

FIG. 1

Program : CLUSTALW

http://npsa-pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=/NPSA/npsa_clustalw.html

Tau Isoform

	10	20	30	40	50	60	
3RON (Seq. ID:6)	MAEPRQEF	EVME	DHAGTYGL	GDRKDQ	GGYTMH	QDQEGD	TDAGLK----- 44
3R1N (Seq. ID:5)	MAEPRQEF	EVME	DHAGTYGL	GDRKDQ	GGYTMH	QDQEGD	TDAGLKESPLQTPTE
3R2N (Seq. ID:4)	MAEPRQEF	EVME	DHAGTYGL	GDRKDQ	GGYTMH	QDQEGD	TDAGLKESPLQTPTE
4RON (Seq. ID:3)	MAEPRQEF	EVME	DHAGTYGL	GDRKDQ	GGYTMH	QDQEGD	TDAGLK----- 44
4R1N (Seq. ID:2)	MAEPRQEF	EVME	DHAGTYGL	GDRKDQ	GGYTMH	QDQEGD	TDAGLKESPLQTPTE
4R2N (Seq. ID:1)	MAEPRQEF	EVME	DHAGTYGL	GDRKDQ	GGYTMH	QDQEGD	TDAGLKESPLQTPTE

Prim. cons. MAEPRQEF EVME DHAGTYGL GDRKDQ GGYTMH QDQEGD TDAGLKESPLQTPTE DGSEEPG

	70	80	90	100	110	120	
3RON (Seq. ID:6)	-----	-----	-----	-----	AEEAGIGD	TPSLEDEAAG 62	
3R1N (Seq. ID:5)	SETSDAKSTPTAE-----	-----	-----	-----	AEEAGIGD	TPSLEDEAAG 91	
3R2N (Seq. ID:4)	SETSDAKSTPTAE	DVTAPLV	DEGAPGK	QAAAPHTEI	PEGTTAEE	AGIGDTPSLEDEAAG 120	
4RON (Seq. ID:3)	-----	-----	-----	-----	AEEAGIGD	TPSLEDEAAG 62	
4R1N (Seq. ID:2)	SETSDAKSTPTAE-----	-----	-----	-----	AEEAGIGD	TPSLEDEAAG 91	
4R2N (Seq. ID:1)	SETSDAKSTPTAE	DVTAPLV	DEGAPGK	QAAAPHTEI	PEGTTAEE	AGIGDTPSLEDEAAG 120	

Prim. cons. SETSDAKSTPTAE DVTAPLV DEGAPGK QAAAPHTEI PEGTTAEE AGIGDTPSLEDEAAG

	130	140	150	160	170	180	
3RON (Seq. ID:6)	HVTQARMV	SKSKDGT	GSDDKKA	KAGADGK	TKIATPR	GAAAPP	GQKGQANATRIPAKTTPPAPK 122
3R1N (Seq. ID:5)	HVTQARMV	SKSKDGT	GSDDKKA	KAGADGK	TKIATPR	GAAAPP	GQKGQANATRIPAKTTPPAPK 151
3R2N (Seq. ID:4)	HVTQARMV	SKSKDGT	GSDDKKA	KAGADGK	TKIATPR	GAAAPP	GQKGQANATRIPAKTTPPAPK 180
4RON (Seq. ID:3)	HVTQARMV	SKSKDGT	GSDDKKA	KAGADGK	TKIATPR	GAAAPP	GQKGQANATRIPAKTTPPAPK 122
4R1N (Seq. ID:2)	HVTQARMV	SKSKDGT	GSDDKKA	KAGADGK	TKIATPR	GAAAPP	GQKGQANATRIPAKTTPPAPK 151
4R2N (Seq. ID:1)	HVTQARMV	SKSKDGT	GSDDKKA	KAGADGK	TKIATPR	GAAAPP	GQKGQANATRIPAKTTPPAPK 180

Prim. cons. HVTQARMV SKSKDGT GSDDKKA KAGADGK TKIATPR GAAAPP GQKGQANATRIPAKTTPPAPK

	190	200	210	220	230	240	
3RON (Seq. ID:6)	TPPSSGE	PPKSGDR	SGYSSPG	SPGTPG	SRSRTP	SLPTPT	TREPKKVAVVRTPPKSPSSAK 182
3R1N (Seq. ID:5)	TPPSSGE	PPKSGDR	SGYSSPG	SPGTPG	SRSRTP	SLPTPT	TREPKKVAVVRTPPKSPSSAK 211
3R2N (Seq. ID:4)	TPPSSGE	PPKSGDR	SGYSSPG	SPGTPG	SRSRTP	SLPTPT	TREPKKVAVVRTPPKSPSSAK 240
4RON (Seq. ID:3)	TPPSSGE	PPKSGDR	SGYSSPG	SPGTPG	SRSRTP	SLPTPT	TREPKKVAVVRTPPKSPSSAK 182
4R1N (Seq. ID:2)	TPPSSGE	PPKSGDR	SGYSSPG	SPGTPG	SRSRTP	SLPTPT	TREPKKVAVVRTPPKSPSSAK 211
4R2N (Seq. ID:1)	TPPSSGE	PPKSGDR	SGYSSPG	SPGTPG	SRSRTP	SLPTPT	TREPKKVAVVRTPPKSPSSAK 240

Prim. cons. TPPSSGE PPKSGDR SGYSSPG SPGTPG SRSRTP SLPTPT TREPKKVAVVRTPPKSPSSAK

FIG. 2

	250	260	270	280	290	300	
3R0N (Seq. ID:6)	SRLQTAPVPM	DLKNVKS	IGSTENLKHQ	PGGGK	-----	216	
3R1N (Seq. ID:5)	SRLQTAPVPM	DLKNVKS	IGSTENLKHQ	PGGGK	-----	245	
3R2N (Seq. ID:4)	SRLQTAPVPM	DLKNVKS	IGSTENLKHQ	PGGGK	-----	274	
4R0N (Seq. ID:3)	SRLQTAPVPM	DLKNVKS	IGSTENLKHQ	PGGGKVQI	INKKLDLSNVQSKCGSKDNI	242	
4R1N (Seq. ID:2)	SRLQTAPVPM	DLKNVKS	IGSTENLKHQ	PGGGKVQI	INKKLDLSNVQSKCGSKDNI	271	
4R2N (Seq. ID:1)	SRLQTAPVPM	DLKNVKS	IGSTENLKHQ	PGGGKVQI	INKKLDLSNVQSKCGSKDNI	300	

Prim. cons.	SRLQTAPVPM						DLKNVKSIGSTENLKHQPGGGKVQIINKKLDLSNVQSKCGSKDNI
	310	320	330	340	350	360	
3R0N (Seq. ID:6)	-----VQIVYK	PVDLSKVT	SKCGSLGNI	HHKPGGGQ	VEVKSEKLD	FKDRVQSKIGSLDNI	271
3R1N (Seq. ID:5)	-----VQIVYK	PVDLSKVT	SKCGSLGNI	HHKPGGGQ	VEVKSEKLD	FKDRVQSKIGSLDNI	300
3R2N (Seq. ID:4)	-----VQIVYK	PVDLSKVT	SKCGSLGNI	HHKPGGGQ	VEVKSEKLD	FKDRVQSKIGSLDNI	329
4R0N (Seq. ID:3)	PGGGSVQIVYK	PVDLSKVT	SKCGSLGNI	HHKPGGGQ	VEVKSEKLD	FKDRVQSKIGSLDNI	302
4R1N (Seq. ID:2)	PGGGSVQIVYK	PVDLSKVT	SKCGSLGNI	HHKPGGGQ	VEVKSEKLD	FKDRVQSKIGSLDNI	331
4R2N (Seq. ID:1)	PGGGSVQIVYK	PVDLSKVT	SKCGSLGNI	HHKPGGGQ	VEVKSEKLD	FKDRVQSKIGSLDNI	360

Prim. cons.	PGGGSVQIVYK						PVDLSKVTSKCGSLGNIHHKPGGGQVEVKSEKLDFKDRVQSKIGSLDNI
	370	380	390	400	410	420	
3R0N (Seq. ID:6)	THVPGGGNKKI	ETHKLT	FRENAKA	KTDHGAEIVYK	SPVVS	SGDTS	SPRHLSNV
3R1N (Seq. ID:5)	THVPGGGNKKI	ETHKLT	FRENAKA	KTDHGAEIVYK	SPVVS	SGDTS	SPRHLSNV
3R2N (Seq. ID:4)	THVPGGGNKKI	ETHKLT	FRENAKA	KTDHGAEIVYK	SPVVS	SGDTS	SPRHLSNV
4R0N (Seq. ID:3)	THVPGGGNKKI	ETHKLT	FRENAKA	KTDHGAEIVYK	SPVVS	SGDTS	SPRHLSNV
4R1N (Seq. ID:2)	THVPGGGNKKI	ETHKLT	FRENAKA	KTDHGAEIVYK	SPVVS	SGDTS	SPRHLSNV
4R2N (Seq. ID:1)	THVPGGGNKKI	ETHKLT	FRENAKA	KTDHGAEIVYK	SPVVS	SGDTS	SPRHLSNV

Prim. cons.	THVPGGGNKKI						ETHKLTFRENAKA
	430	440					
3R0N (Seq. ID:1)	DSPQLATLA	DEV	SAS	LAKQGL	352		
3R1N (Seq. ID:1)	DSPQLATLA	DEV	SAS	LAKQGL	381		
3R2N (Seq. ID:1)	DSPQLATLA	DEV	SAS	LAKQGL	410		
4R0N (Seq. ID:1)	DSPQLATLA	DEV	SAS	LAKQGL	383		
4R1N (Seq. ID:1)	DSPQLATLA	DEV	SAS	LAKQGL	412		
4R2N (Seq. ID:1)	DSPQLATLA	DEV	SAS	LAKQGL	441		

