \times 100$; specificity was estimated by the formula: $[\text{True negatives}/(\text{False positives} + \text{True negatives})] \times 100$; positive predictive value was estimated by the formula: $[\text{True positives}/(\text{True positives} + \text{False positives})] \times 100$; negative predictive value was estimated by the formula: $[\text{True negatives}/(\text{True negatives} + \text{False negatives})] \times 100$
3. Controls refers to the samples from NND plus NAND.

FIG. 5

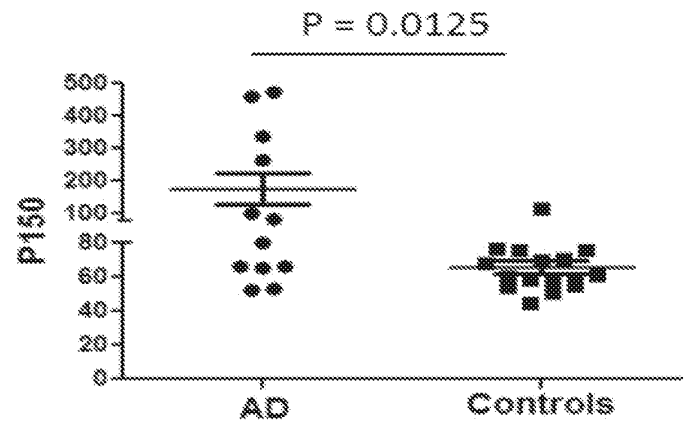


FIG. 6

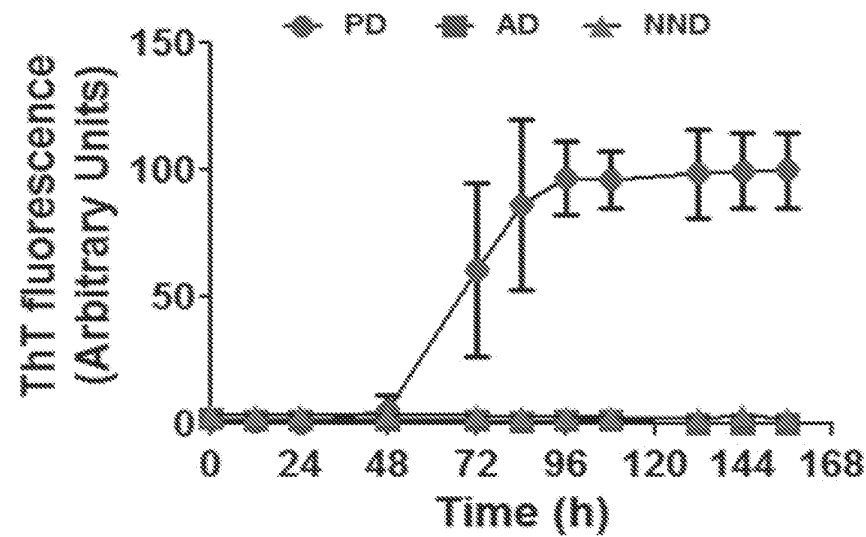


FIG. 14

