

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	DHAGTYGLGDRKDQGGYTMHQDQEGD	TDAGLK-----			44
3R1N (Seq. ID:5)	MAEPRQEF	EVME	DHAGTYGLGDRKDQGGYTMHQDQEGD	TDAGLKESPLQTPTEDGSEEPG			60
3R2N (Seq. ID:4)	MAEPRQEF	EVME	DHAGTYGLGDRKDQGGYTMHQDQEGD	TDAGLKESPLQTPTEDGSEEPG			60
4RON (Seq. ID:3)	MAEPRQEF	EVME	DHAGTYGLGDRKDQGGYTMHQDQEGD	TDAGLK-----			44
4R1N (Seq. ID:2)	MAEPRQEF	EVME	DHAGTYGLGDRKDQGGYTMHQDQEGD	TDAGLKESPLQTPTEDGSEEPG			60
4R2N (Seq. ID:1)	MAEPRQEF	EVME	DHAGTYGLGDRKDQGGYTMHQDQEGD	TDAGLKESPLQTPTEDGSEEPG			60

Prim. cons. MAEPRQEFEVME DHAGTYGLGDRKDQGGYTMHQDQEGD TDAGLKESPLQTPTEDGSEEPG

	70	80	90	100	110	120	
3RON (Seq. ID:6)	-----				AEEAGIGDTPSLEDEAAG		62
3R1N (Seq. ID:5)	SETSDAKSTPTAE-----				AEEAGIGDTPSLEDEAAG		91
3R2N (Seq. ID:4)	SETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHT				IEPGTTAEEAGIGDTPSLEDEAAG		120
4RON (Seq. ID:3)	-----				AEEAGIGDTPSLEDEAAG		62
4R1N (Seq. ID:2)	SETSDAKSTPTAE-----				AEEAGIGDTPSLEDEAAG		91
4R2N (Seq. ID:1)	SETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHT				IEPGTTAEEAGIGDTPSLEDEAAG		120

Prim. cons. SETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHTIEPGTTAEEAGIGDTPSLEDEAAG

	130	140	150	160	170	180	
3RON (Seq. ID:6)	HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP				GQKGQANATRIPAKTPPAPK		122
3R1N (Seq. ID:5)	HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP				GQKGQANATRIPAKTPPAPK		151
3R2N (Seq. ID:4)	HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP				GQKGQANATRIPAKTPPAPK		180
4RON (Seq. ID:3)	HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP				GQKGQANATRIPAKTPPAPK		122
4R1N (Seq. ID:2)	HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP				GQKGQANATRIPAKTPPAPK		151
4R2N (Seq. ID:1)	HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP				GQKGQANATRIPAKTPPAPK		180

Prim. cons. HVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPPGQKGQANATRIPAKTPPAPK

	190	200	210	220	230	240	
3RON (Seq. ID:6)	TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREP				KKVAVVRTPPKSPSSAK		182
3R1N (Seq. ID:5)	TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREP				KKVAVVRTPPKSPSSAK		211
3R2N (Seq. ID:4)	TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREP				KKVAVVRTPPKSPSSAK		240
4RON (Seq. ID:3)	TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREP				KKVAVVRTPPKSPSSAK		182
4R1N (Seq. ID:2)	TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREP				KKVAVVRTPPKSPSSAK		211
4R2N (Seq. ID:1)	TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREP				KKVAVVRTPPKSPSSAK		240

Prim. cons. TPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREPKKVAVVRTPPKSPSSAK

FIG. 2

	250	260	270	280	290	300
3R0N (Seq. ID:6)	SRLQTAPVMPDLKNVKS	IGSTENLKHQPGGGK	-----			216
3R1N (Seq. ID:5)	SRLQTAPVMPDLKNVKS	IGSTENLKHQPGGGK	-----			245
3R2N (Seq. ID:4)	SRLQTAPVMPDLKNVKS	IGSTENLKHQPGGGK	-----			274
4R0N (Seq. ID:3)	SRLQTAPVMPDLKNVKS	IGSTENLKHQPGGGKVQI	INKKLDLSNVQSKCGSKDNI	KHV		242
4R1N (Seq. ID:2)	SRLQTAPVMPDLKNVKS	IGSTENLKHQPGGGKVQI	INKKLDLSNVQSKCGSKDNI	KHV		271
4R2N (Seq. ID:1)	SRLQTAPVMPDLKNVKS	IGSTENLKHQPGGGKVQI	INKKLDLSNVQSKCGSKDNI	KHV		300

Prim. cons.	SRLQTAPVMPDLKNVKSIGSTENLKHQPGGGKVQIINKKLDLSNVQSKCGSKDNI					KHV
	310	320	330	340	350	360
3R0N (Seq. ID:6)	-----VQIVYK	PVDLSKVT	SKCGSLGNIHHK	PGGGQVEVKSEK	LDFKDRVQSKIGSLDNI	271
3R1N (Seq. ID:5)	-----VQIVYK	PVDLSKVT	SKCGSLGNIHHK	PGGGQVEVKSEK	LDFKDRVQSKIGSLDNI	300
3R2N (Seq. ID:4)	-----VQIVYK	PVDLSKVT	SKCGSLGNIHHK	PGGGQVEVKSEK	LDFKDRVQSKIGSLDNI	329
4R0N (Seq. ID:3)	PGGGSVQIVYK	PVDLSKVT	SKCGSLGNIHHK	PGGGQVEVKSEK	LDFKDRVQSKIGSLDNI	302
4R1N (Seq. ID:2)	PGGGSVQIVYK	PVDLSKVT	SKCGSLGNIHHK	PGGGQVEVKSEK	LDFKDRVQSKIGSLDNI	331
4R2N (Seq. ID:1)	PGGGSVQIVYK	PVDLSKVT	SKCGSLGNIHHK	PGGGQVEVKSEK	LDFKDRVQSKIGSLDNI	360

Prim. cons.	PGGGSVQIVYKPVDSLKVT					SKCGSLGNIHHKPGGGQVEVKSEKLDKDRVQSKIGSLDNI
	370	380	390	400	410	420
3R0N (Seq. ID:6)	THVPGGGNKKIETHKLT	FRENAKAKTDHGAE	IVYKSPVVS	SGDTS	SPRHLSNV	SSTGSIDMV 331
3R1N (Seq. ID:5)	THVPGGGNKKIETHKLT	FRENAKAKTDHGAE	IVYKSPVVS	SGDTS	SPRHLSNV	SSTGSIDMV 360
3R2N (Seq. ID:4)	THVPGGGNKKIETHKLT	FRENAKAKTDHGAE	IVYKSPVVS	SGDTS	SPRHLSNV	SSTGSIDMV 389
4R0N (Seq. ID:3)	THVPGGGNKKIETHKLT	FRENAKAKTDHGAE	IVYKSPVVS	SGDTS	SPRHLSNV	SSTGSIDMV 362
4R1N (Seq. ID:2)	THVPGGGNKKIETHKLT	FRENAKAKTDHGAE	IVYKSPVVS	SGDTS	SPRHLSNV	SSTGSIDMV 391
4R2N (Seq. ID:1)	THVPGGGNKKIETHKLT	FRENAKAKTDHGAE	IVYKSPVVS	SGDTS	SPRHLSNV	SSTGSIDMV 420