Prim. cons.	DSPQLATLA				DEV	SAS	LAKQGL

FIG. 3

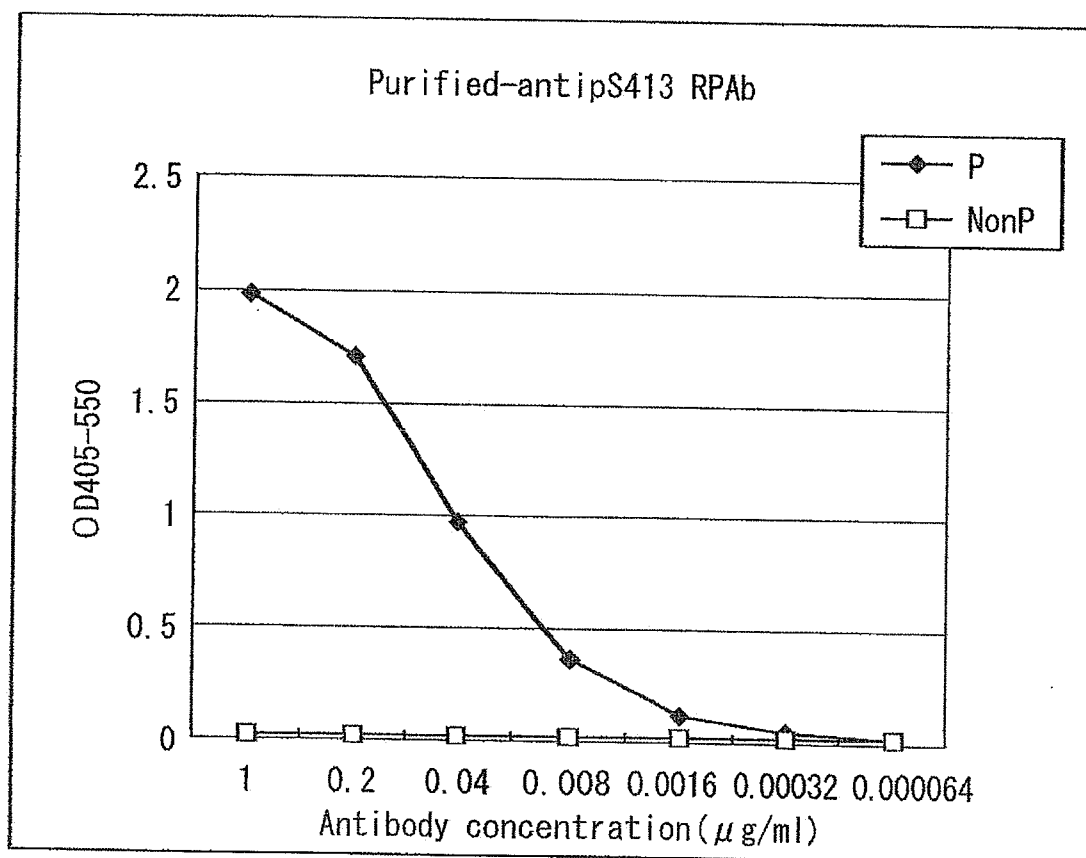
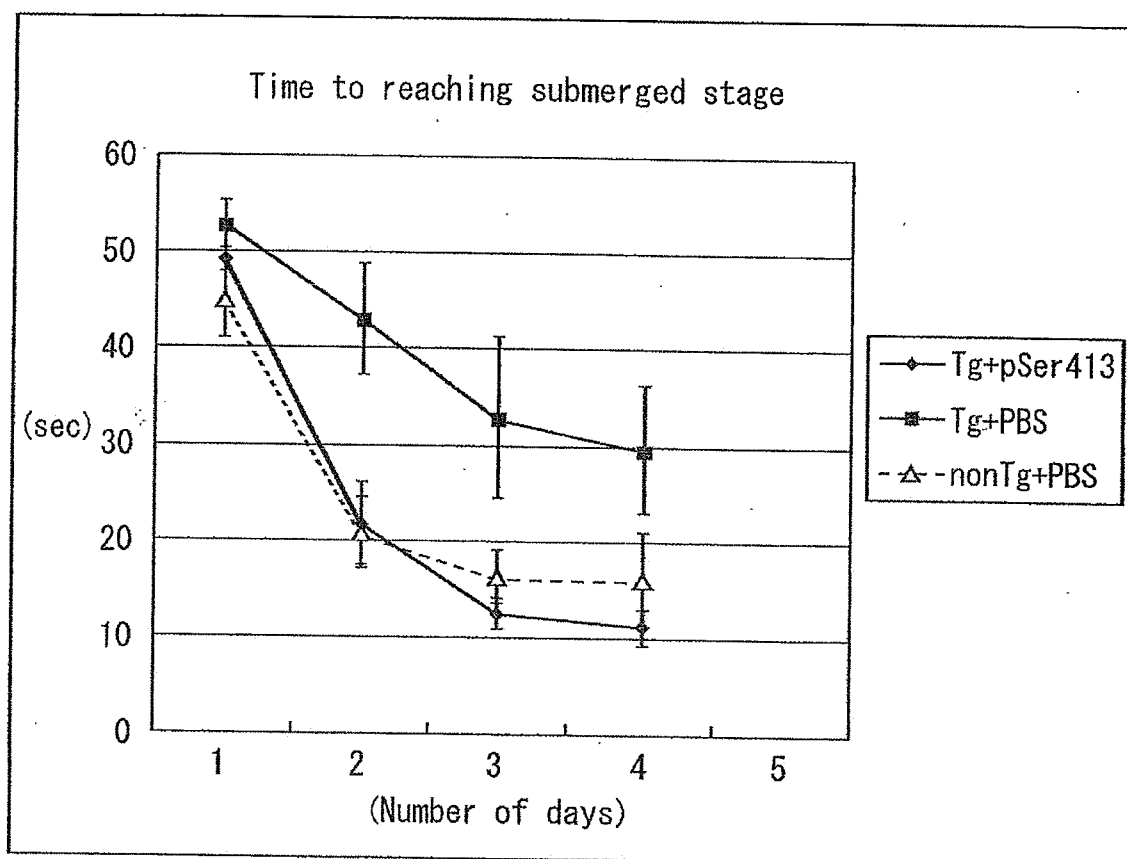


FIG. 4

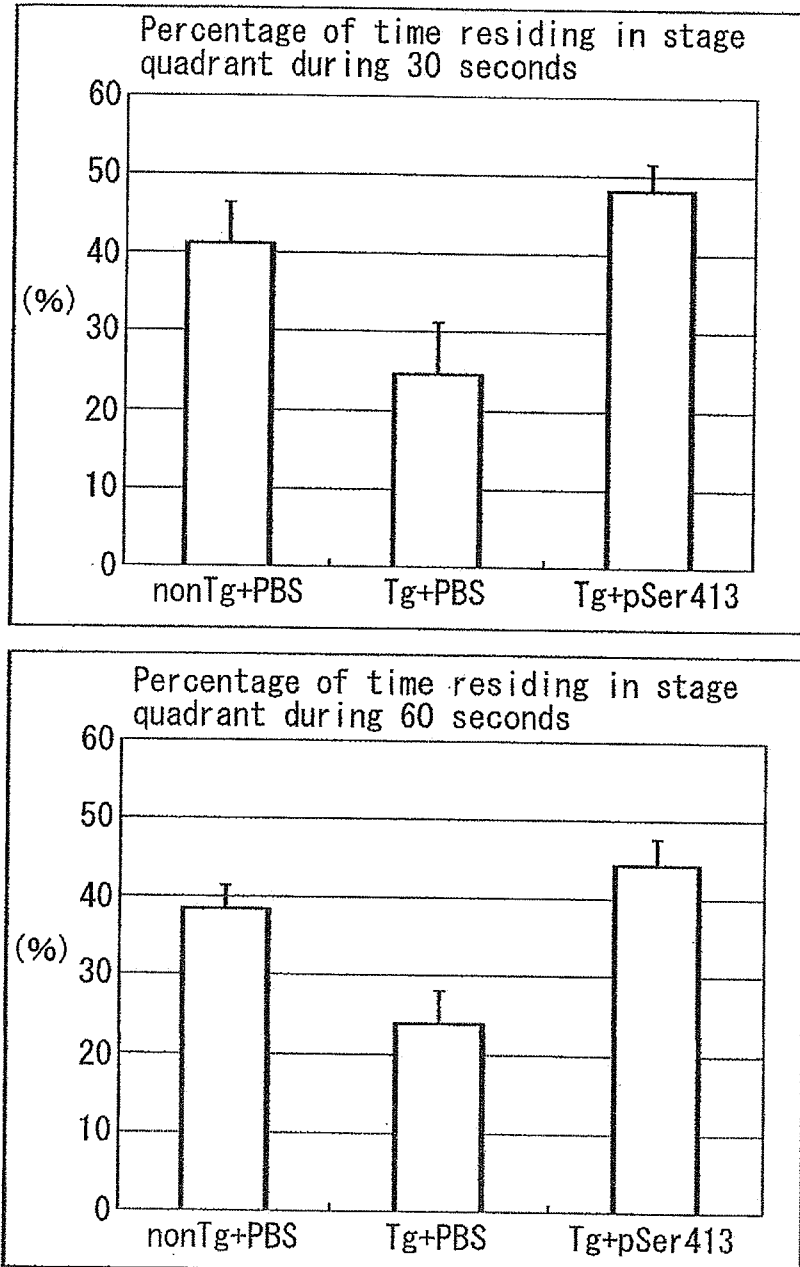
(1-1) Trial test



Significant difference
non Tg vs Tg : $p=0.0071$
Tg vs Immunized Tg : $p=0.0029$

FIG. 5

(1-2) Probe test



Significant difference

Fov 30-second analysis :

non Tg vs Tg : $p=0.0403$ Tg vs Immunized Tg : $p=0.00321$

Fov 60-second analysis :