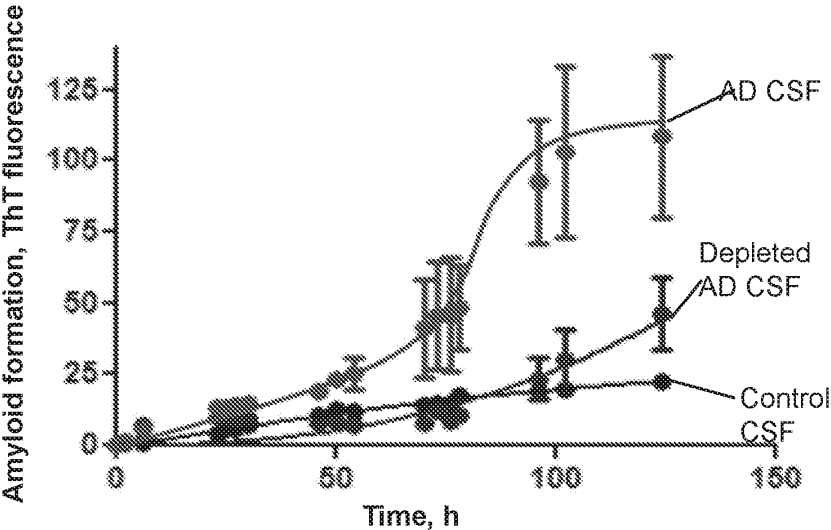


FIG. 7B

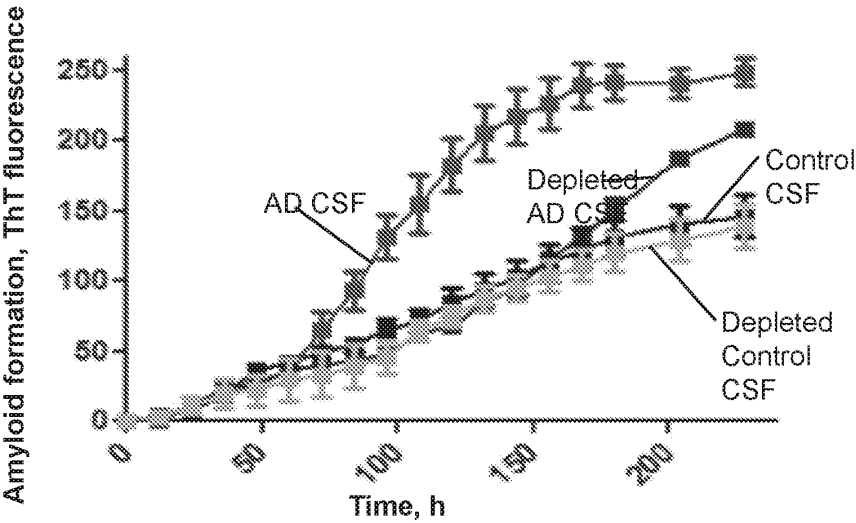


FIG. 7C

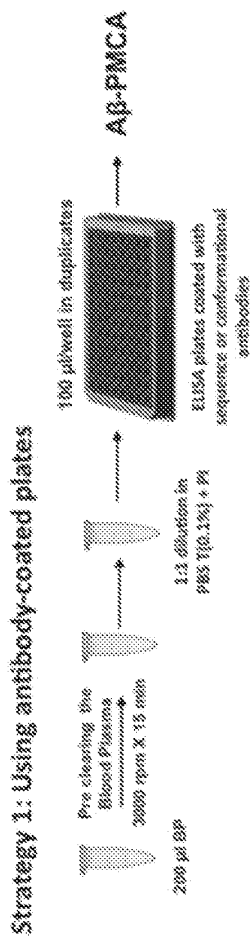


FIG. 8A

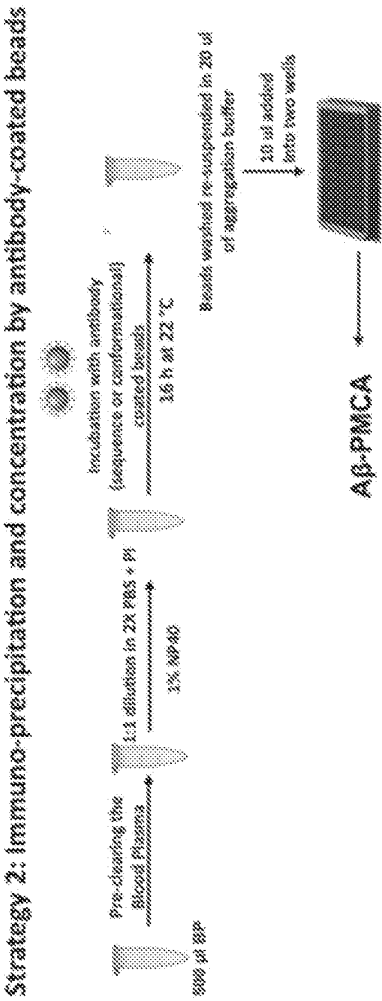


FIG. 8B

Table 2

<div><div>82E1</div><div>DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA</div><div>8E10</div></div> <div><div>4G8</div><div></div><div>X-40/42</div></div>			
Antibody	Epitope	Commercial source	Aβ oligomer capturing capacity
82E1	1-5	IBL America	+++
4G8	18-22	Covance	+
6E10	3-8	Covance	++
X-40/42	C-terminal	Mybiosource	-
16 ADV Mouse IgG1	Conformational	Acumen	++
All	Conformational	Invitrogen	-