Prim. cons.	THVPGGGNKKIETHKLT					FRENAKAKTDHGAEIVYKSPVVS
	430	440				
3R0N (Seq. ID:1)	DSPQLATLADEV	SASLAKQGL				352
3R1N (Seq. ID:1)	DSPQLATLADEV	SASLAKQGL				381
3R2N (Seq. ID:1)	DSPQLATLADEV	SASLAKQGL				410
4R0N (Seq. ID:1)	DSPQLATLADEV	SASLAKQGL				383
4R1N (Seq. ID:1)	DSPQLATLADEV	SASLAKQGL				412
4R2N (Seq. ID:1)	DSPQLATLADEV	SASLAKQGL				441

Prim. cons.	DSPQLATLADEV					SASLAKQGL

FIG. 3

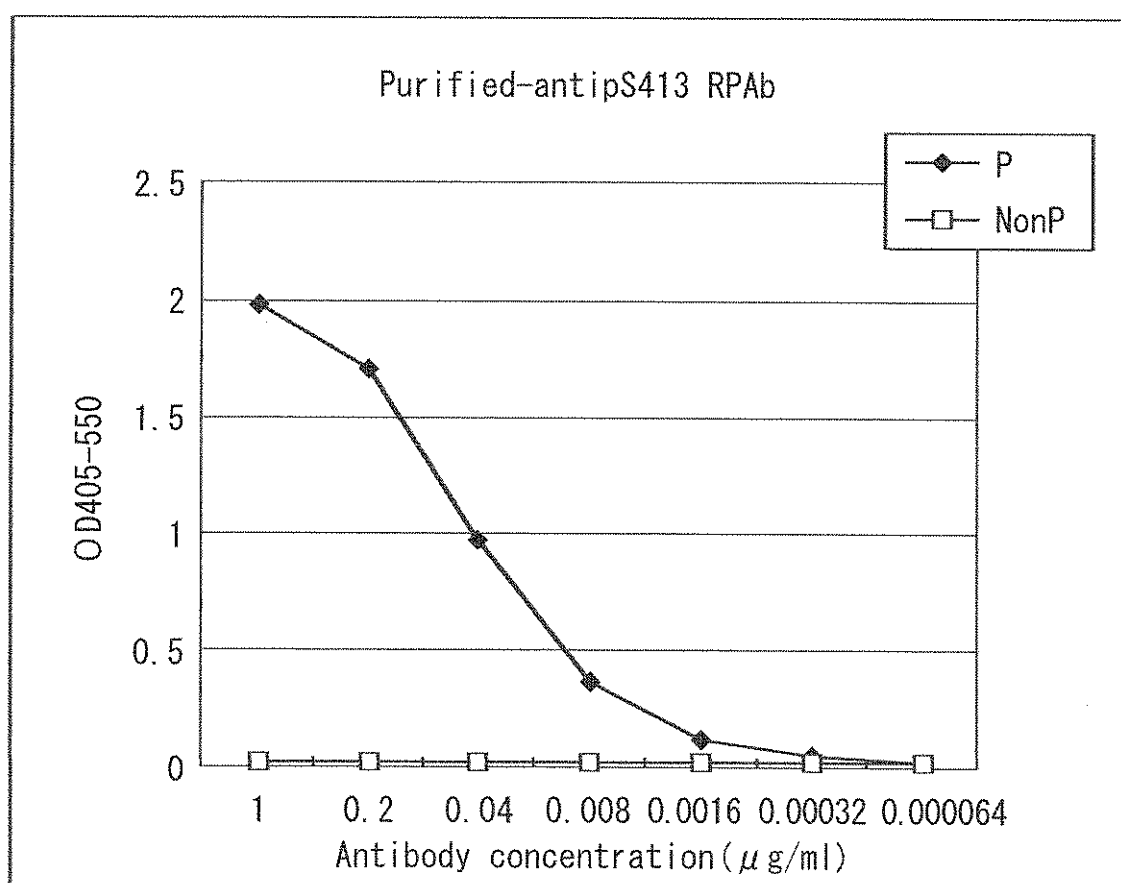
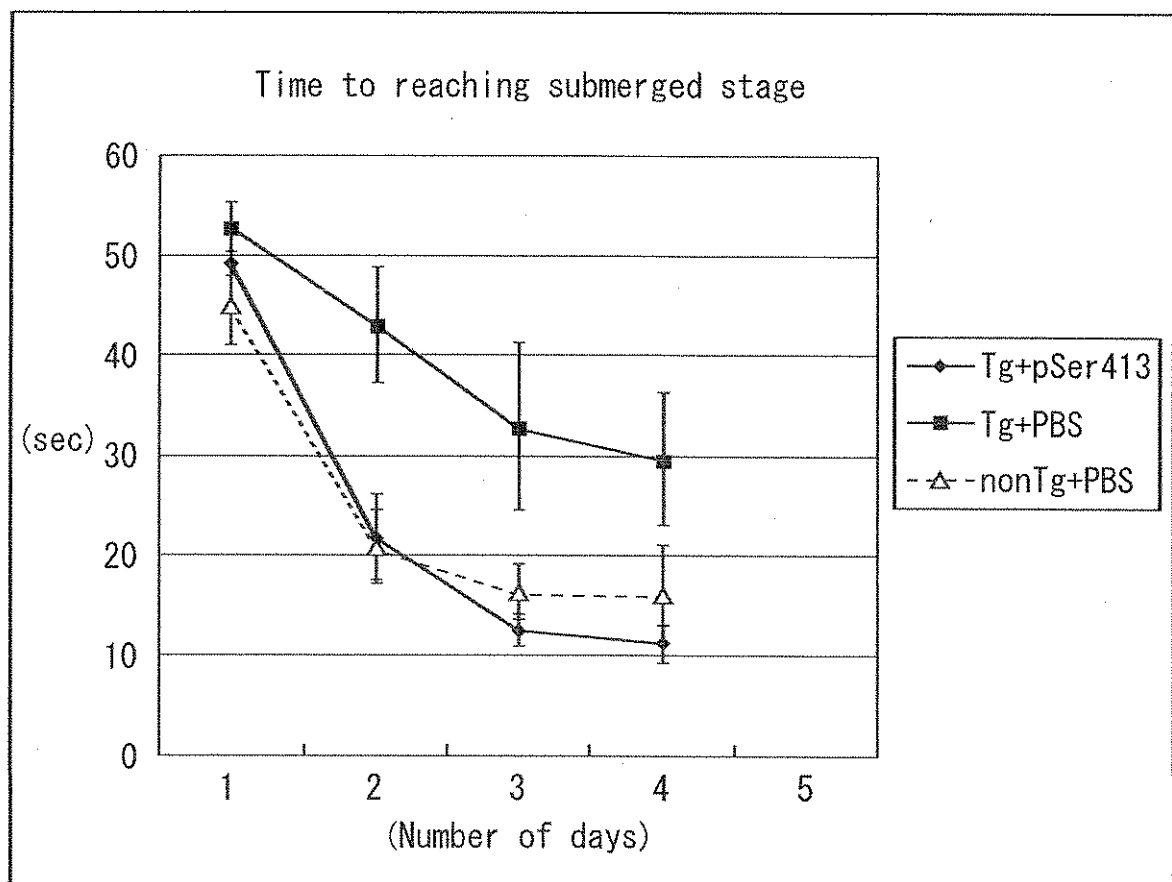