non Tg vs Tg : $p=0.0085$ Tg vs Immunized Tg : $p=0.0003$

FIG. 6

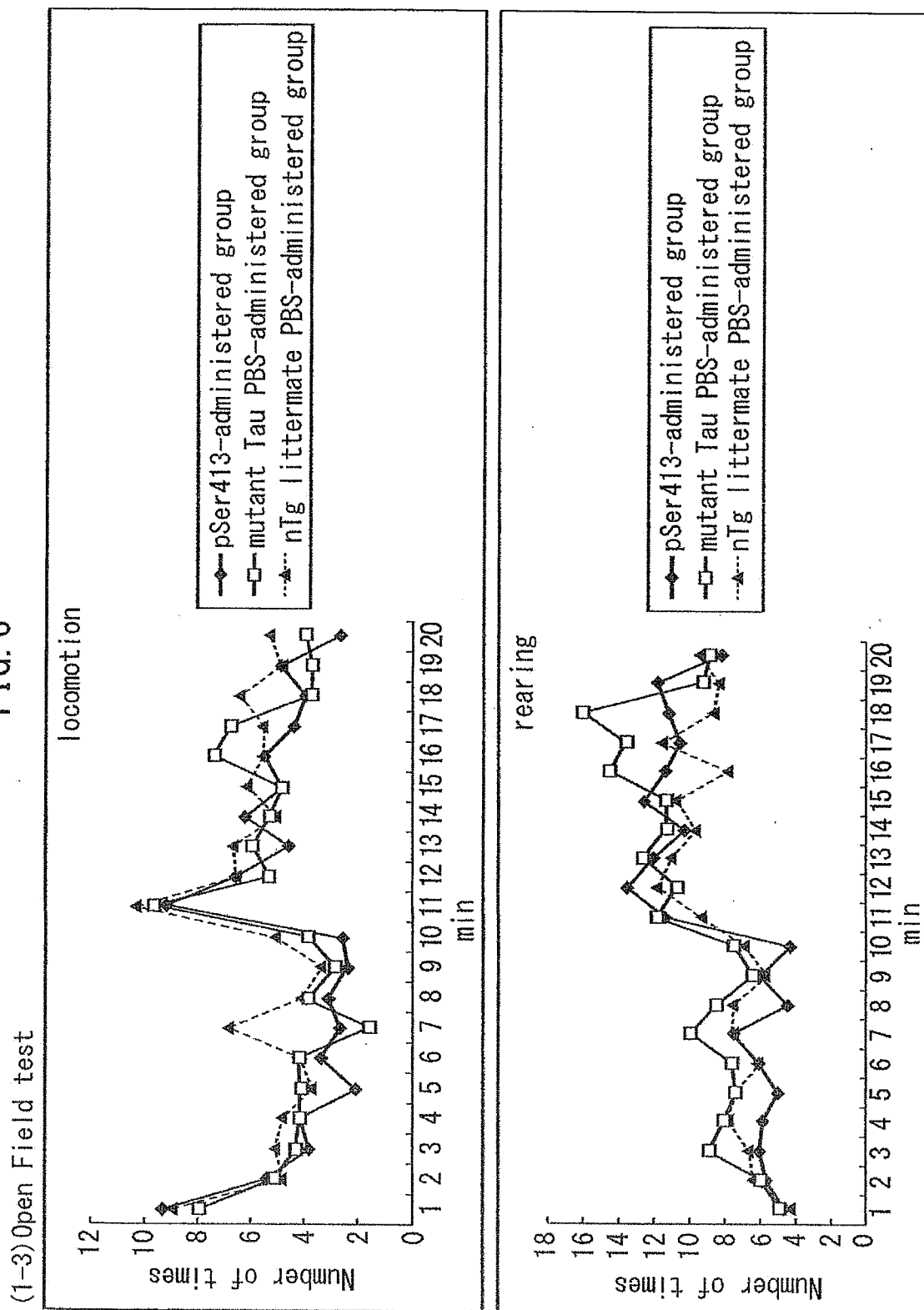


FIG. 7

(1-3) Open Field test

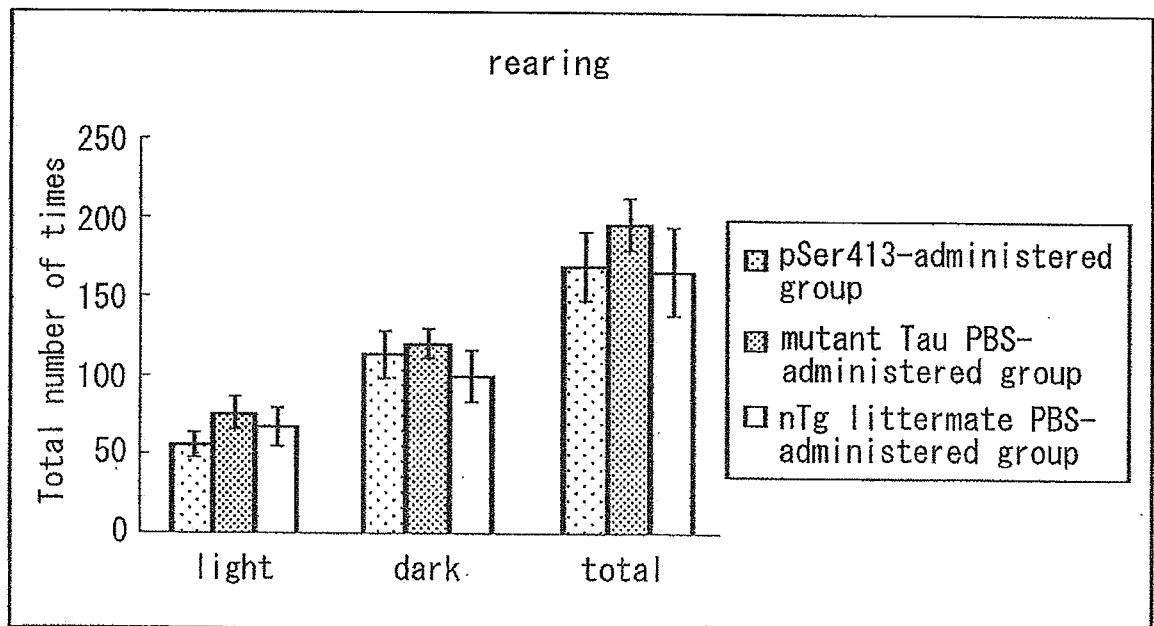
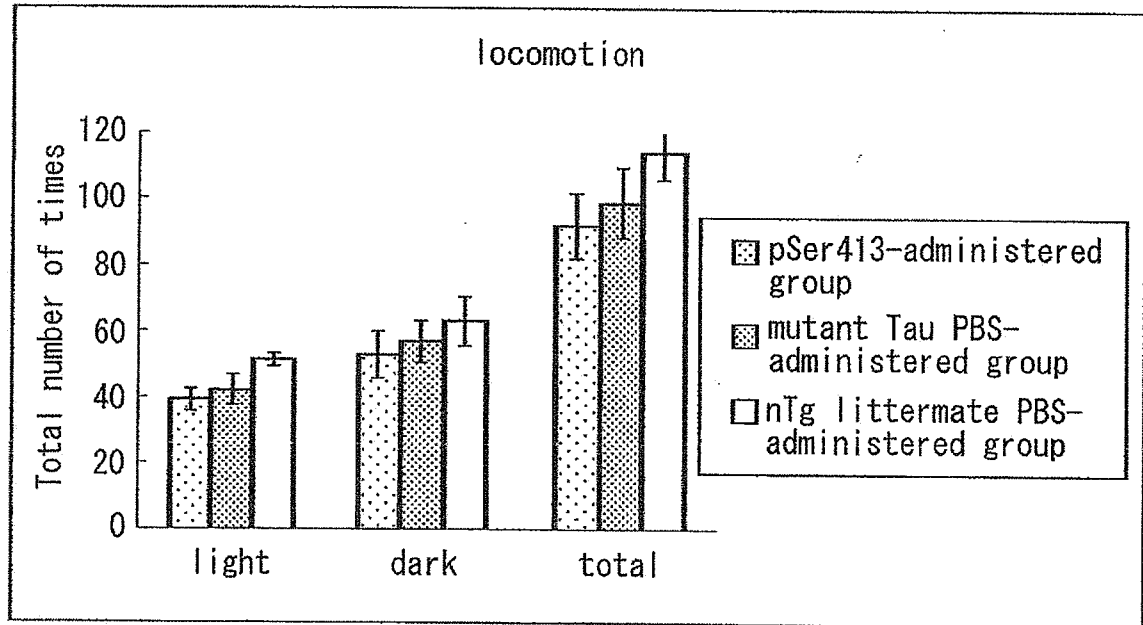
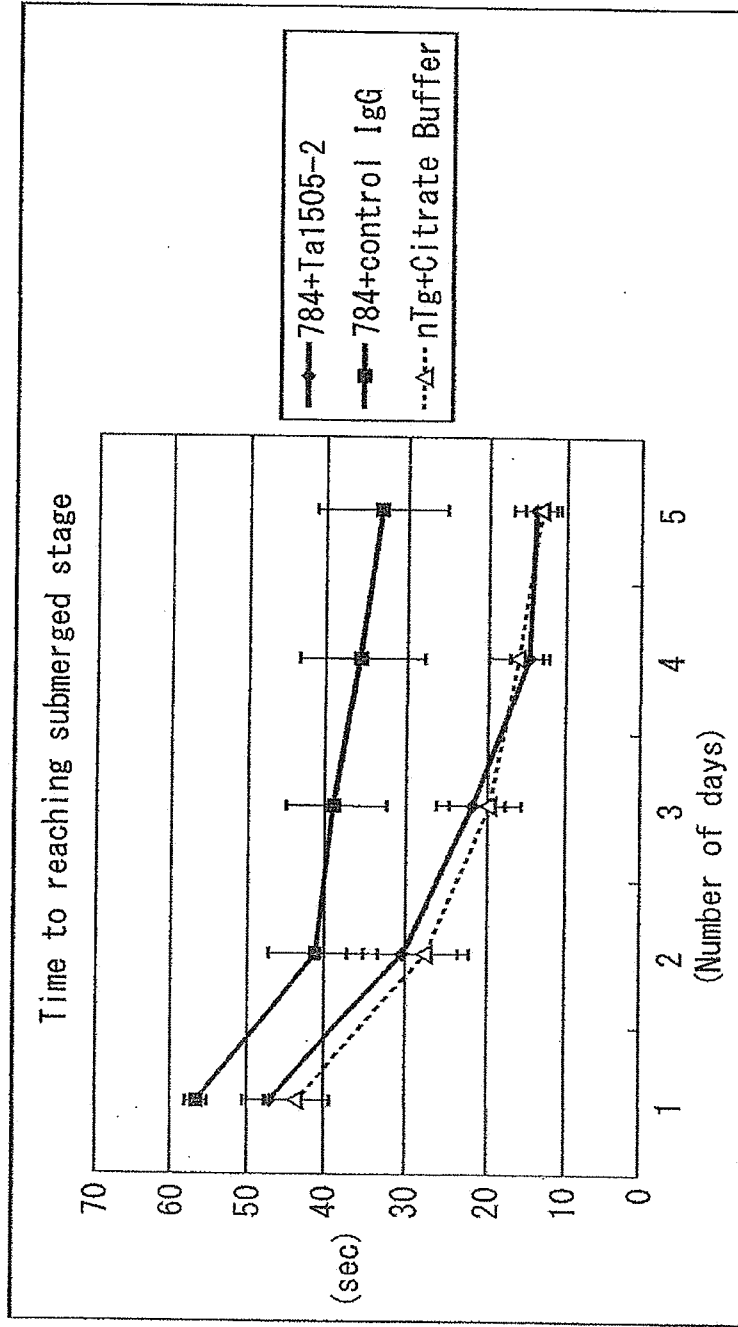


FIG. 8

(2-1) Trial test



Significant difference

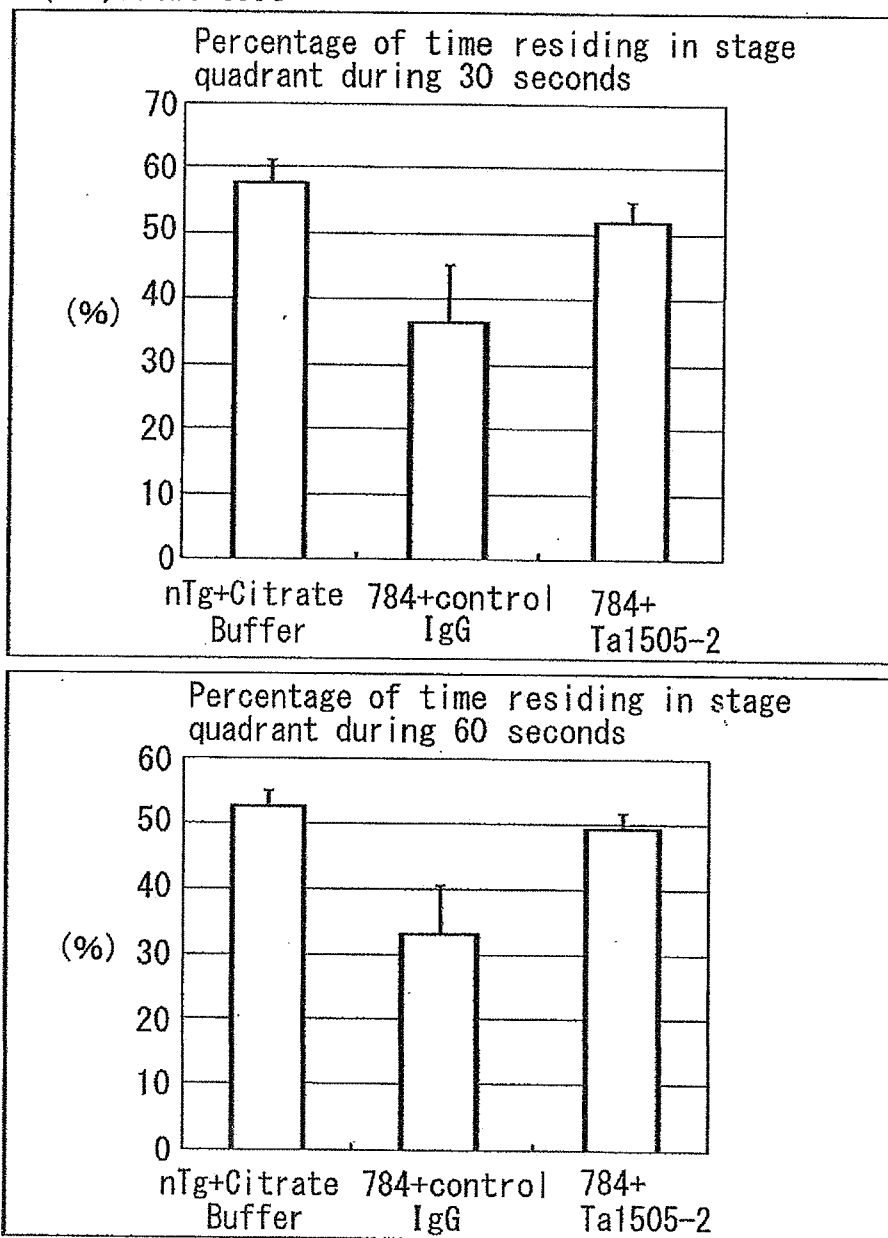
non Ig vs Ig(control IgG) : $p=0.0110$

non Ig vs Ig(Ta1505-2) : $p=0.8259$ (No significant difference)

Ig(Ta1505-2) vs Ig(control IgG) : $p=0.0152$

FIG. 9

(2-2) Probe test



Significant difference

Fov 30-second analysis :

non-Tg vs Tg(control IgG) : $p=0.0199$ non-Tg vs Tg(Ta1505-2) : $p=0.5106$ (No significant difference)Tg(Ta1505-2) vs. Tg(control IgG) : $p=0.0713$ (No significant difference)

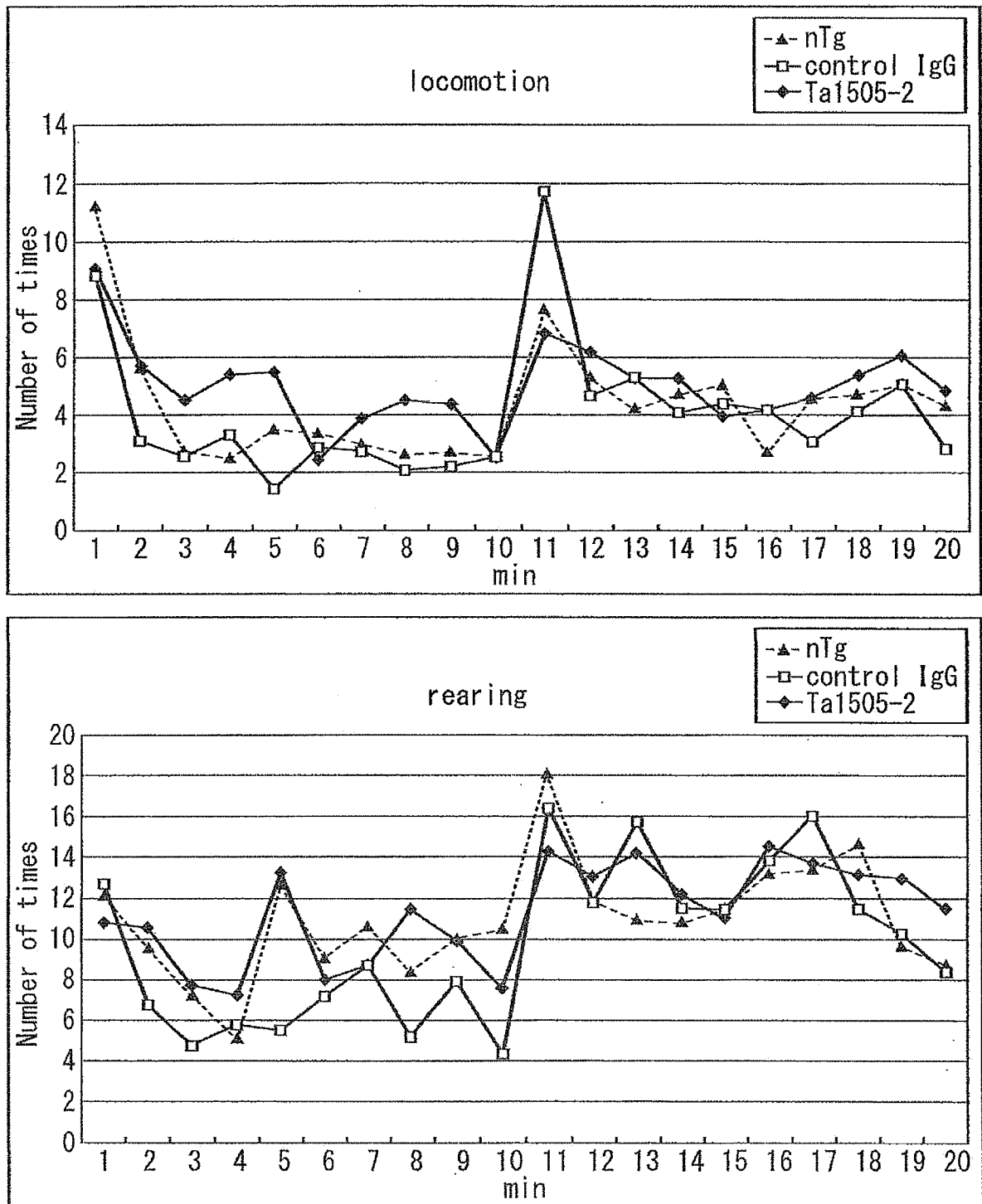
Fov 60-second analysis :

non-Tg vs Tg(control IgG) : $p=0.0120$ non-Tg vs Tg(Ta1505-2) : $p=0.6639$ (No significant difference)Tg(Ta1505-2) vs. Tg(control IgG) : $p=0.273$