+++ Best
++ very good
+ good
- no result

FIG. 9

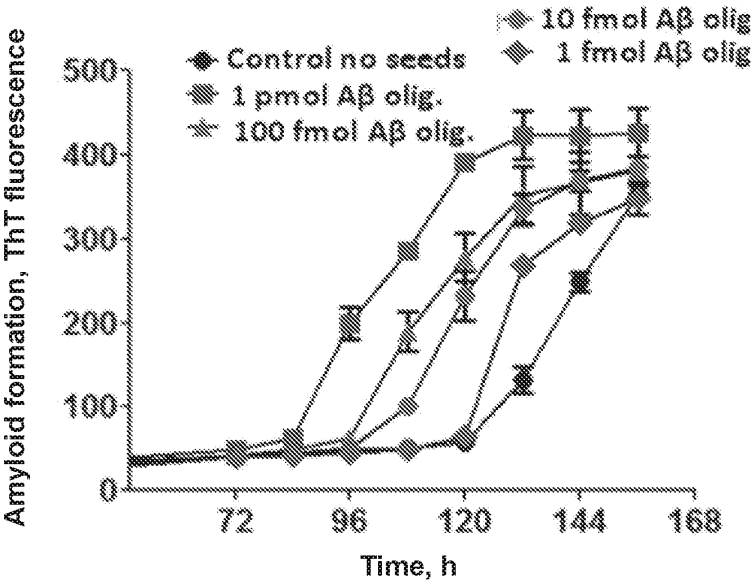


FIG. 10

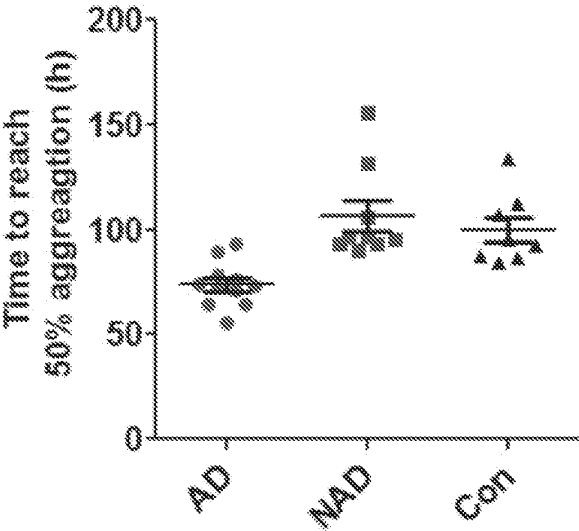


FIG. 11

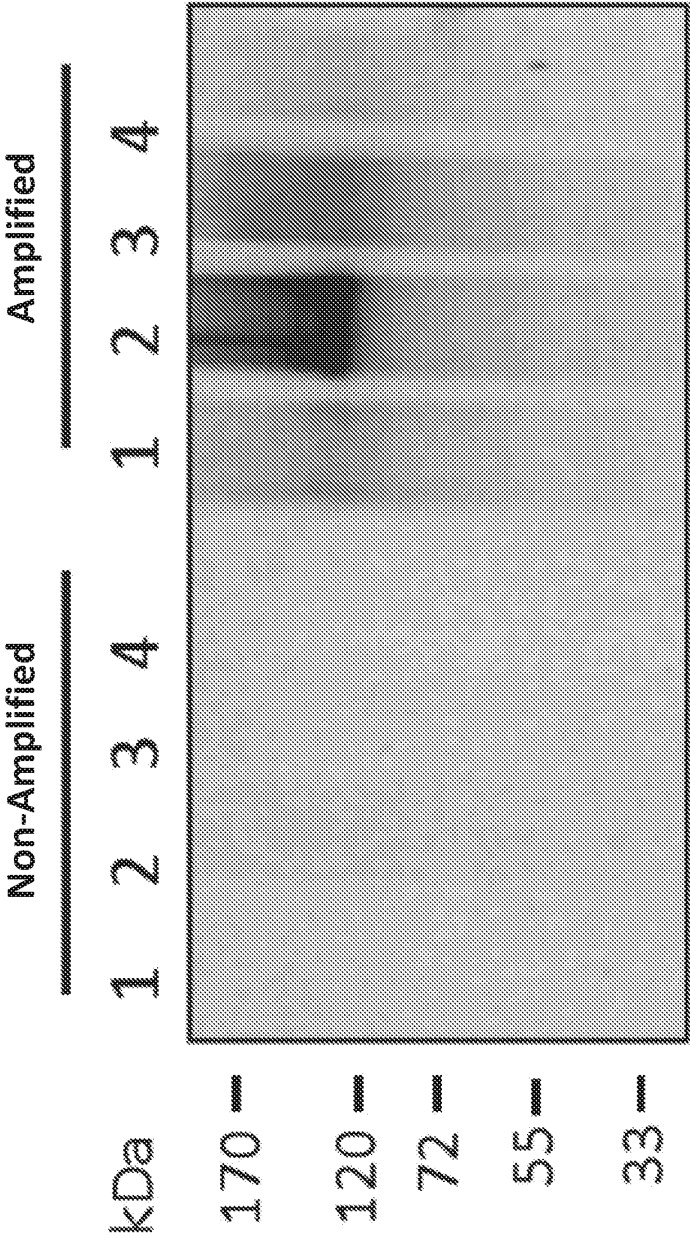


FIG. 12

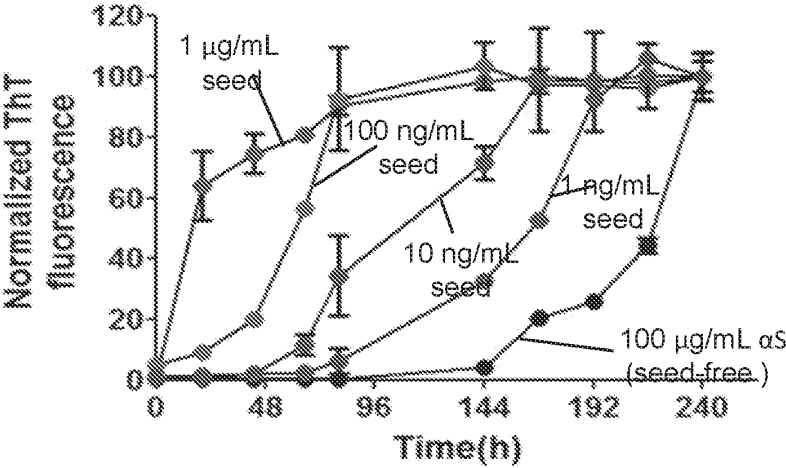


FIG. 13A

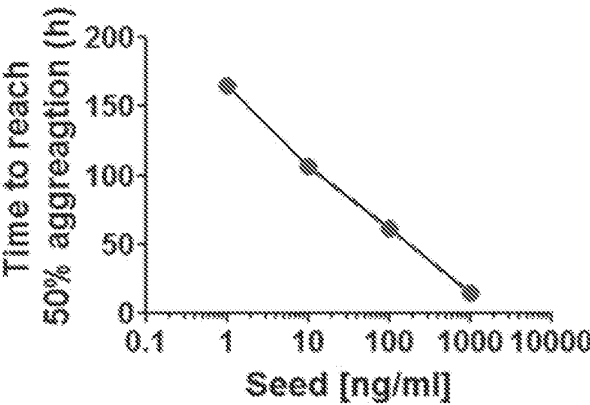


FIG. 13B

Table 3

Antibodies (Company)	Epitope	Alpha-Synuclein oligomer capturing capacity
Alpha/beta-Synuclein Antibody N-19 (Santa Cruz Biotechnology)	N-terminal	+++
Alpha-Synuclein Antibody C-20-R (Santa Cruz Biotechnology)	C-terminal	+++
Alpha-Synuclein Antibody 211 (Santa Cruz Biotechnology)	Amino acids 121-125	++
Alpha-synuclein Antibody Syn-204 (Santa Cruz Biotechnology)	Fragment 1-130	+
16 ADV Mouse IgG1 (Acumen)	Conformational	-