FIG. 4

(1-1) Trial test

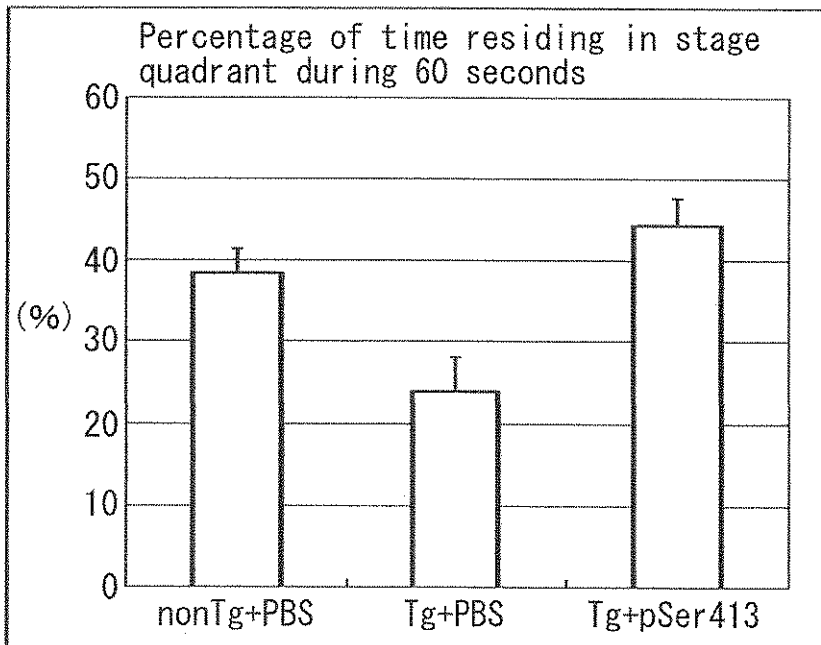
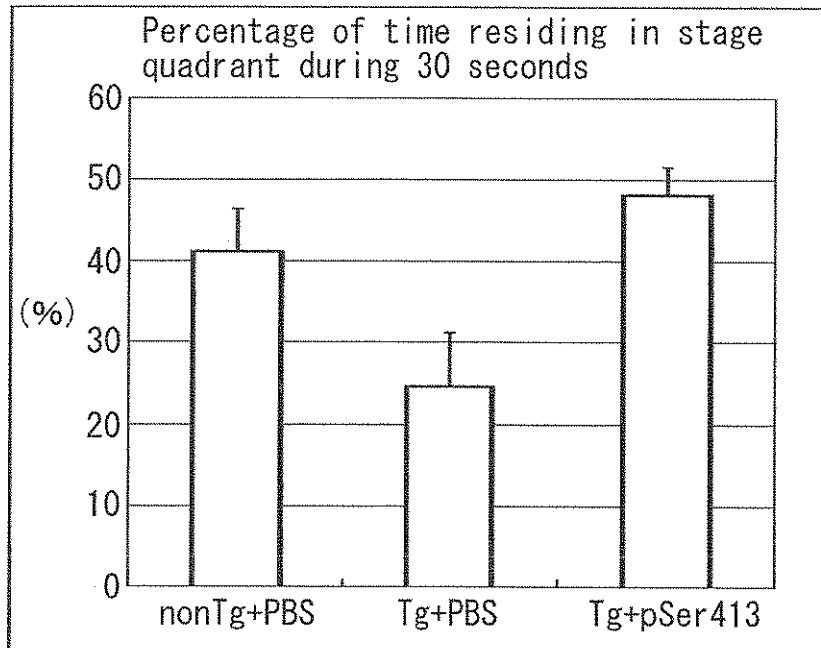