10/29

FIG. 10

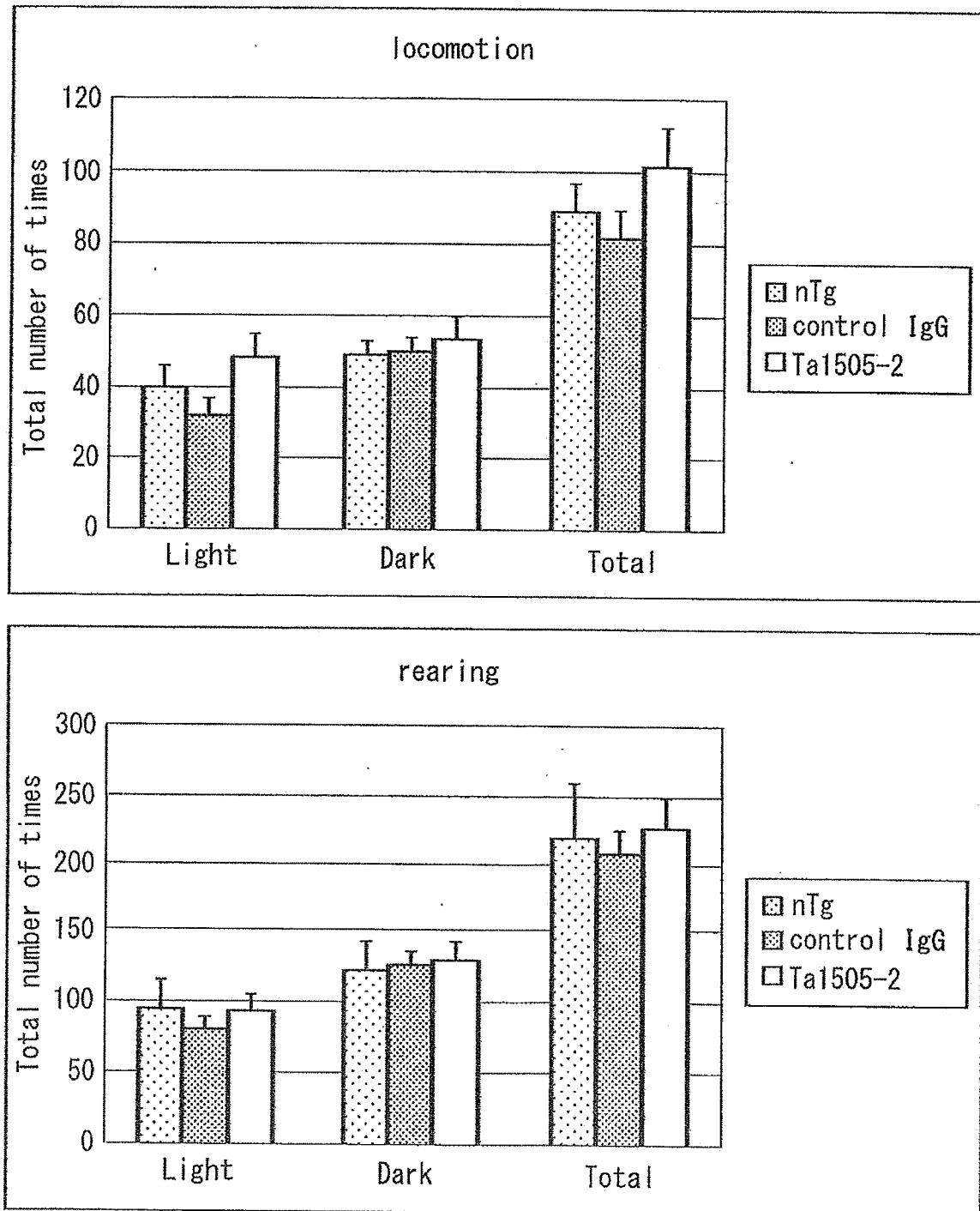
(2-3) Open Field test



11/29

FIG. 11

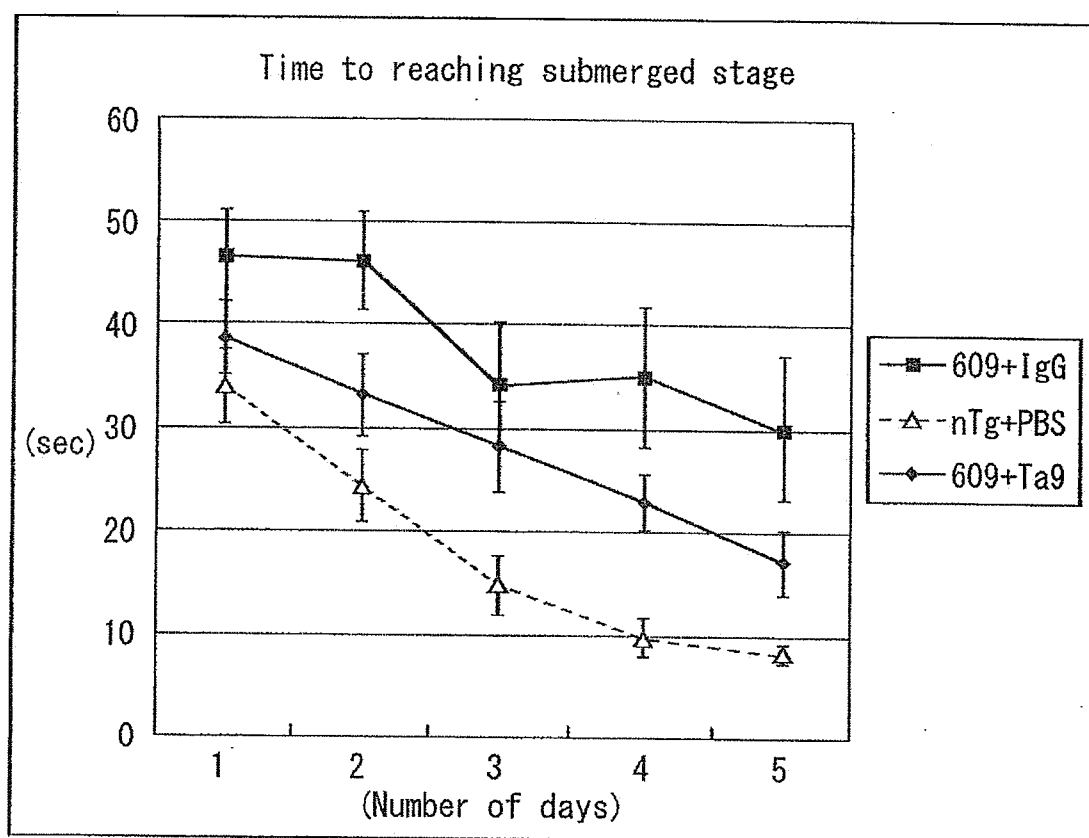
(2-3) Open Field test



12/29

FIG. 12

(3-1) Trial test



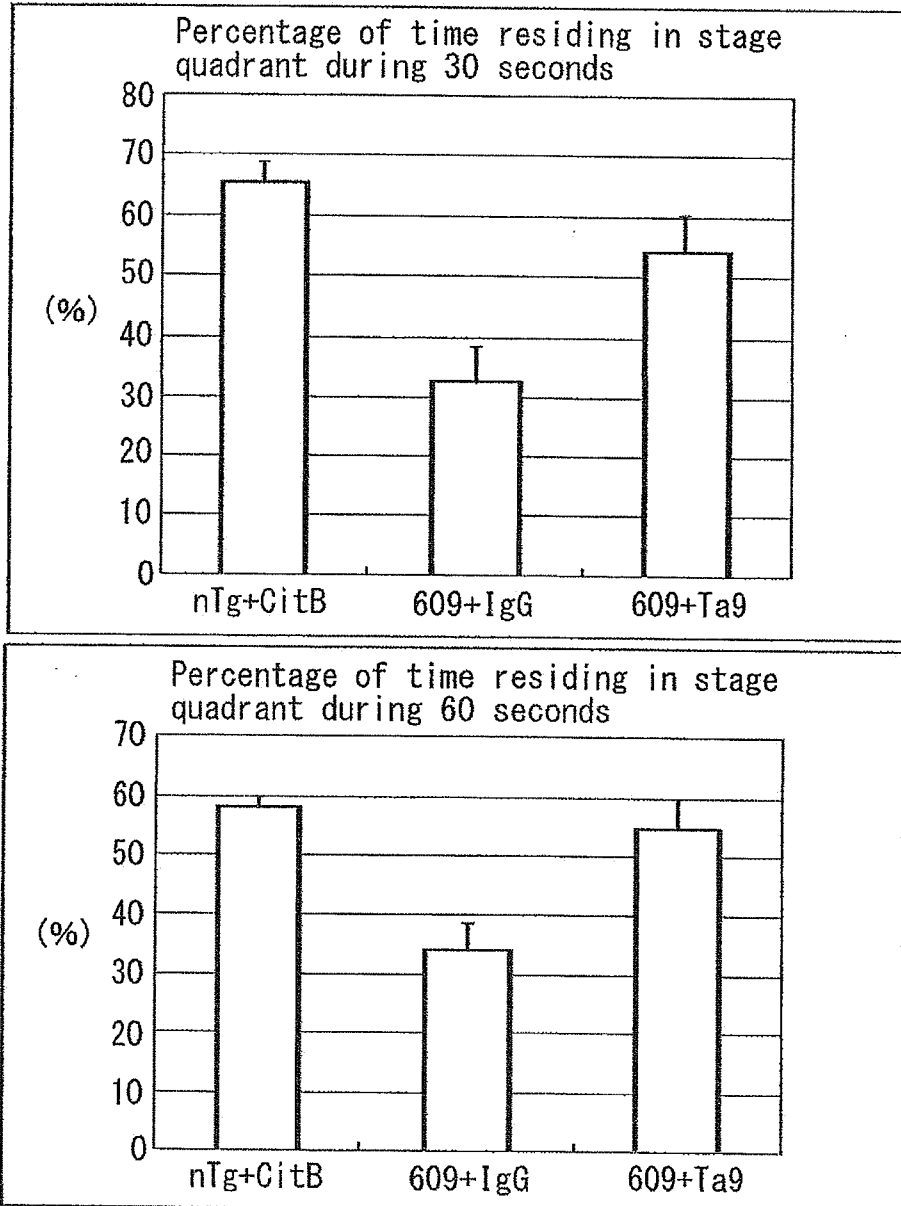
Significant difference

nTg vs Tg+pSer396 : $p=0.0460$

Tg+control IgG vs Tg+pSer396 : $p=0.0402$

FIG. 13

(3-2) Probe test



Significant difference

Fov 30-second analysis:

Ta9 vs IgG, $p=0.0015$ Ta9 vs NonTg, $p=0.8330$ (No significant difference)IgG vs NonTg, $p=0.0007$

Fov 60-second analysis:

Ta9 vs IgG, $p=0.0061$ Ta9 vs NonTg, $p=0.1637$ (No significant difference)IgG vs NonTg, $p=0.0001$