+++ *Best*
 ++ *very good*
 + *good*
 - *no result*

FIG. 15



Using antibody-coated beads

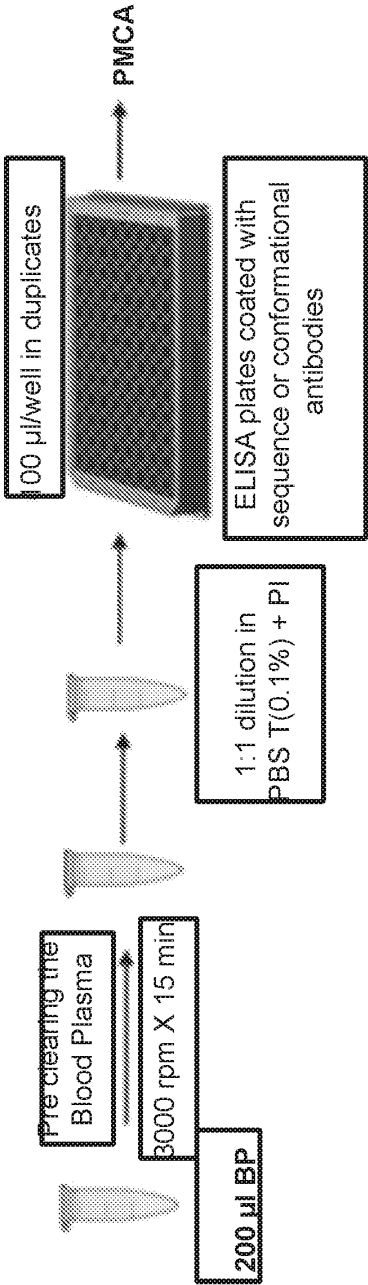
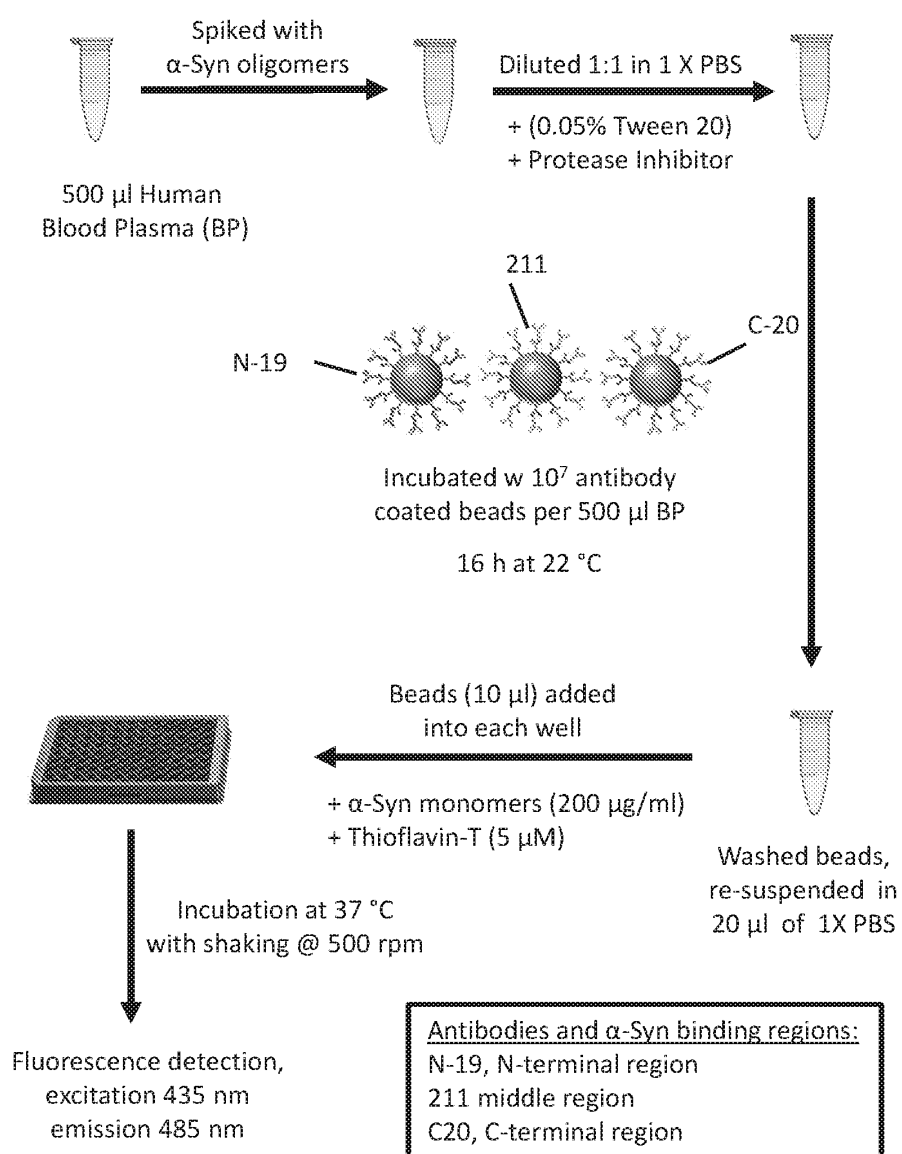