Significant difference

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

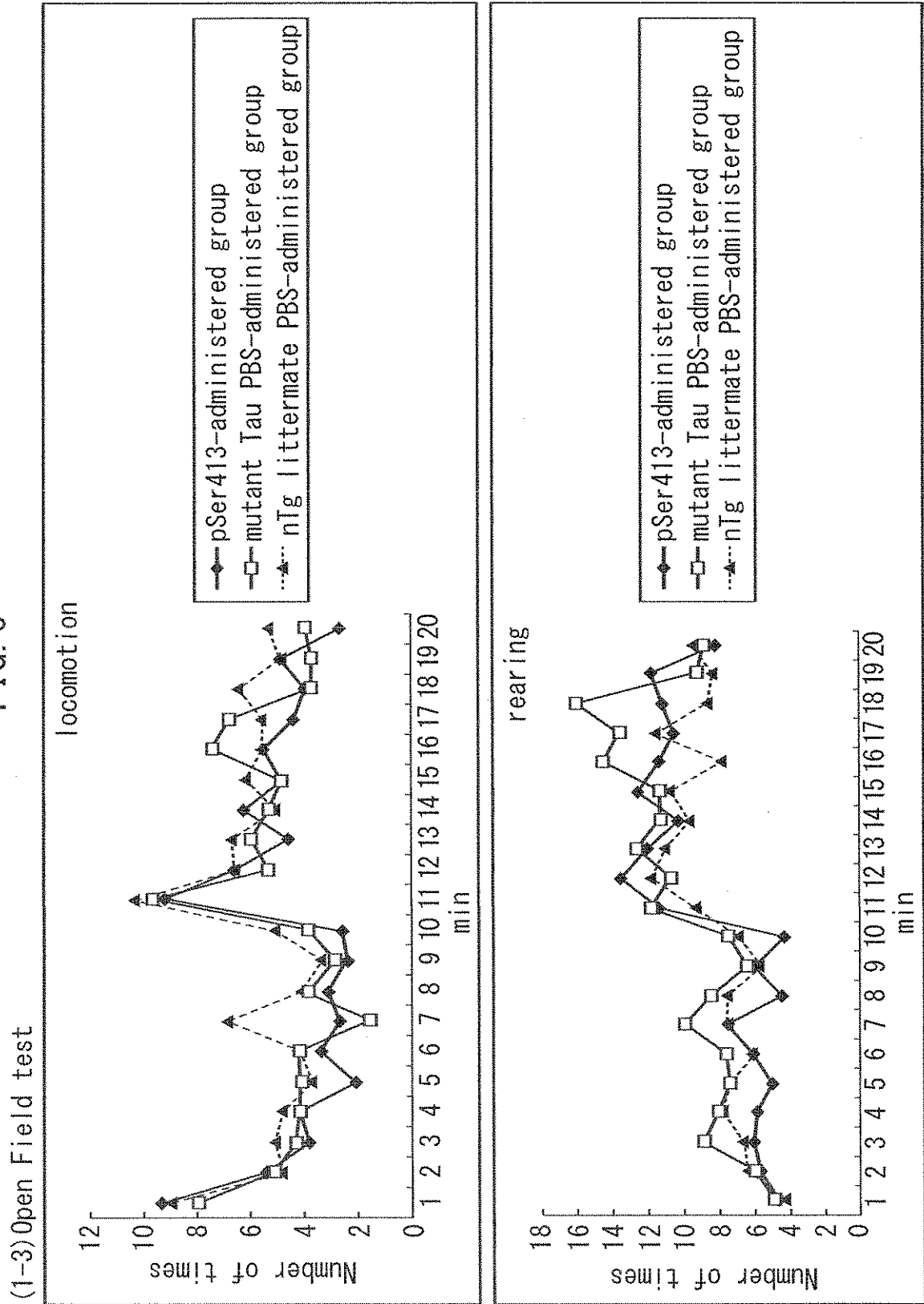


FIG. 7