FIG. 14

(3-3) Open Field test

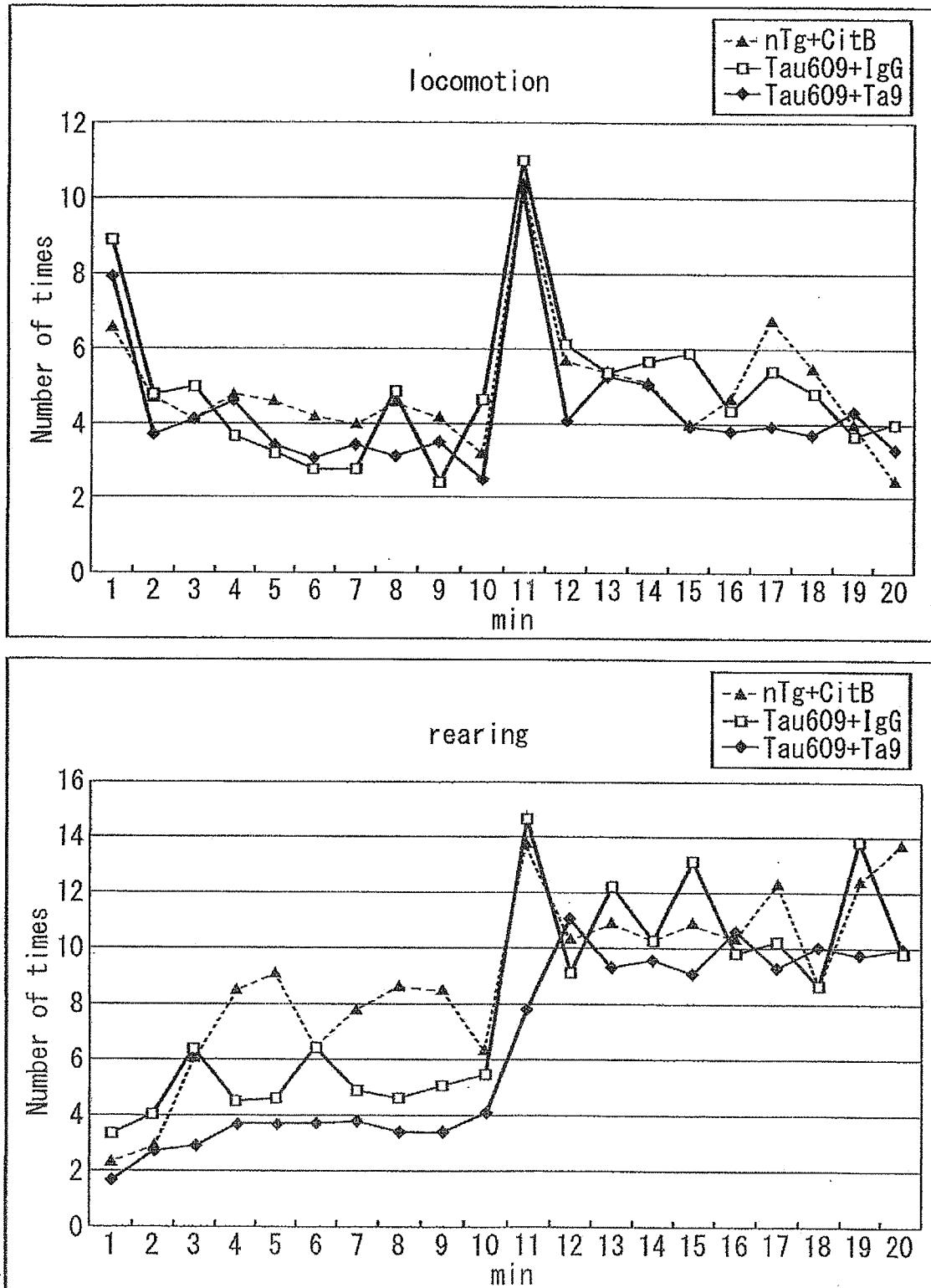


FIG. 15

(3-3) Open Field test

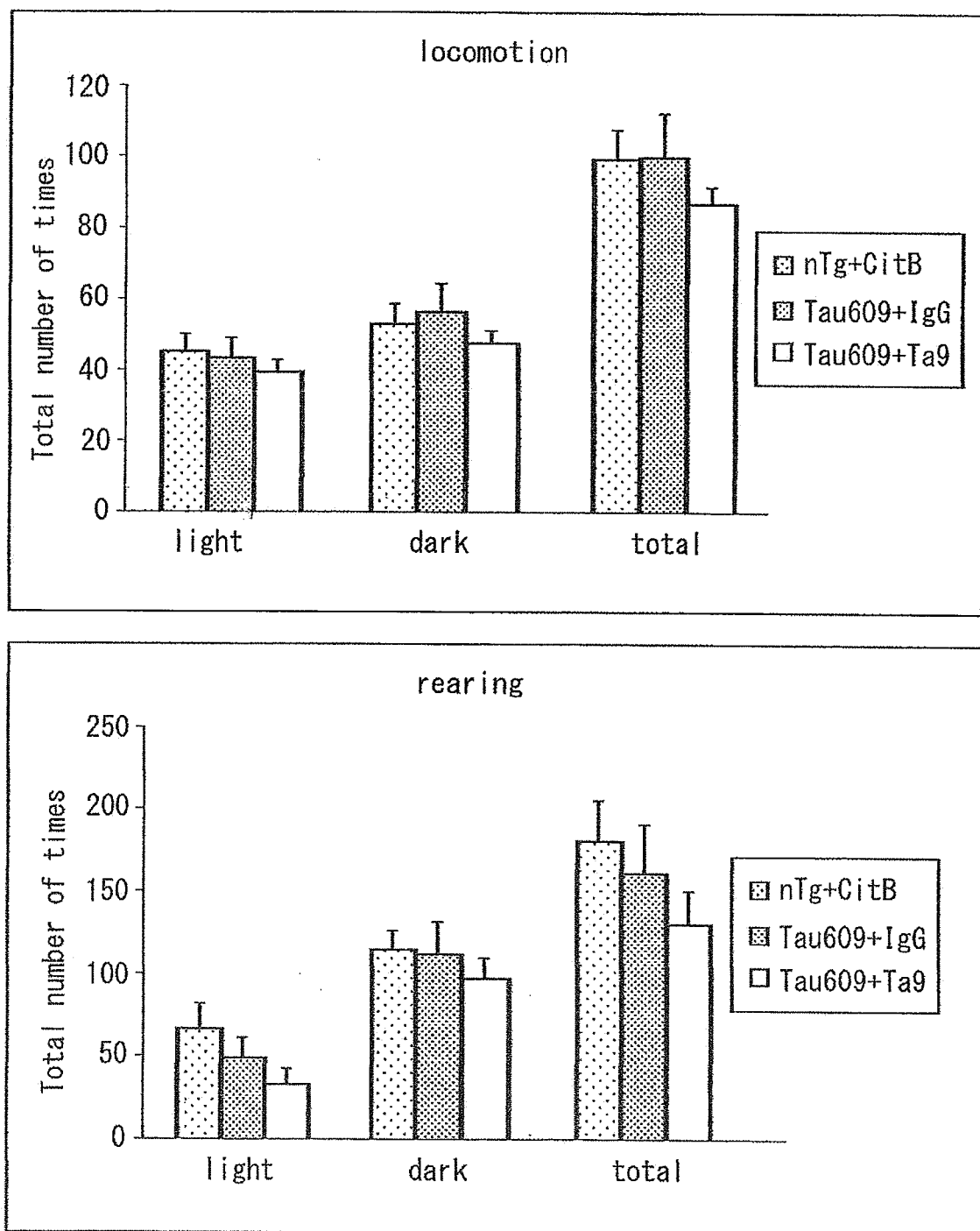
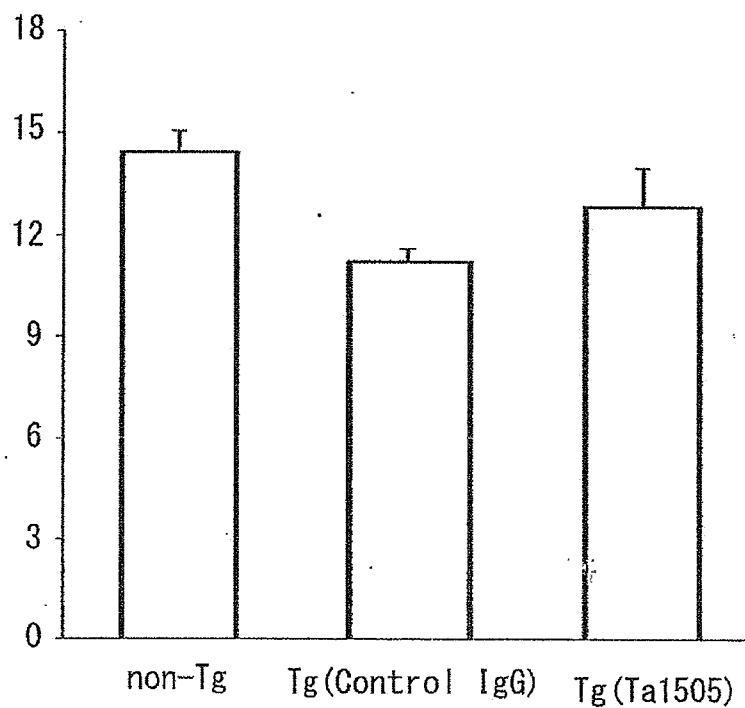


FIG. 16



Vertical axis represents synaptophysin fluorescence
in hippocampal CA3 region(arbitrary units)

Significant difference

non-Tg vs. Tg(control IgG) : $p=0.0138$

non-Tg vs. Tg(Ta1505) : $p=0.1806$ (No significant difference)

Tg(Ta1505) vs. Tg(control IgG) : $p=0.1696$

(No significant difference)

FIG. 17

Tau-conferring nucleic structure

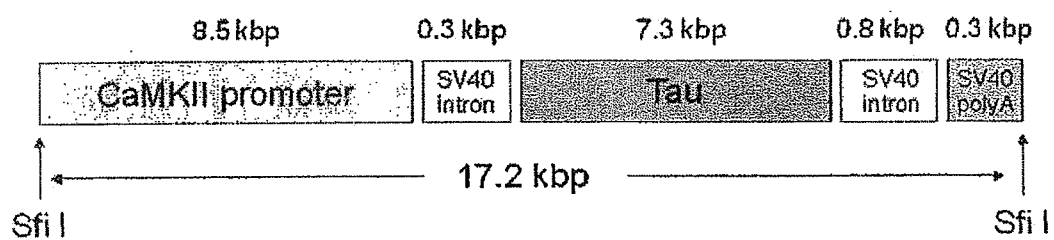
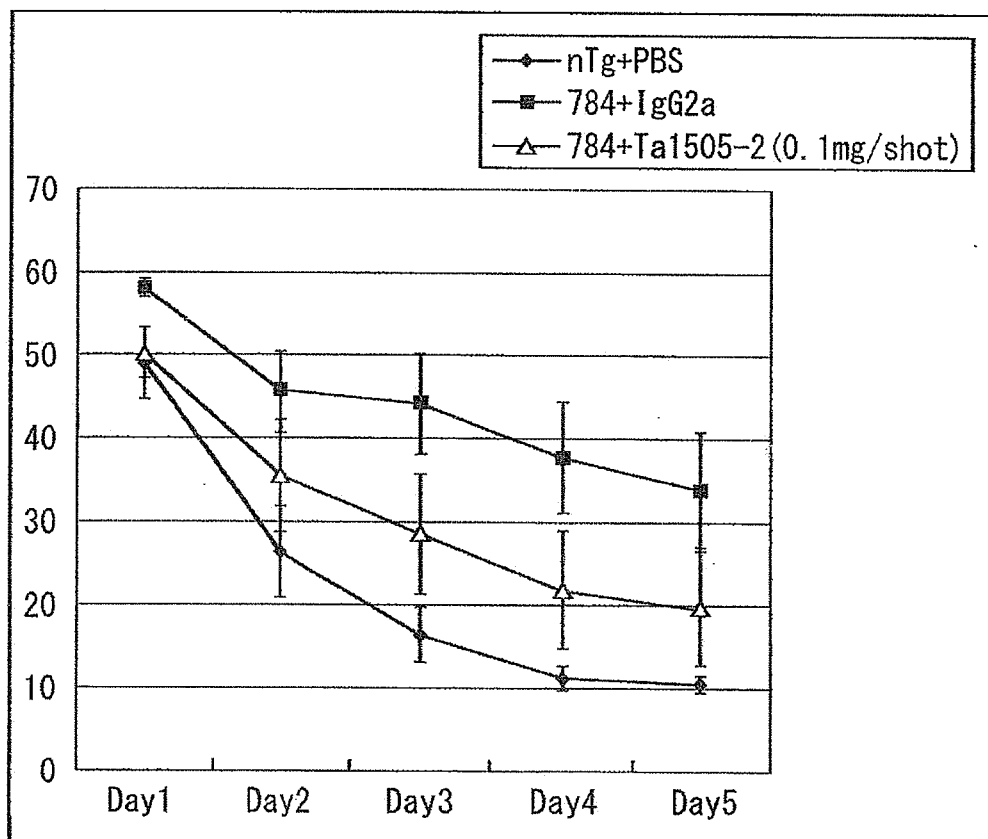