FIG. 16A

Detection of α -Synuclein oligomers spiked in human blood plasma**FIG. 16B**

Immunoprecipitation with N-19 antibody

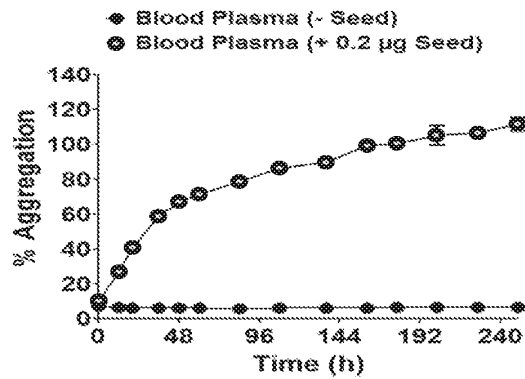


FIG. 17A

Immunoprecipitation with 211 antibody

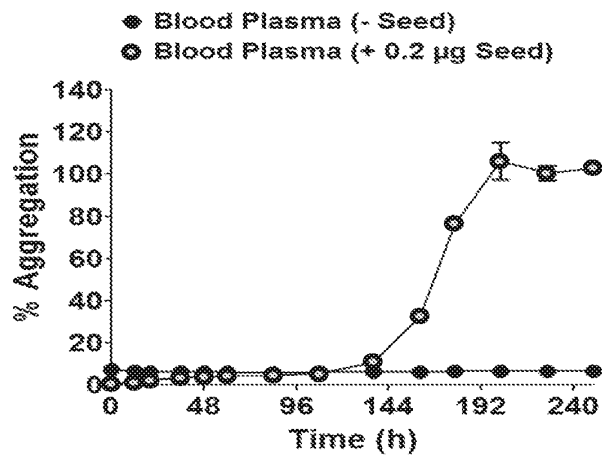


FIG. 17B

Immunoprecipitation with C-20 antibody

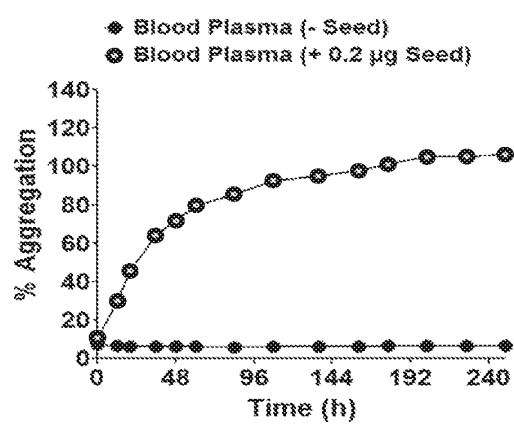


FIG. 17C

Healthy Control

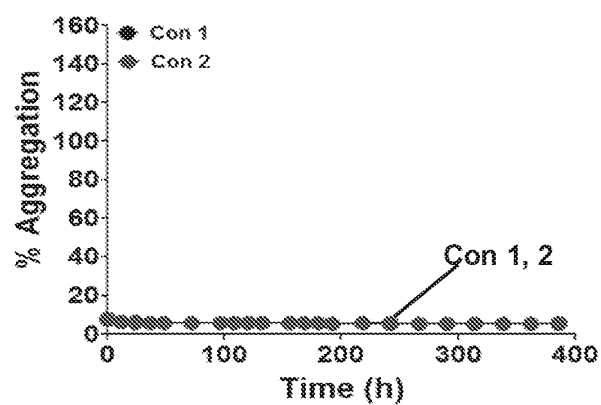


FIG. 18A