(1-3) Open Field test

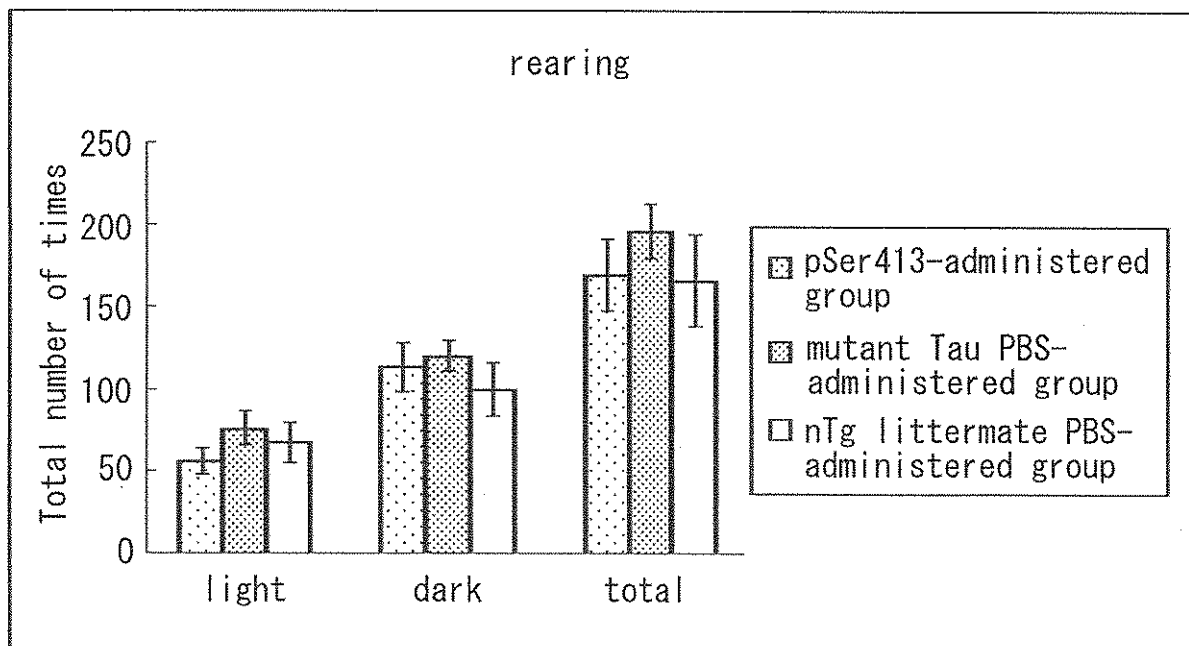
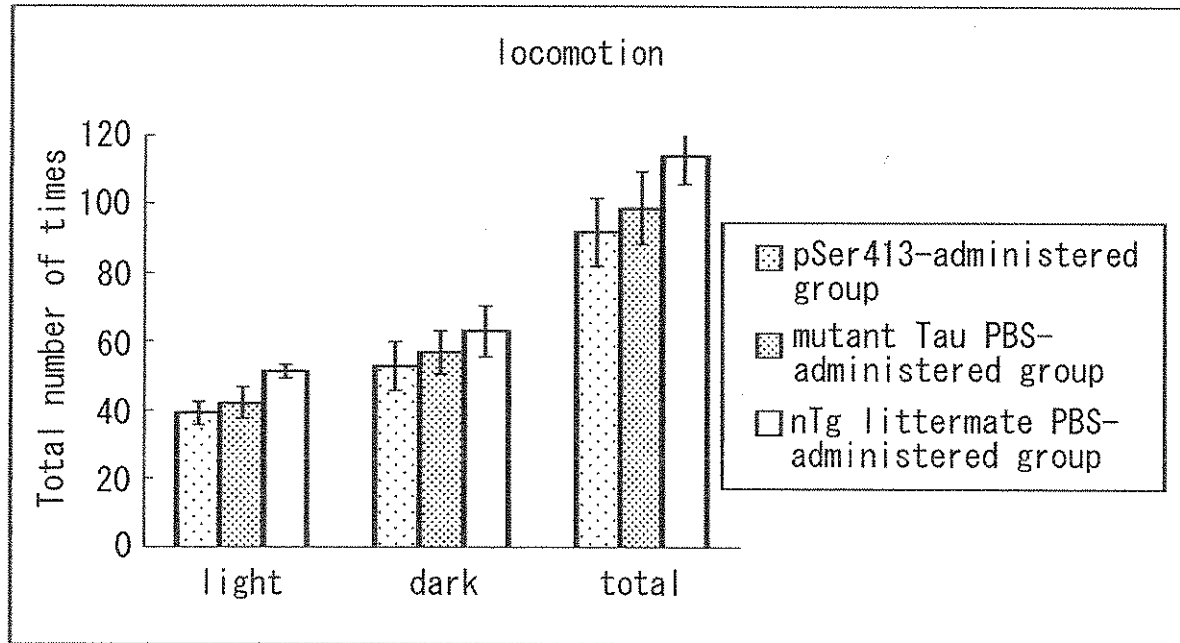
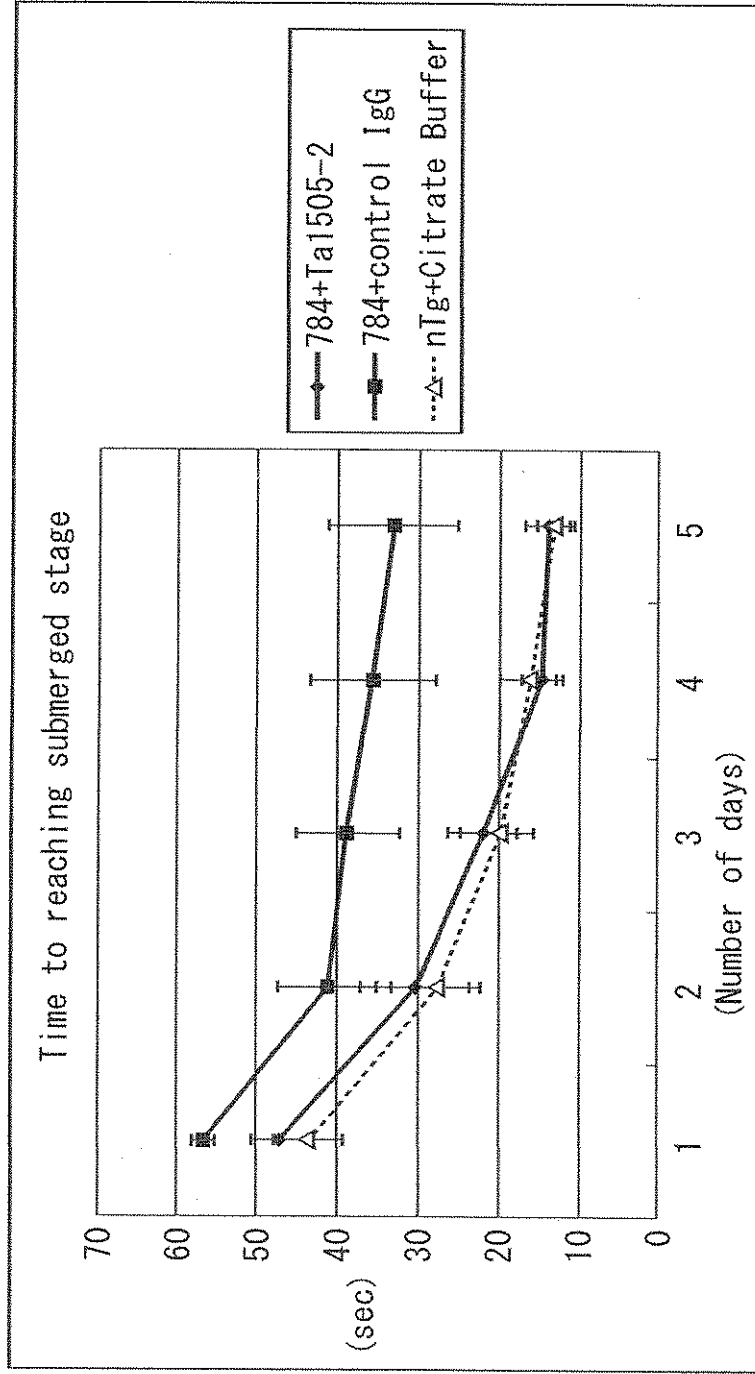