FIG. 18

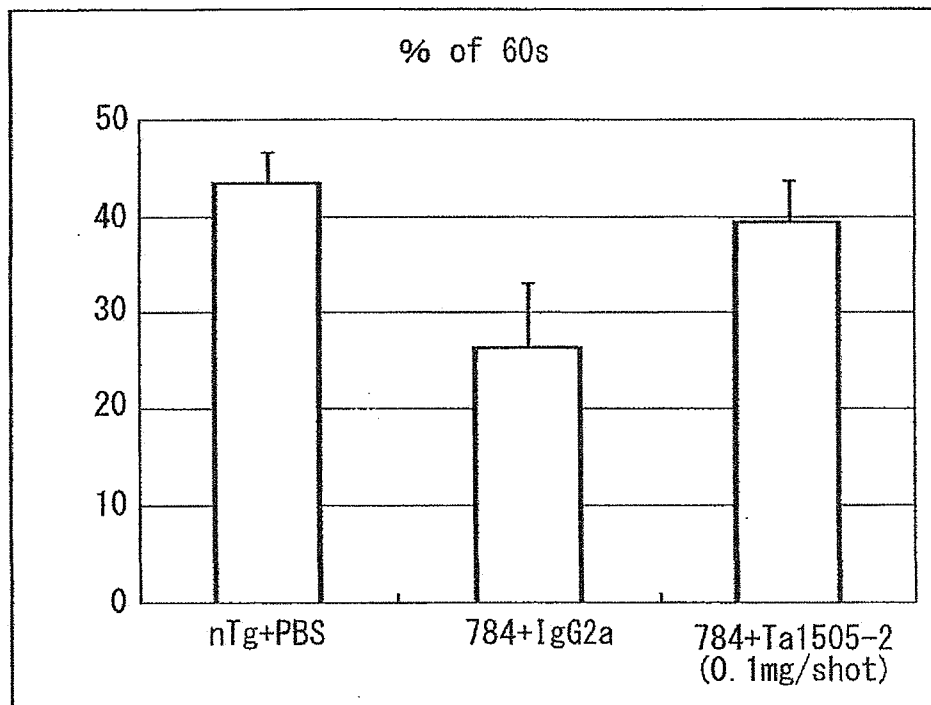
(4-1) Trial test



nonTg vs Tg(Control IgG) $p=0.0025$
nonTg vs Tg(Ta1505) $p=0.1926$ (No significant difference)
Tg(Ta1505) vs Tg(Control IgG) $p=0.0493$

FIG. 19

(4-2) Probe test



nonTg vs Tg(Control IgG)

p=0.0240

nonTg vs Tg(Ta1505)

p=0.5783 (No significant difference)

Tg(Ta1505) vs Tg(Control IgG)

p=0.0708 (No significant difference)

FIG. 20

(5-1) Trial test

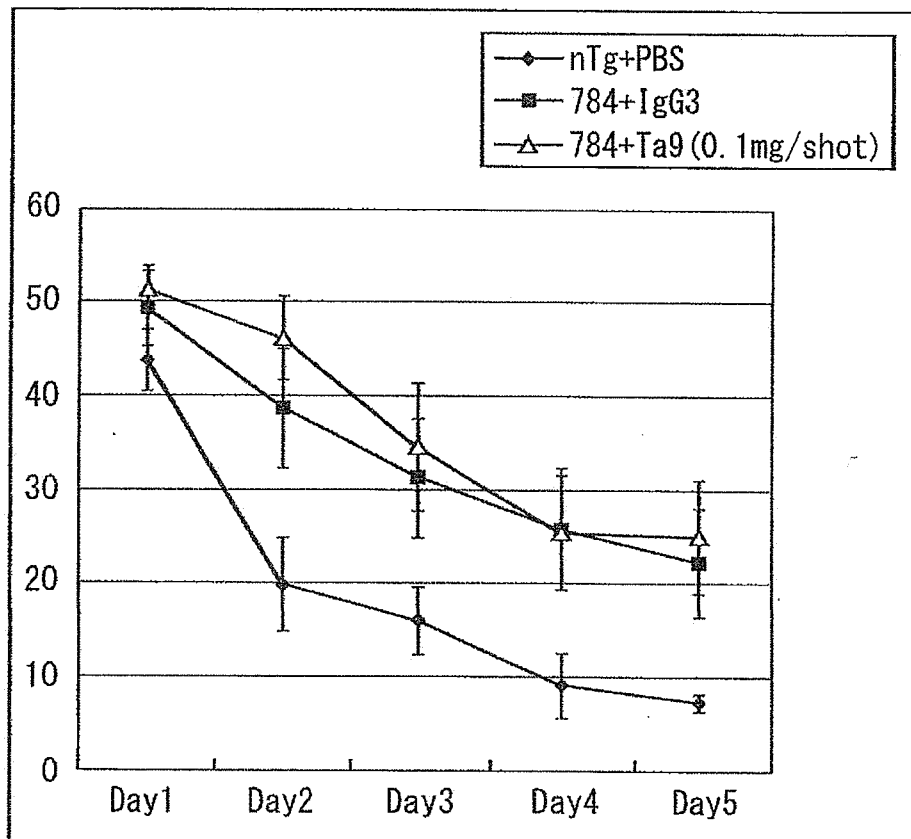
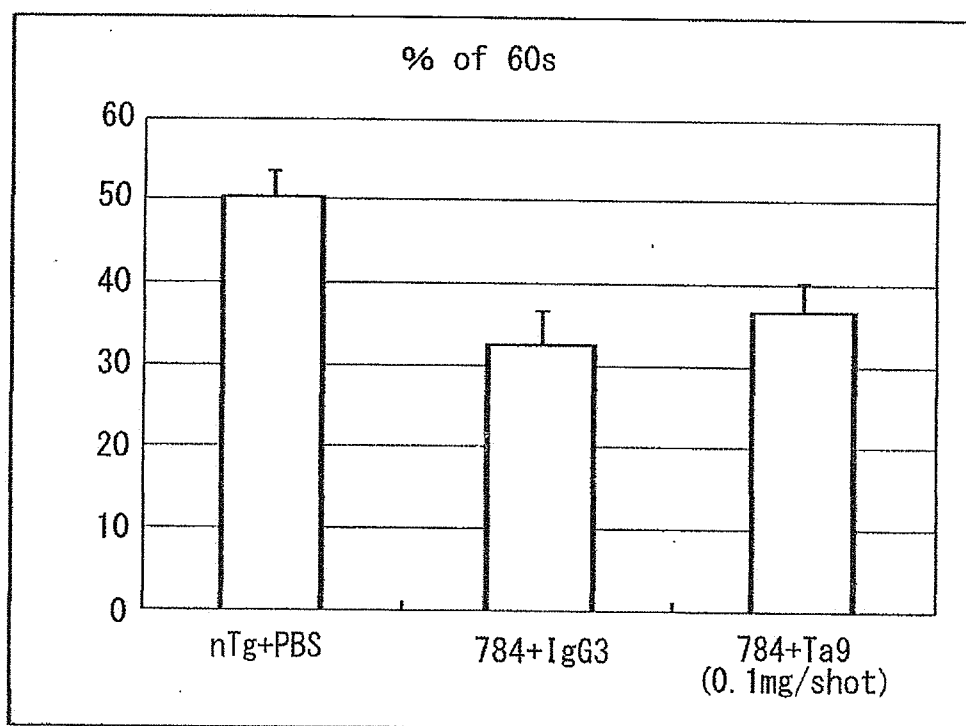
nonTg vs Tg(Control IgG) $p=0.0065$ nonTg vs Tg(Ta9) $p=0.0044$ Tg(Ta9) vs Tg(Control IgG) $p=0.8635$ (No significant difference)

FIG. 21

(5-2) Probe test



nonTg vs Tg(Control IgG)

p=0.0033

nonTg vs Tg(Ta9)

p=0.0100

Tg(Ta9) vs Tg(Control IgG)

p=0.5226 (No significant difference)

FIG. 22

Immunohistostaining of hippocampal region (Ta1505 stain)

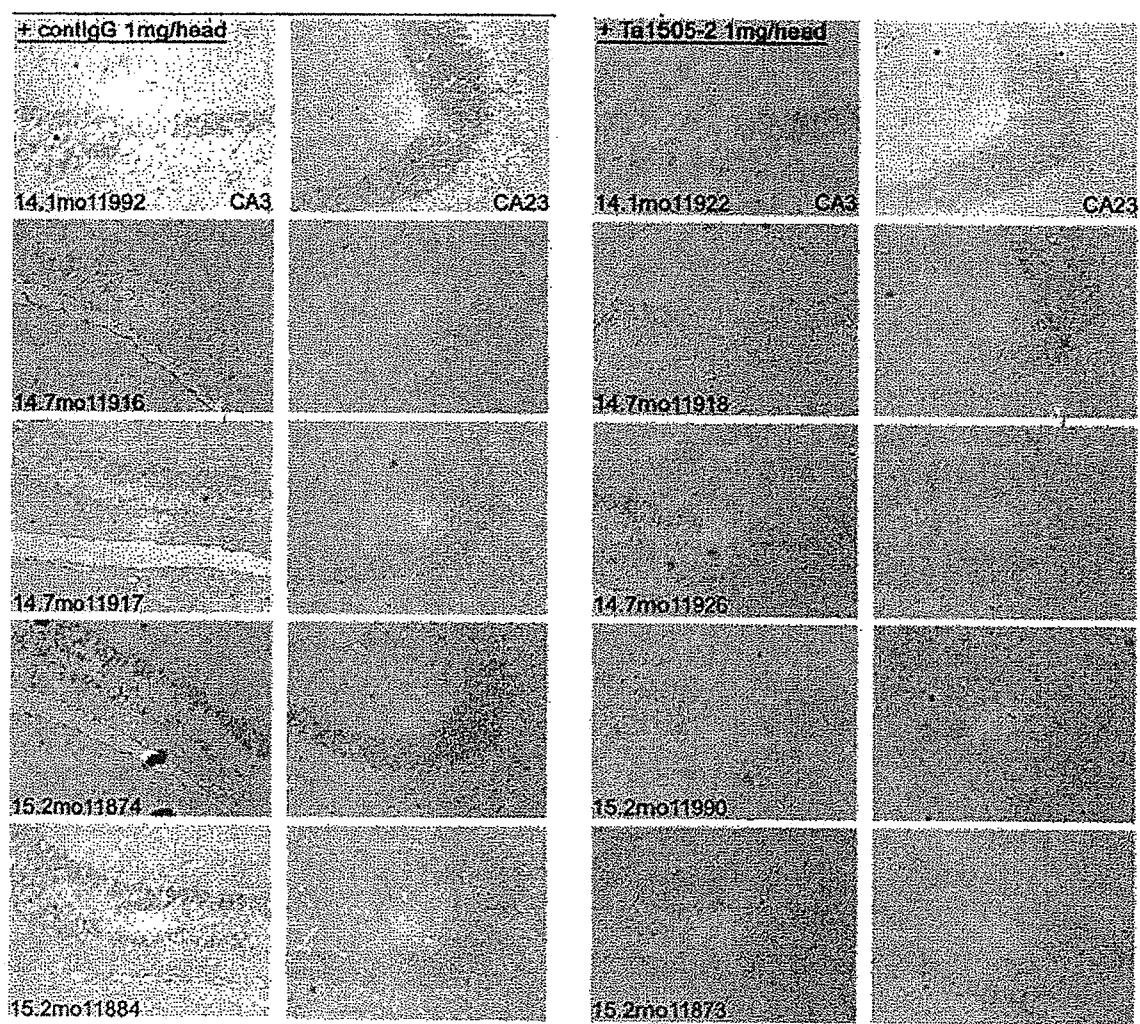


FIG. 23

Immunohistostaining of Cortex region (Ta1505 stain)
Control IgG (1mg/head)