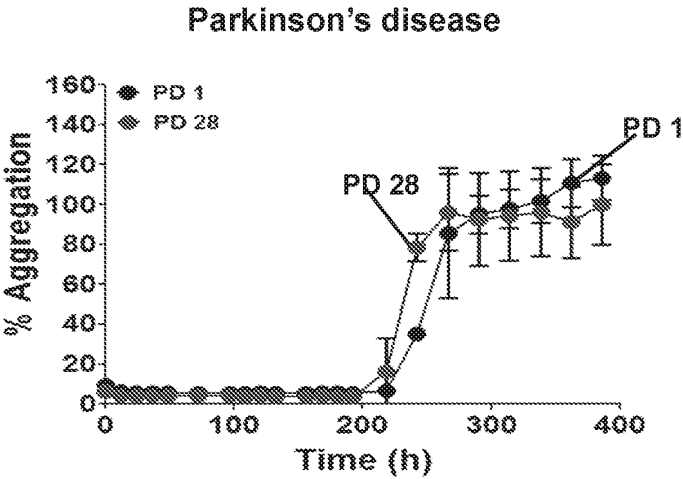


FIG. 18B

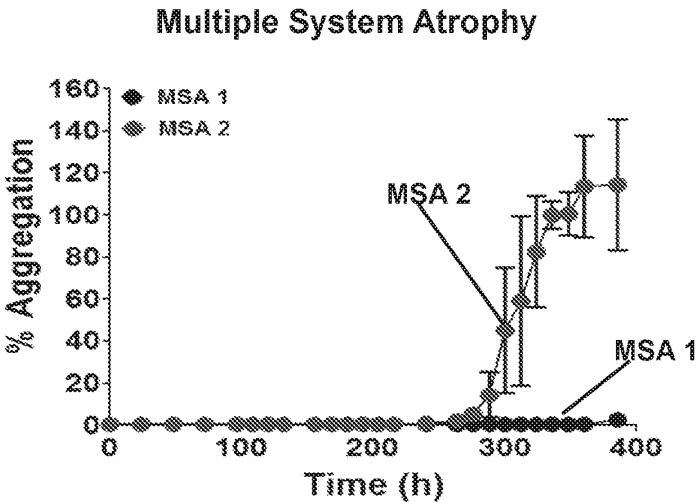


FIG. 18C

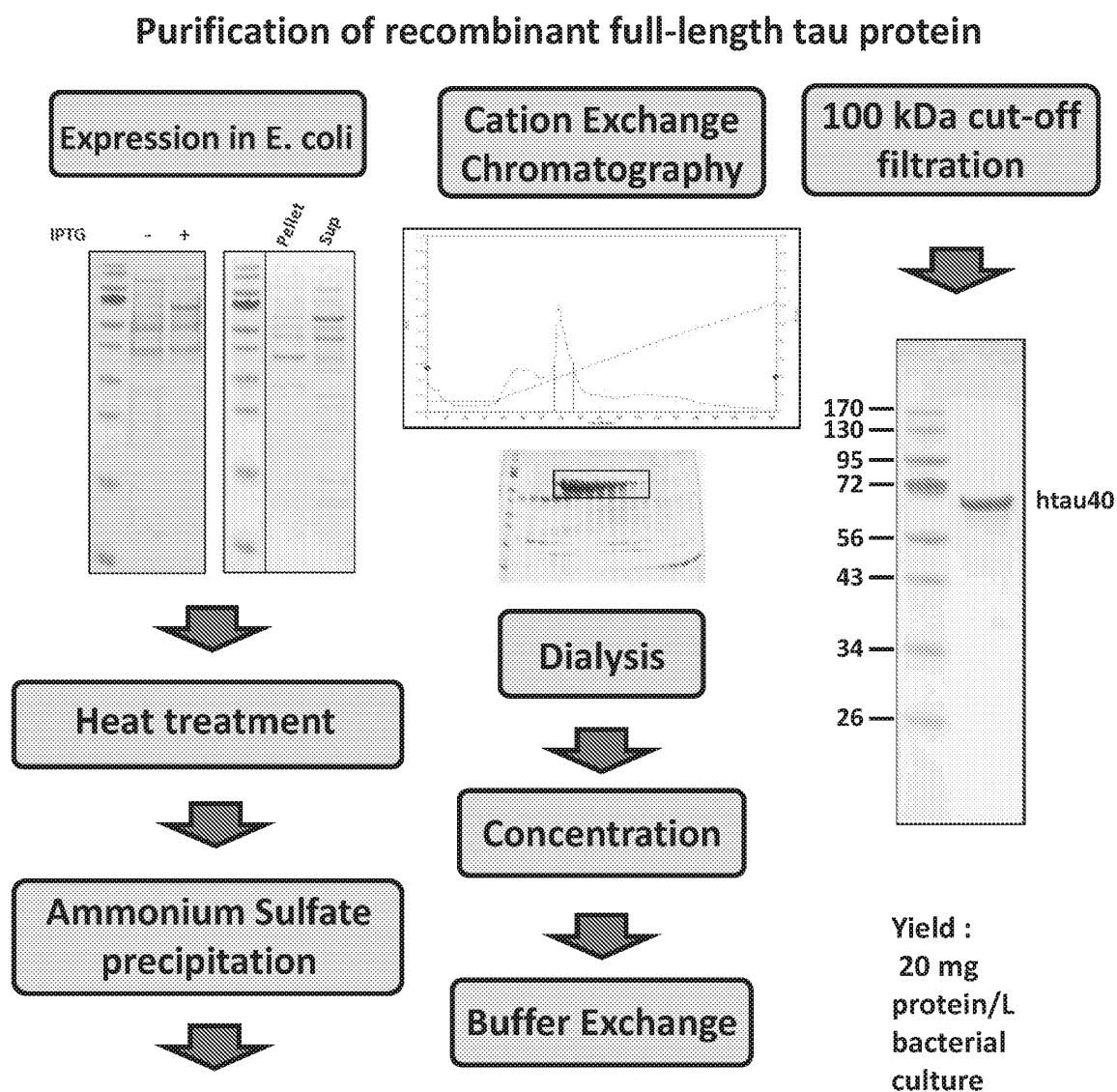


FIG. 19

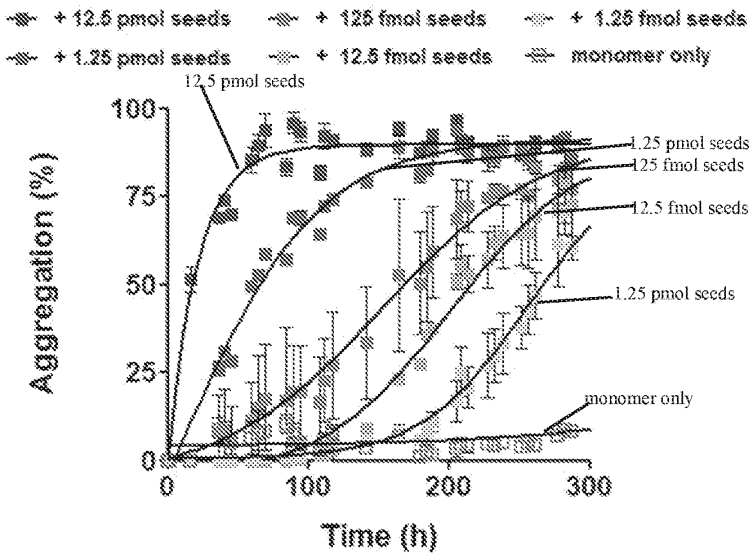


FIG. 20A

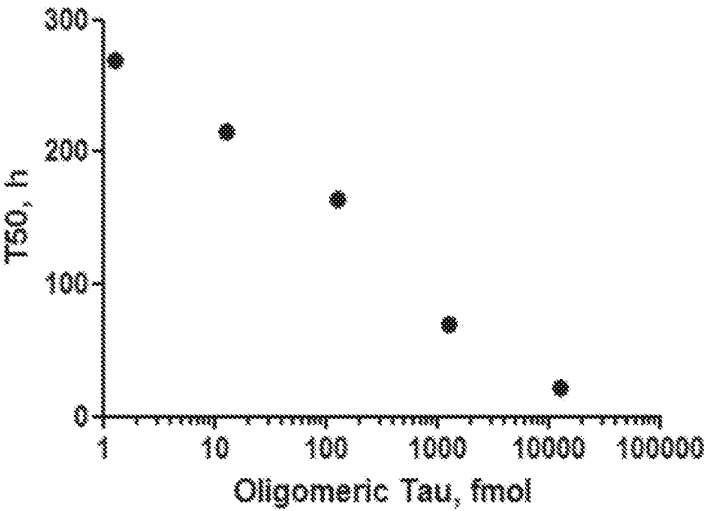


FIG. 20B

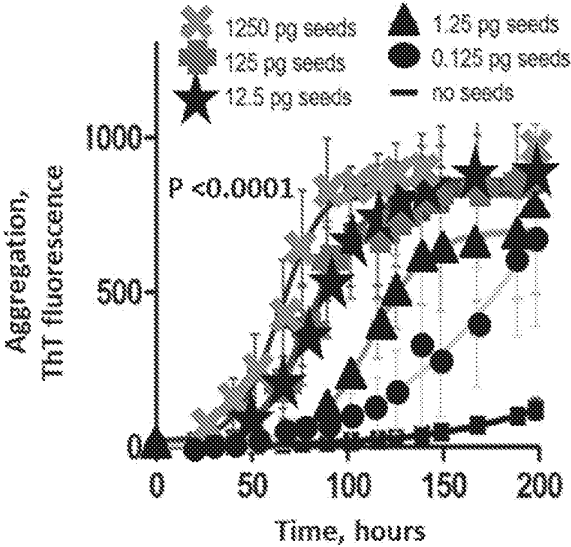


FIG. 20C

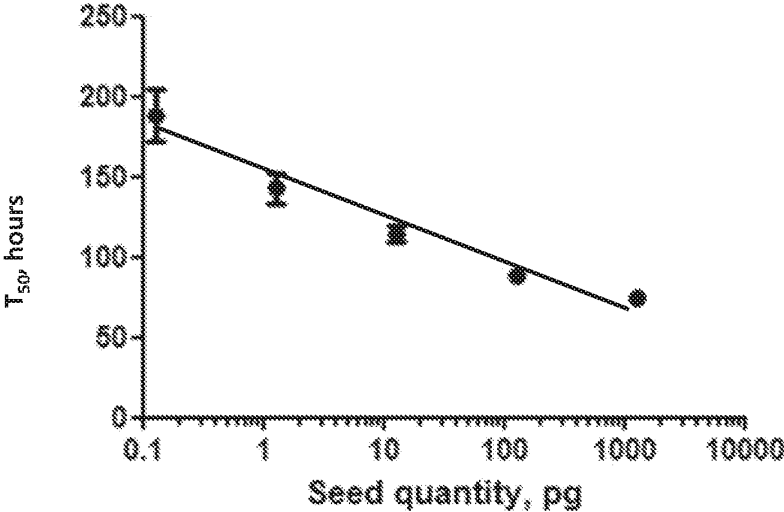
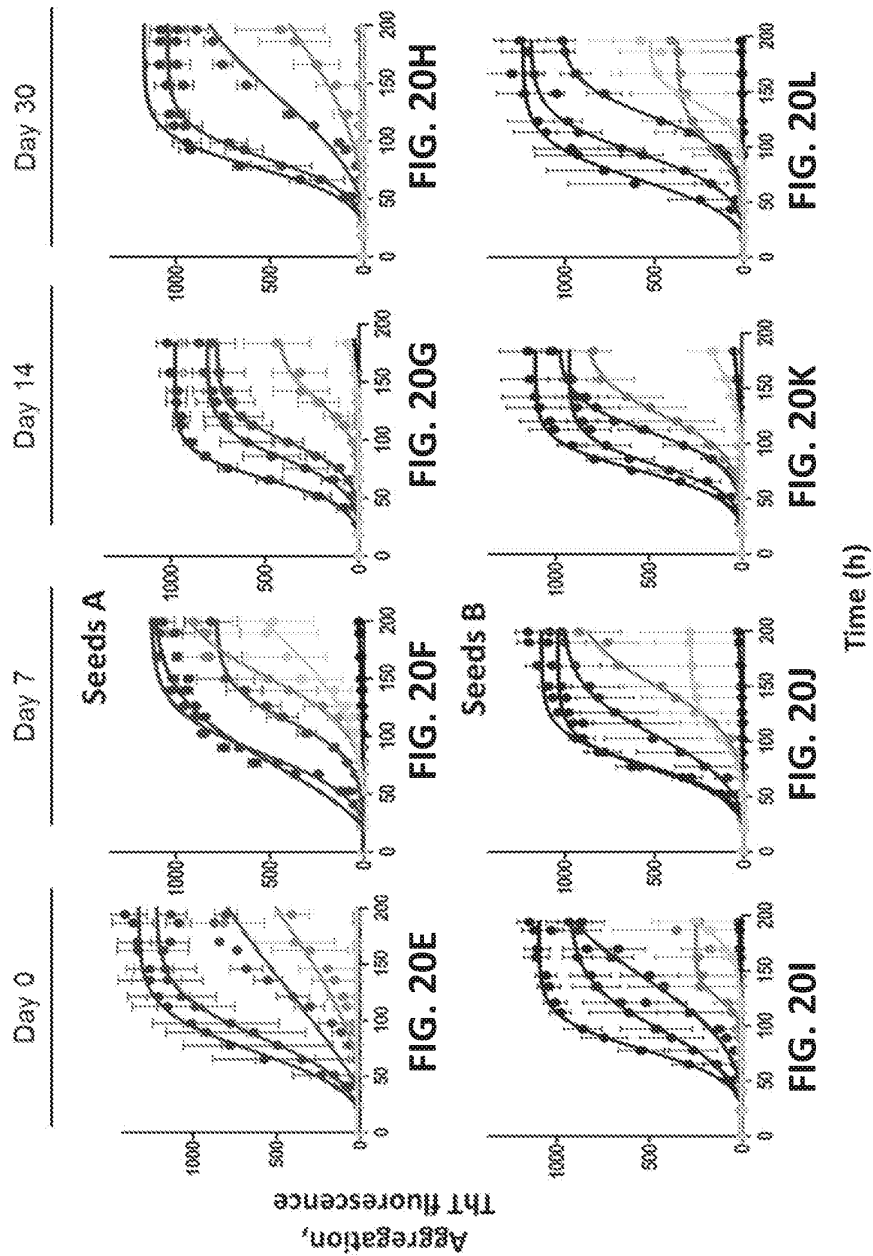


FIG. 20D



$T_{50} \pm \text{s.e.m. (h)}$						
Days	Seeds A		Seeds B		Average	P Value (ns)
	Undiluted standard	Diluted standard	Undiluted standard	Diluted standard		
Day 0	65 ± 5	78 ± 3	72 ± 6	65 ± 3	70 ± 3.1	0.19
Day 7	69 ± 3	74 ± 2	74 ± 4	74 ± 8	72 ± 1.2	0.84
Day 14	63 ± 4	75 ± 3	69 ± 3	63 ± 1	68 ± 2.9	0.06
Day 30	74 ± 2	70 ± 7	88 ± 4	77 ± 3	77 ± 3.9	0.09
Average	67 ± 2.6	74 ± 1.6	75 ± 4.2	70 ± 3.4	71.5 ± 1.8	
P value (ns)	0.14	0.62	0.08	0.16		0.26