FIG. 8

(2-1) Trial test



Significant difference

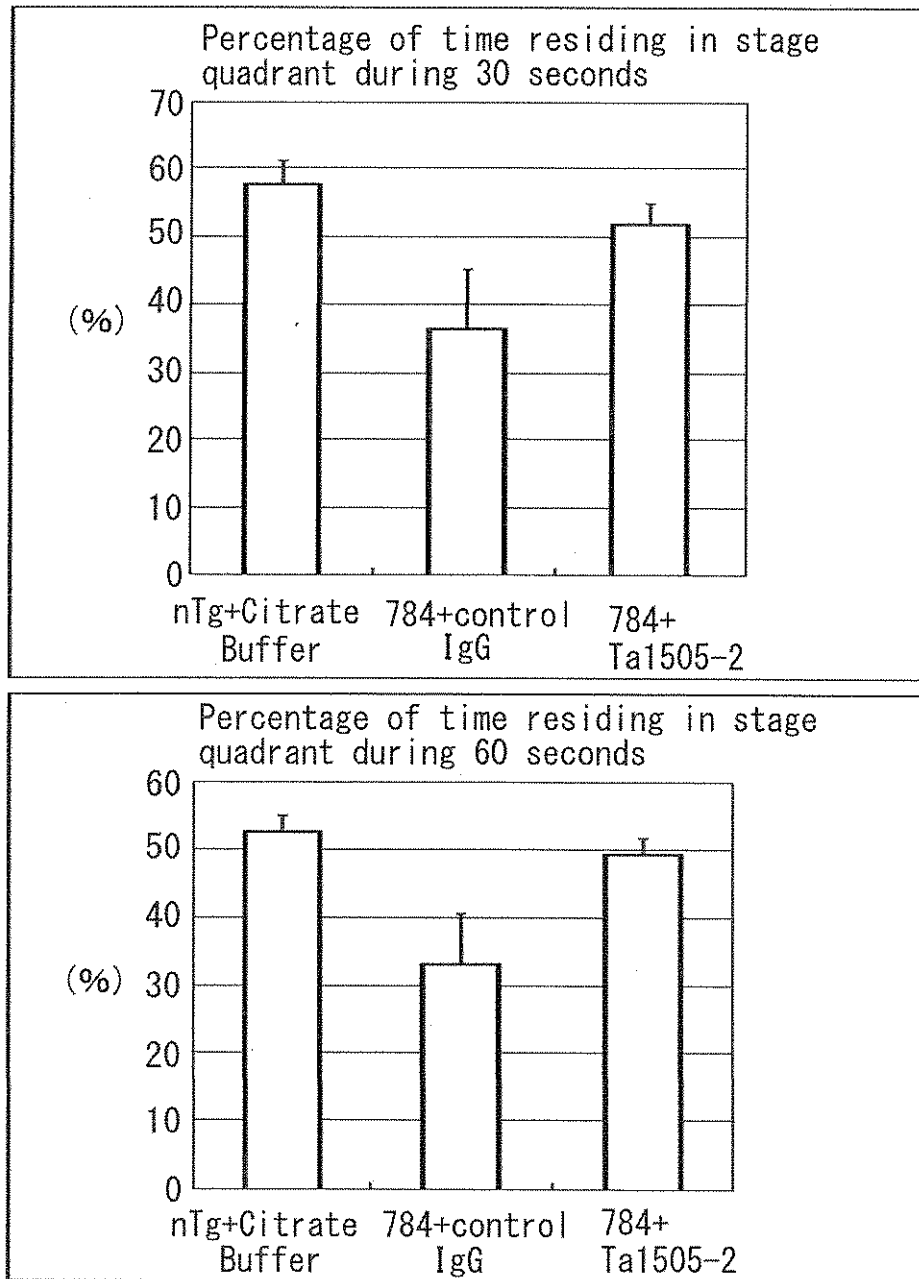
non Tg vs Tg(control IgG) : $p=0.0110$

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

Tg(Ta1505-2) vs Tg(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) : $p=0.273$