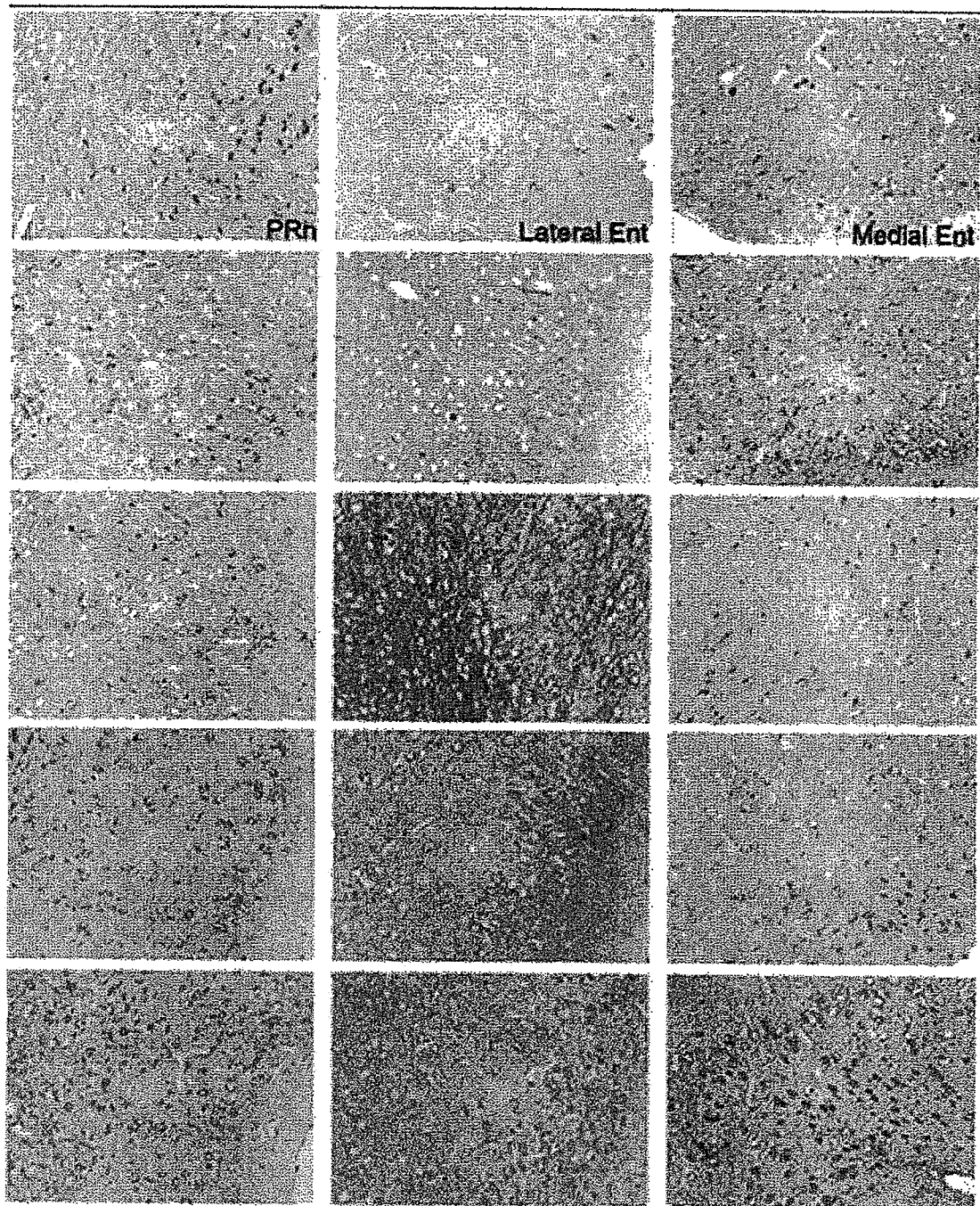


FIG. 24

Ta1505 administration(1mg/head)

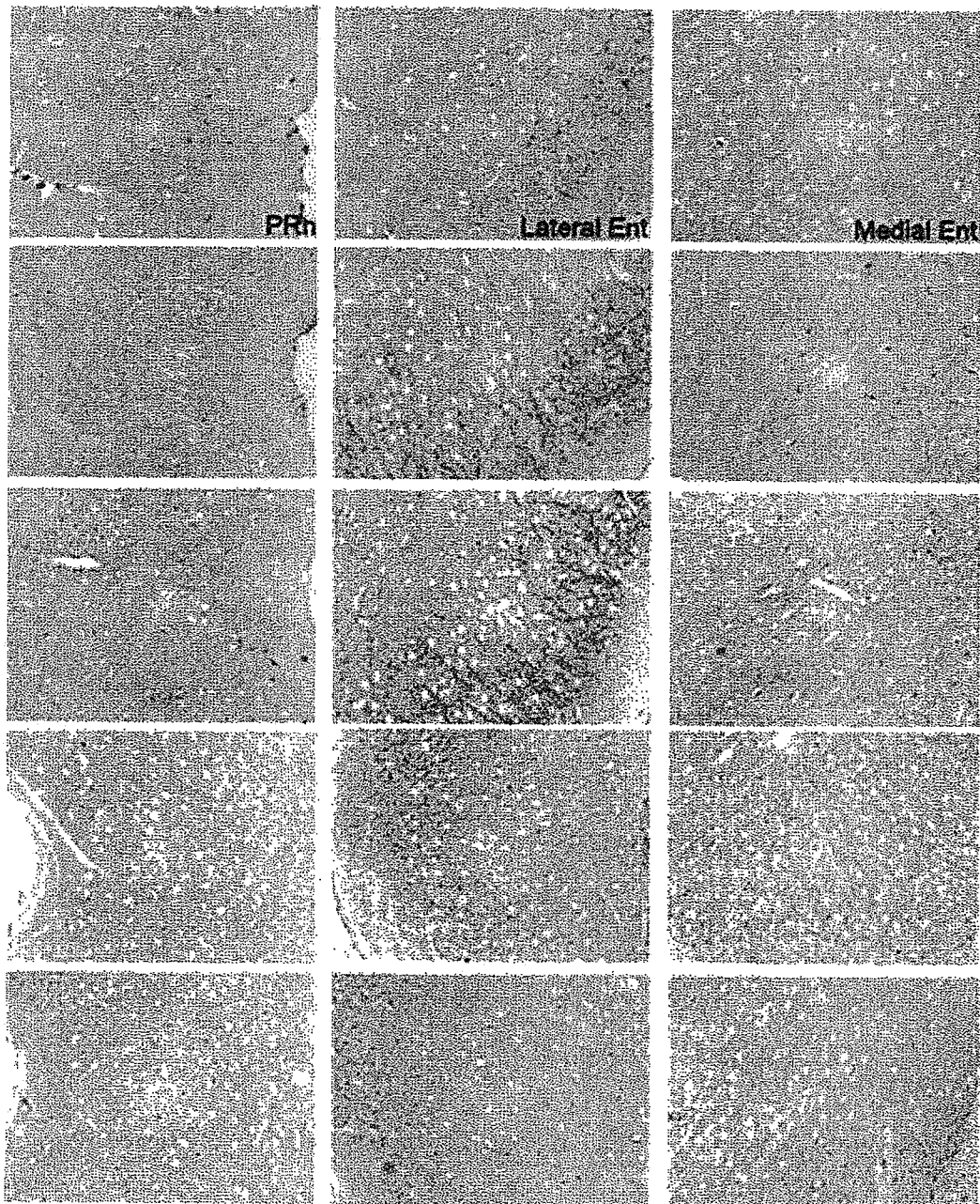
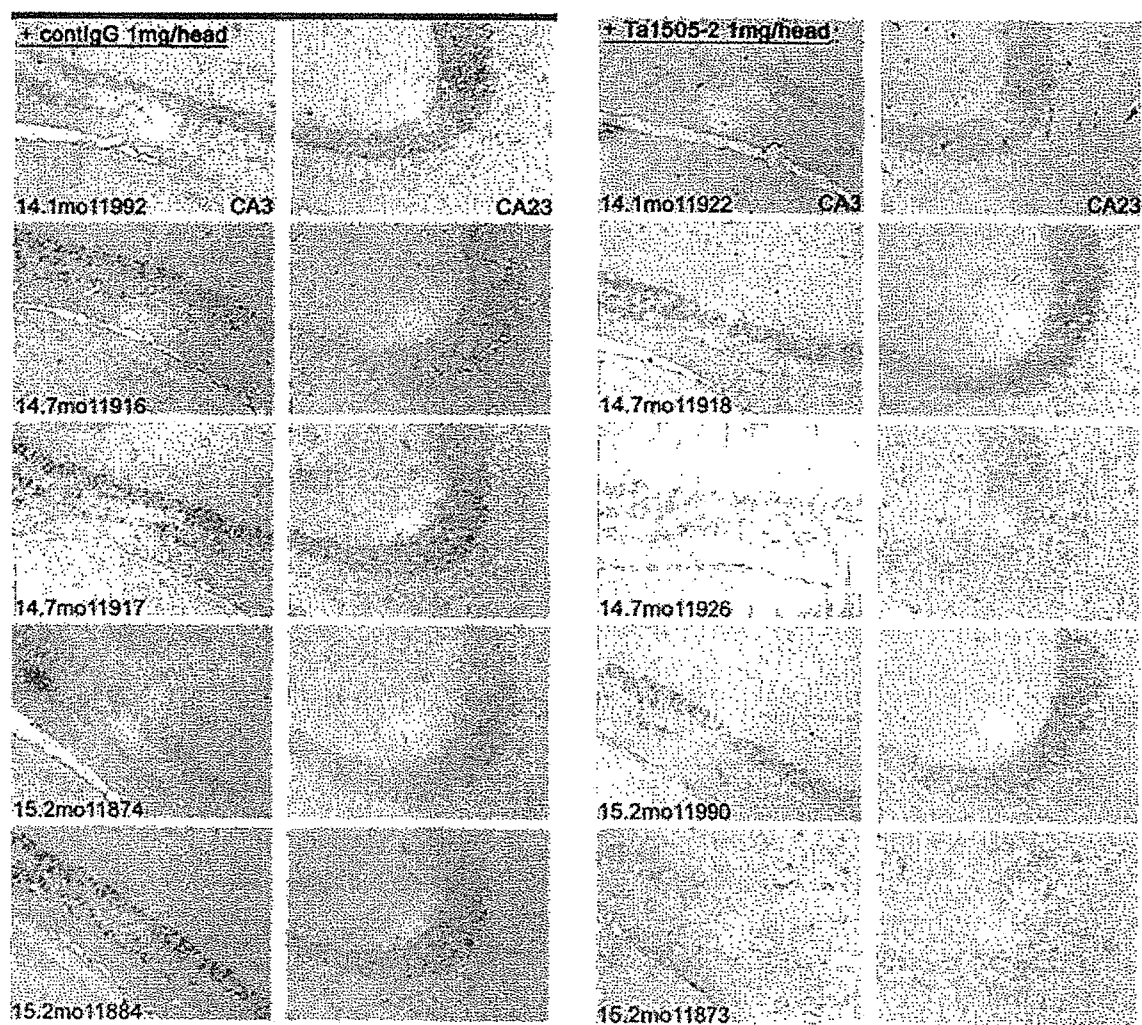


FIG. 25

Immunohistostaining of hippocampal region(AT8 stain)



26/29

FIG. 26

Immunohistostaining of Cortex region(AT8 stain)
Control IgG(1mg/head)

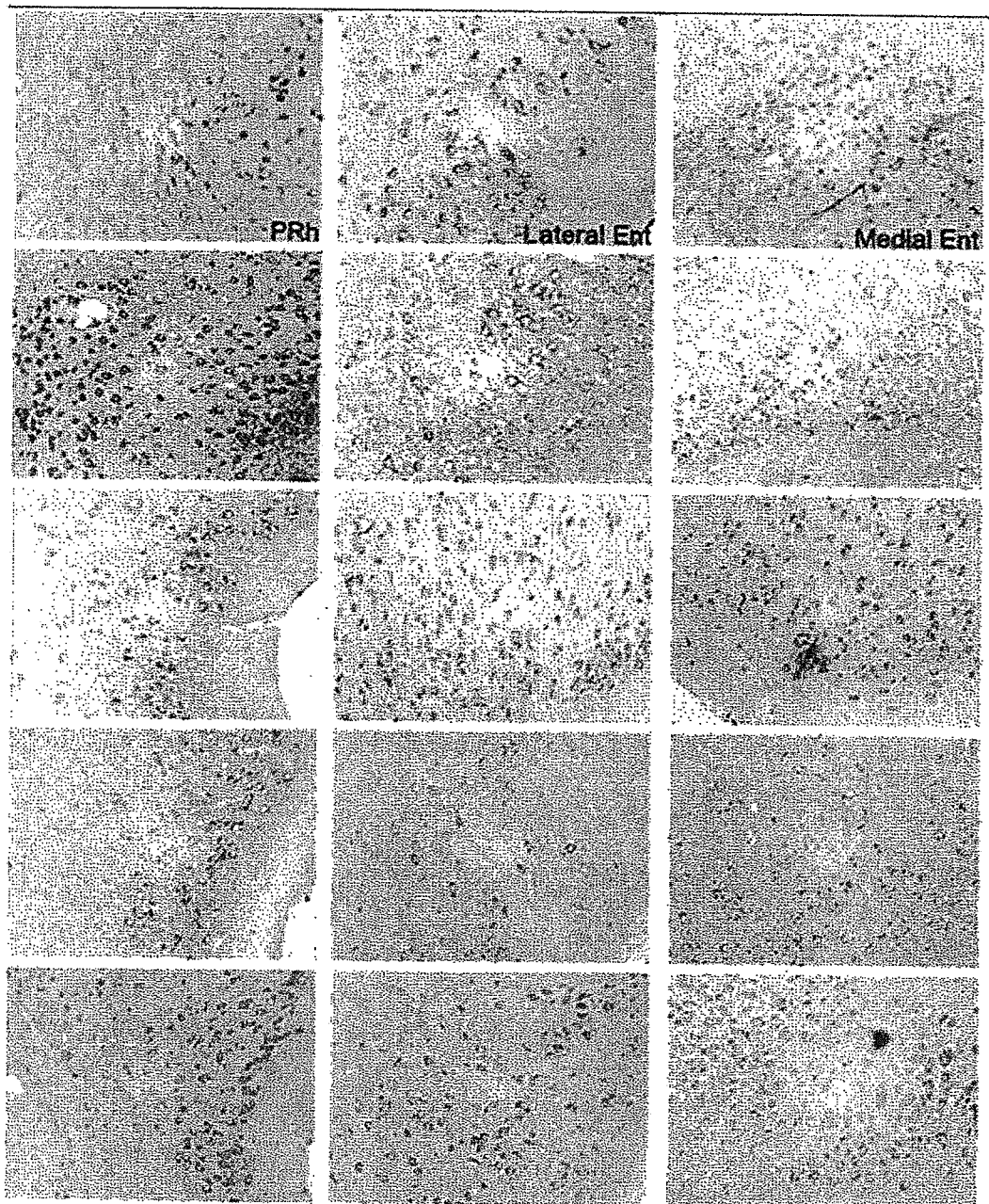


FIG. 27

Ta1505 administration (1mg/head)