FIG. 20M

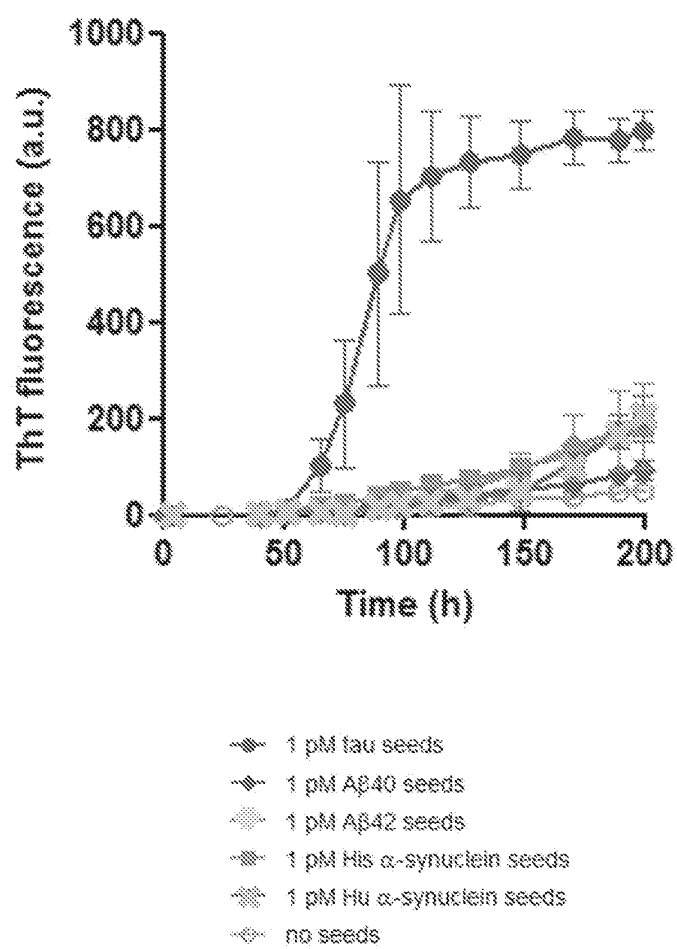


FIG. 20N

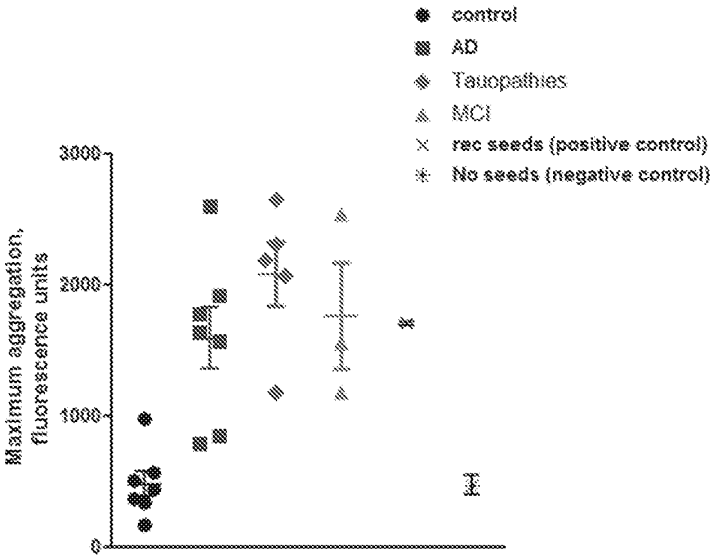


FIG. 21A

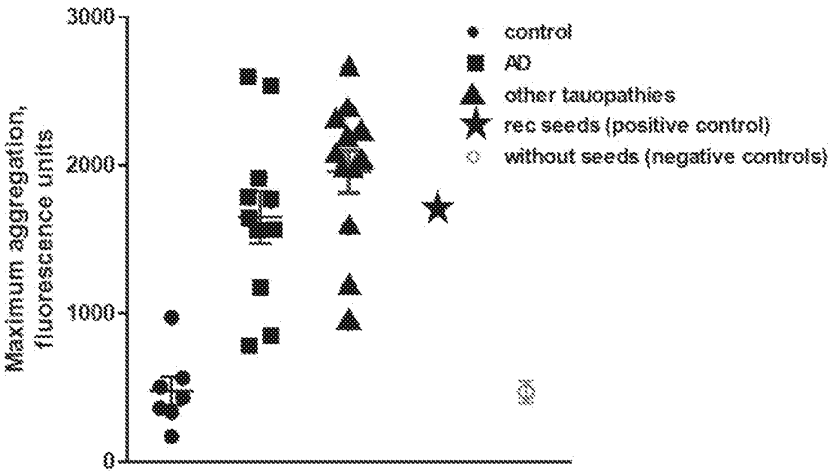


FIG. 21B

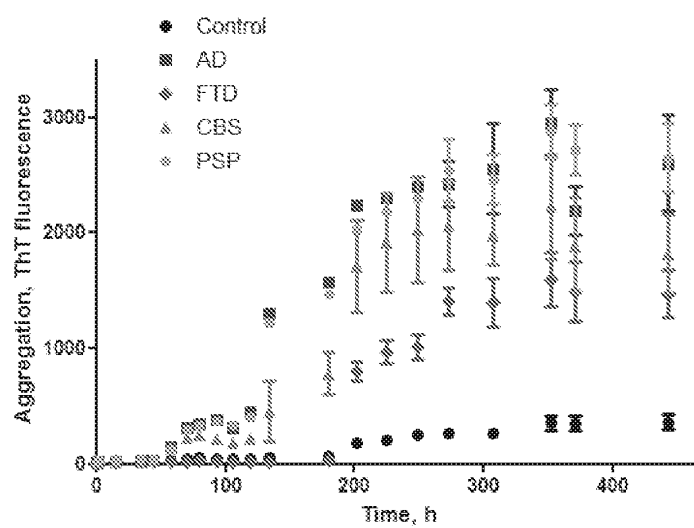


FIG. 22