FIG. 10

(2-3) Open Field test

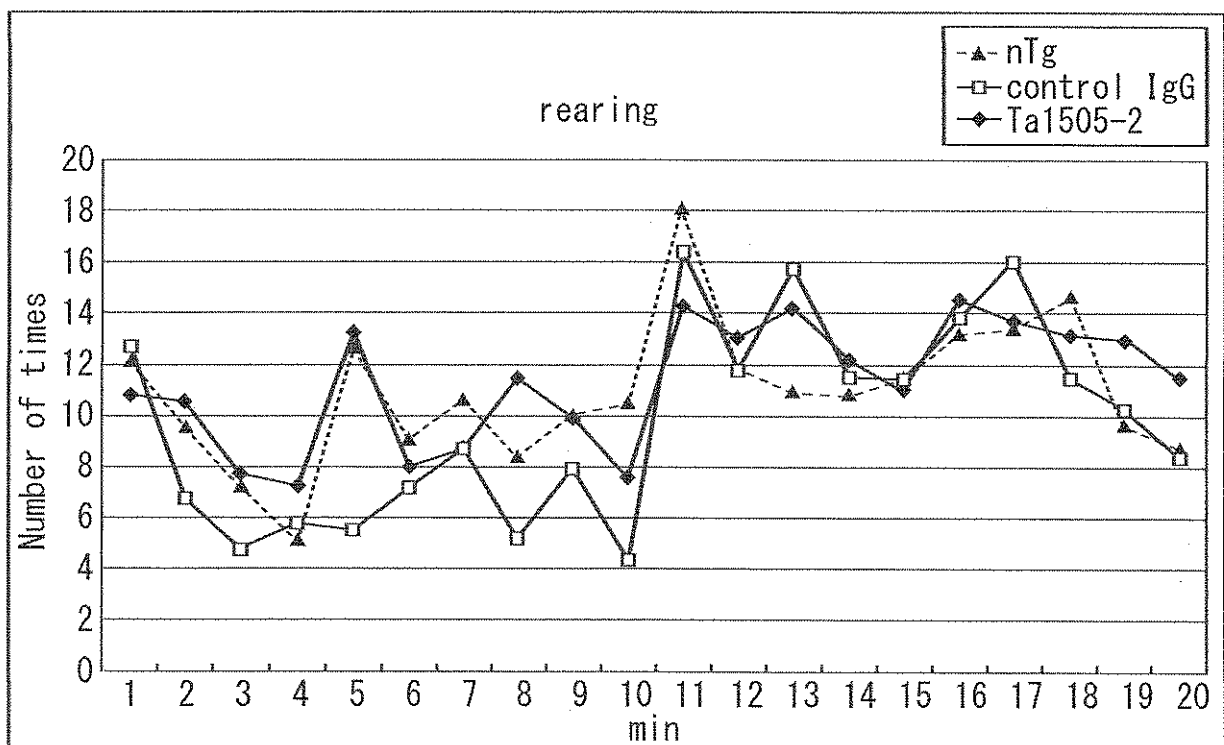
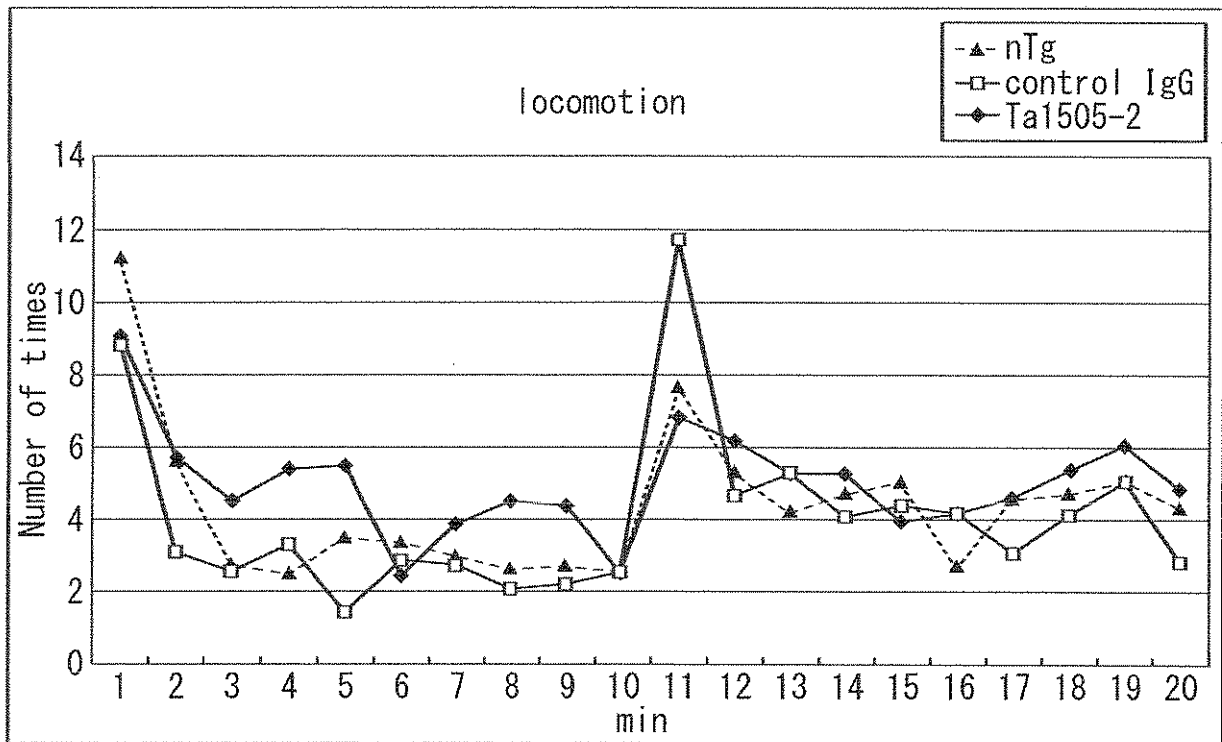
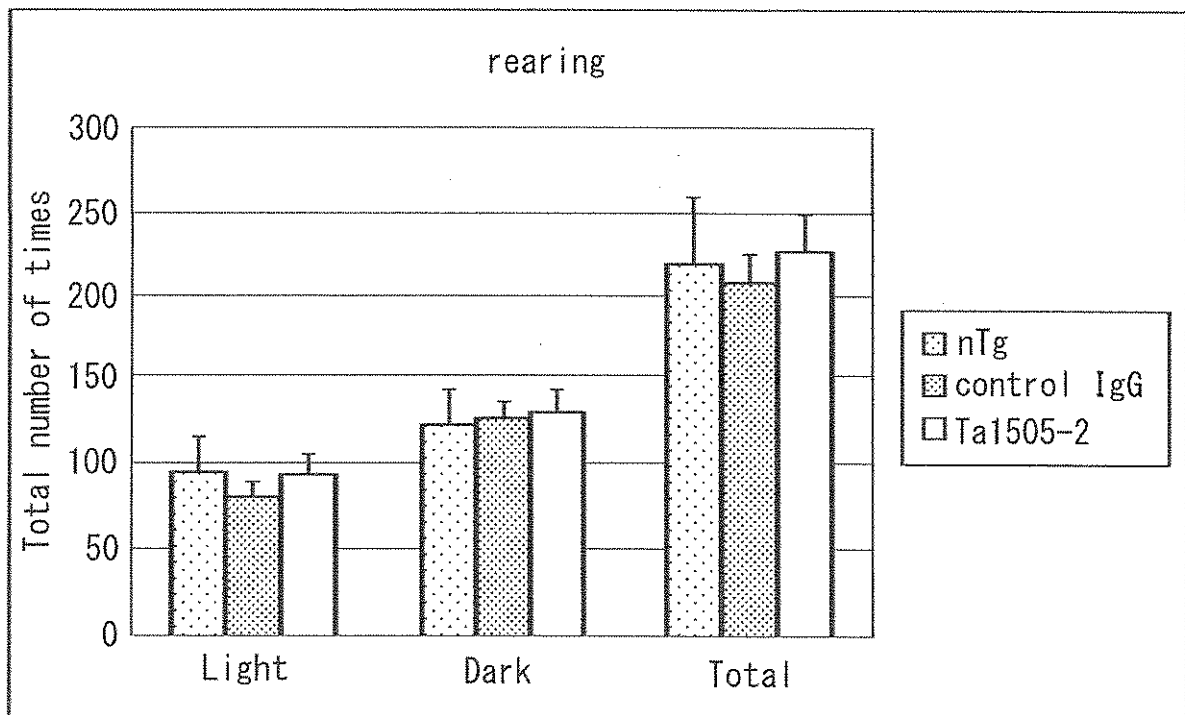
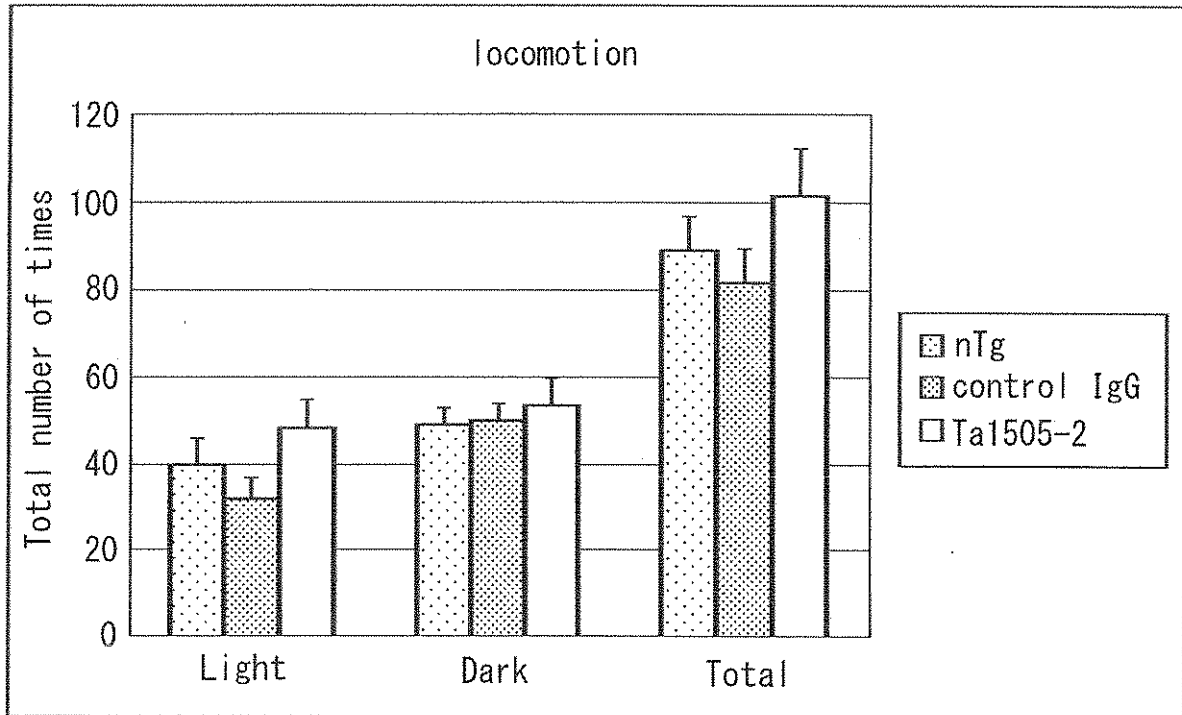