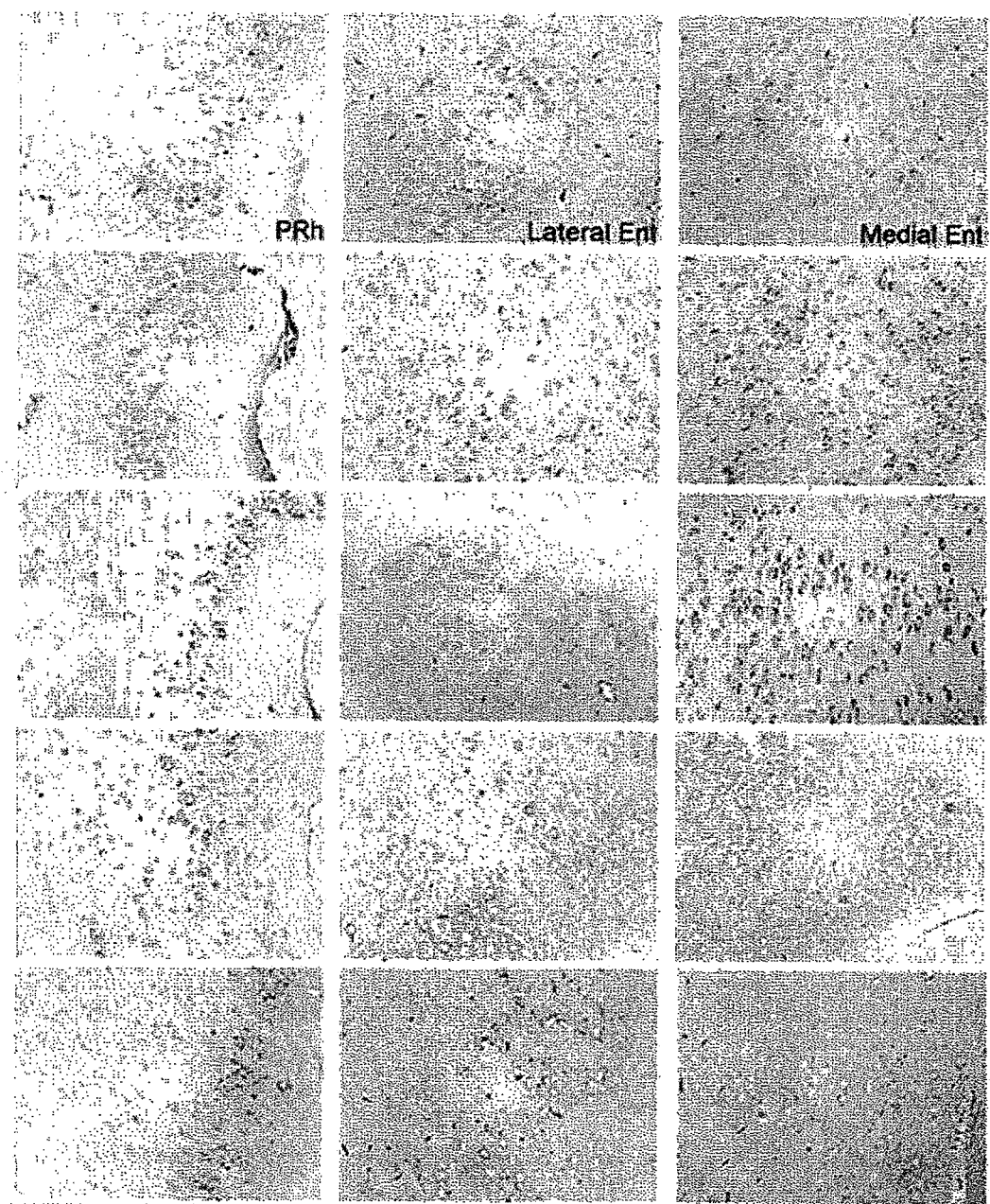
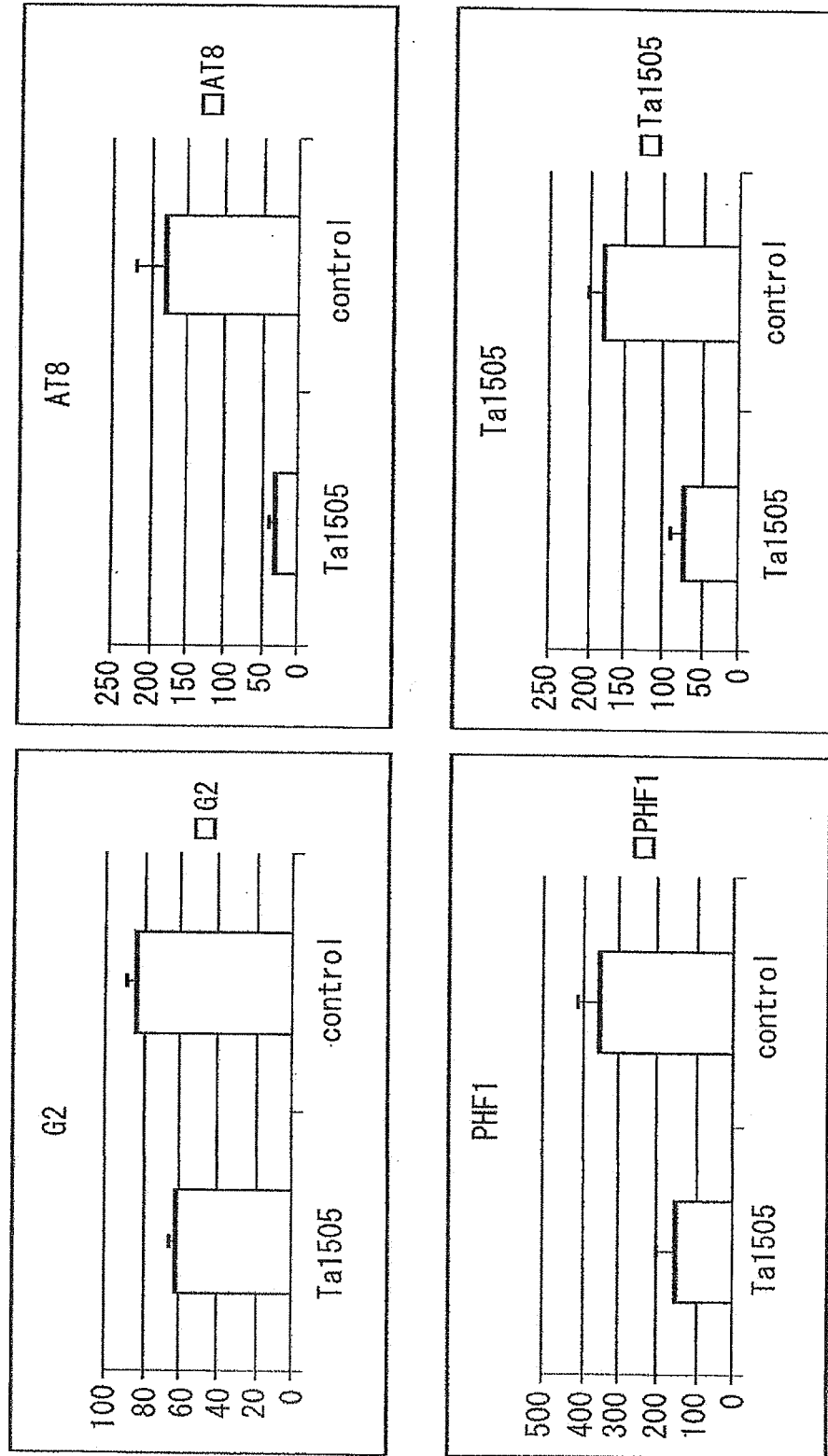


FIG. 28

TBS-soluble fraction



T-test

G2 : Ta1505 vs Control p=0.013276

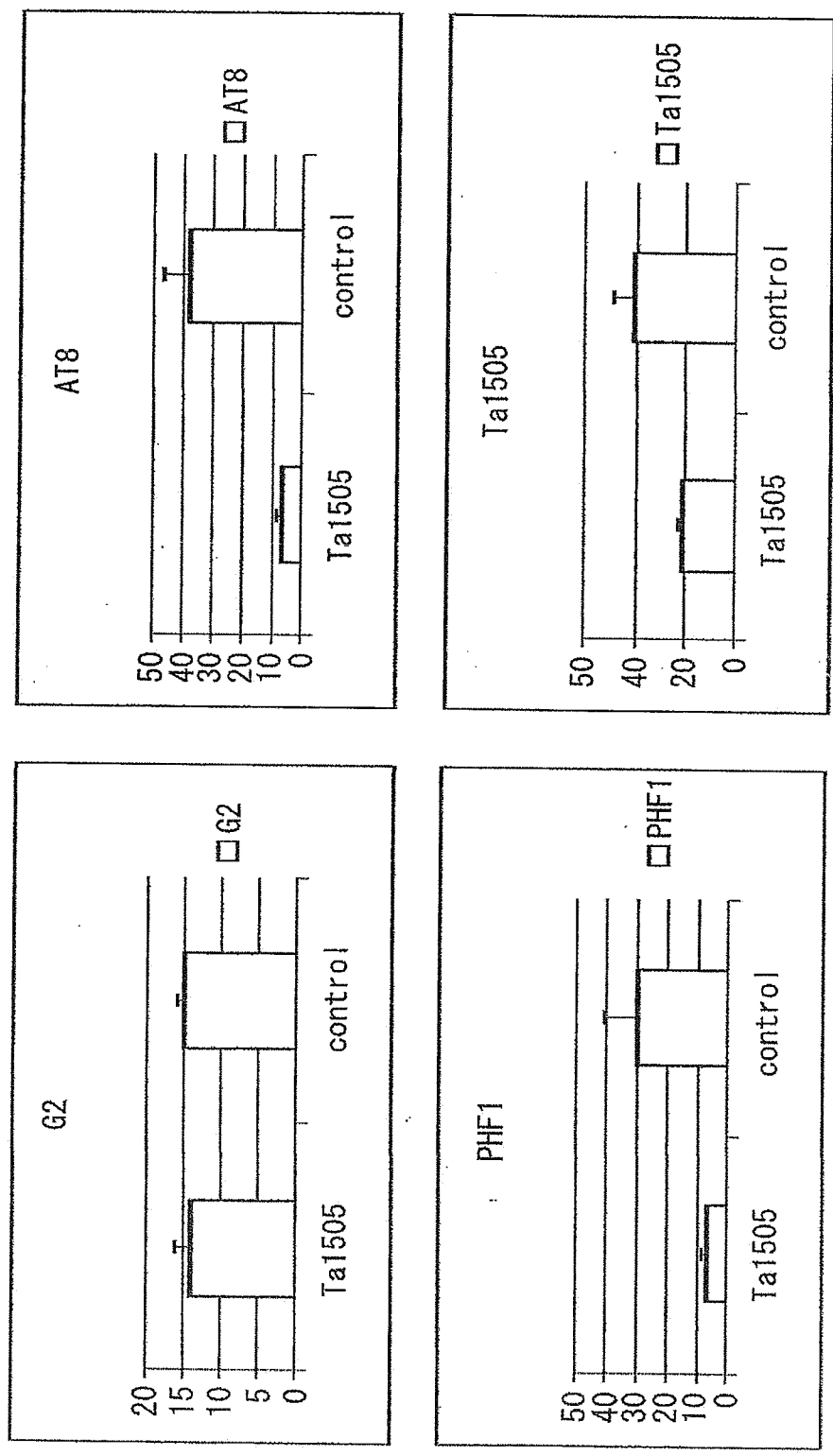
AT8 : Ta1505 vs Control p=0.016886

PHF1 : Ta1505 vs Control p=0.021157

Ta1505 : Ta1505 vs Control p=0.006104

FIG. 29

Sarkosyl-soluble fraction



T-test

G2 : Ta1505 vs Control p=0.804878 (No significant difference)

AT8 : Ta1505 vs Control p=0.012585

PHF1 : Ta1505 vs Control p=0.06155 (Decline)

Ta1505 : Ta1505 vs Control p=0.063603 (Decline)