FIG. 11

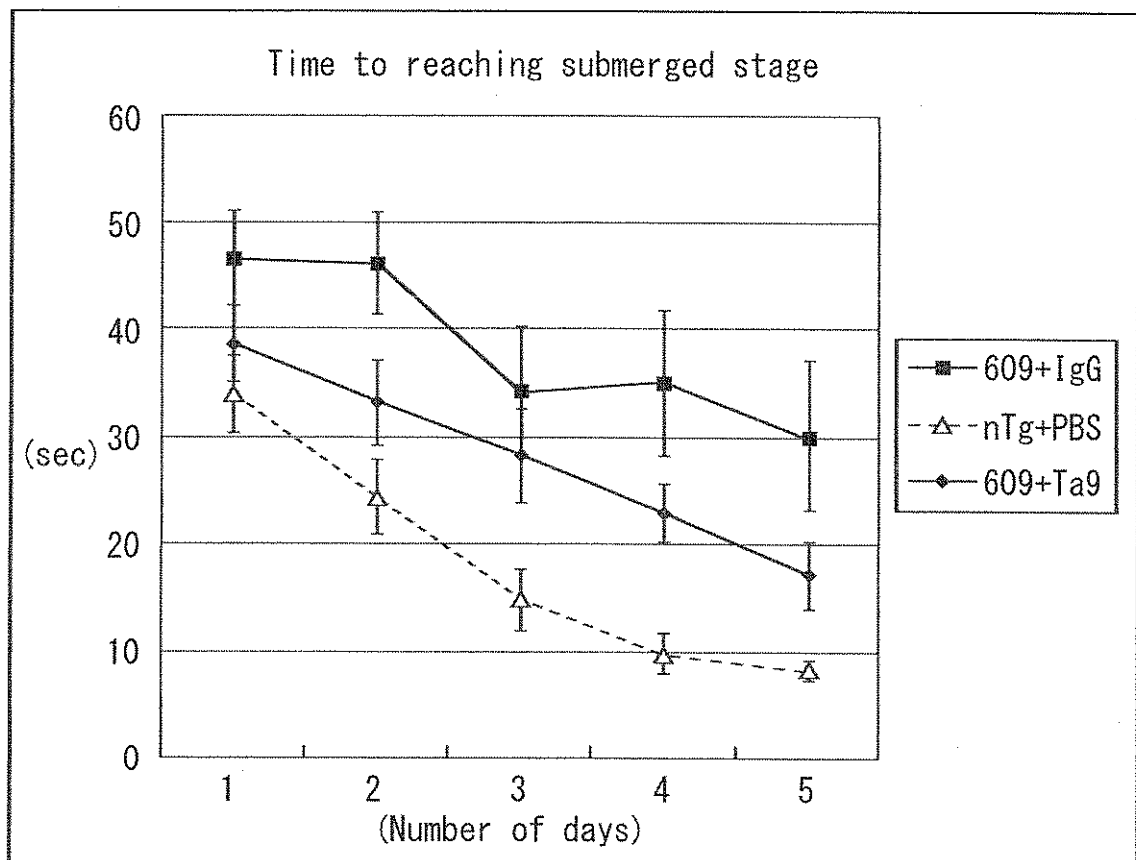
(2-3) Open Field test



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FIG. 12

(3-1) Trial test



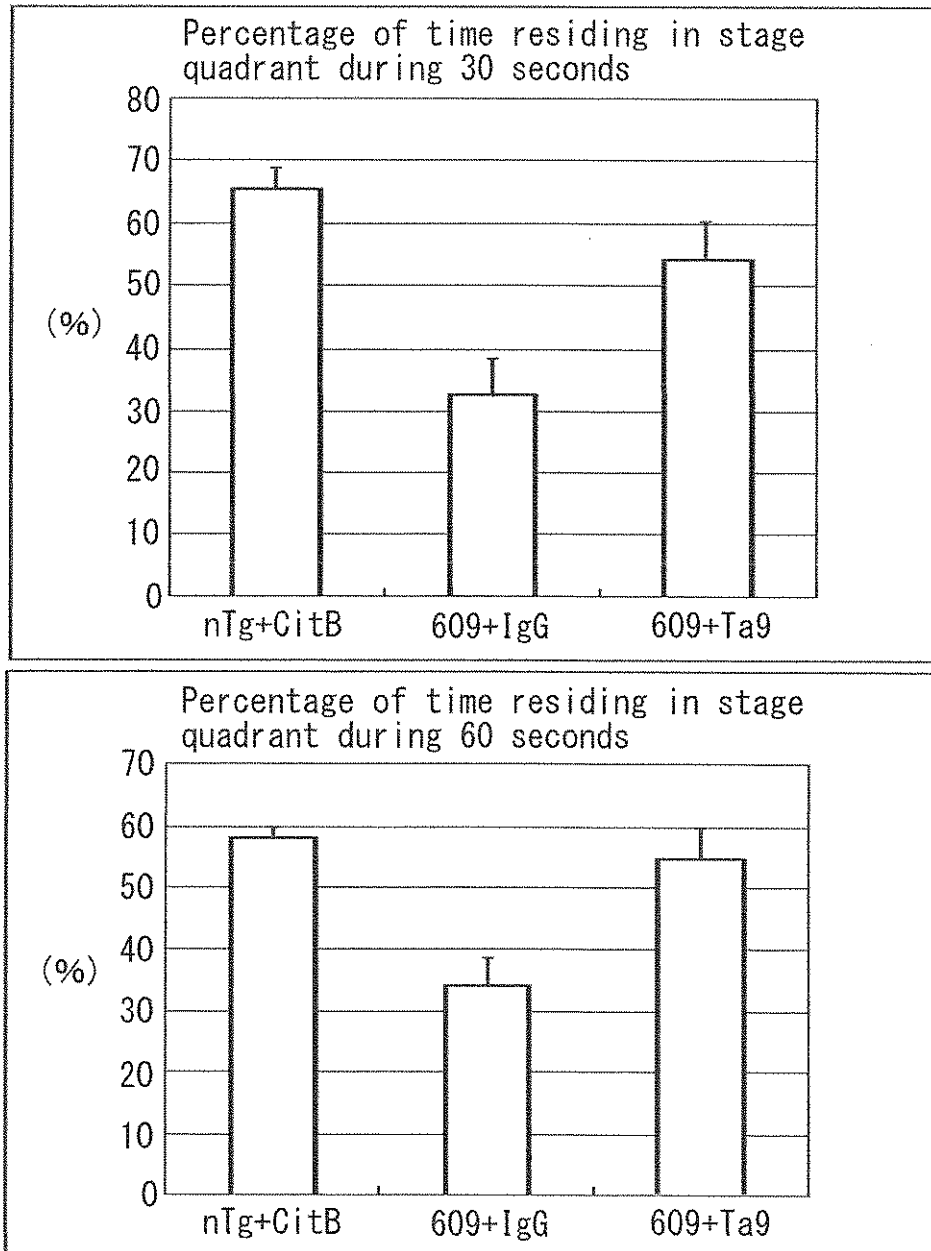
Significant difference

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

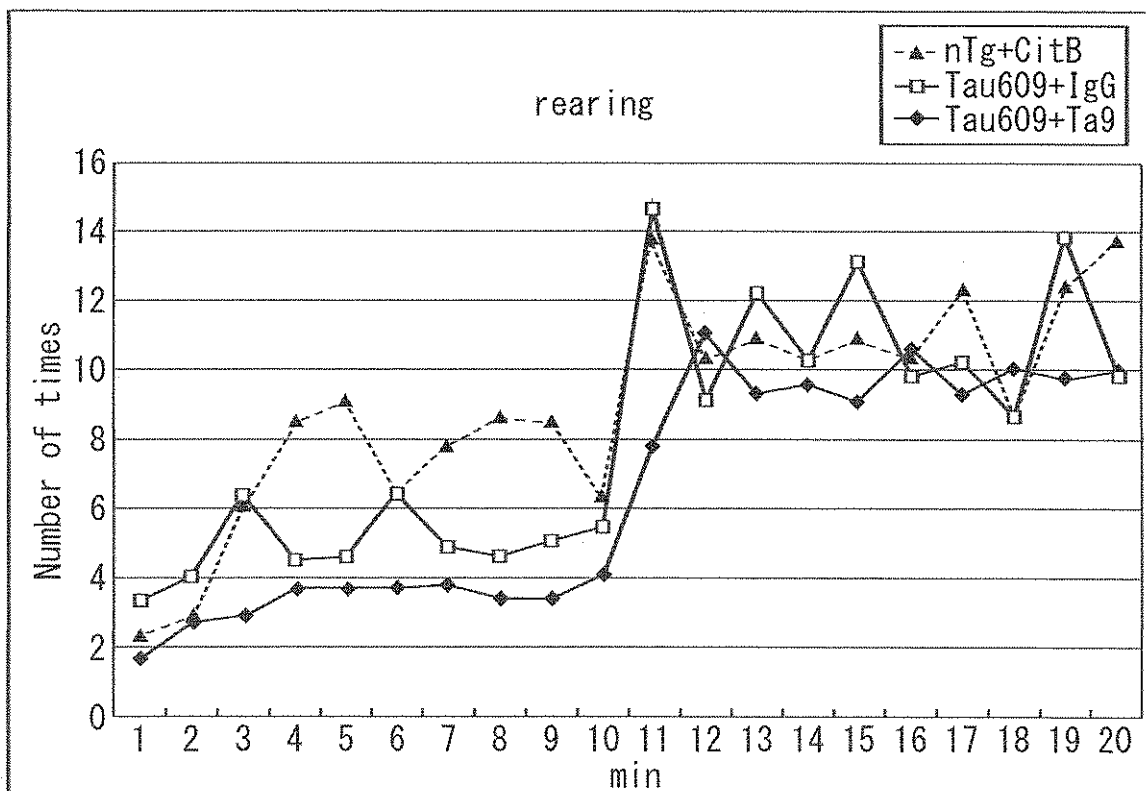
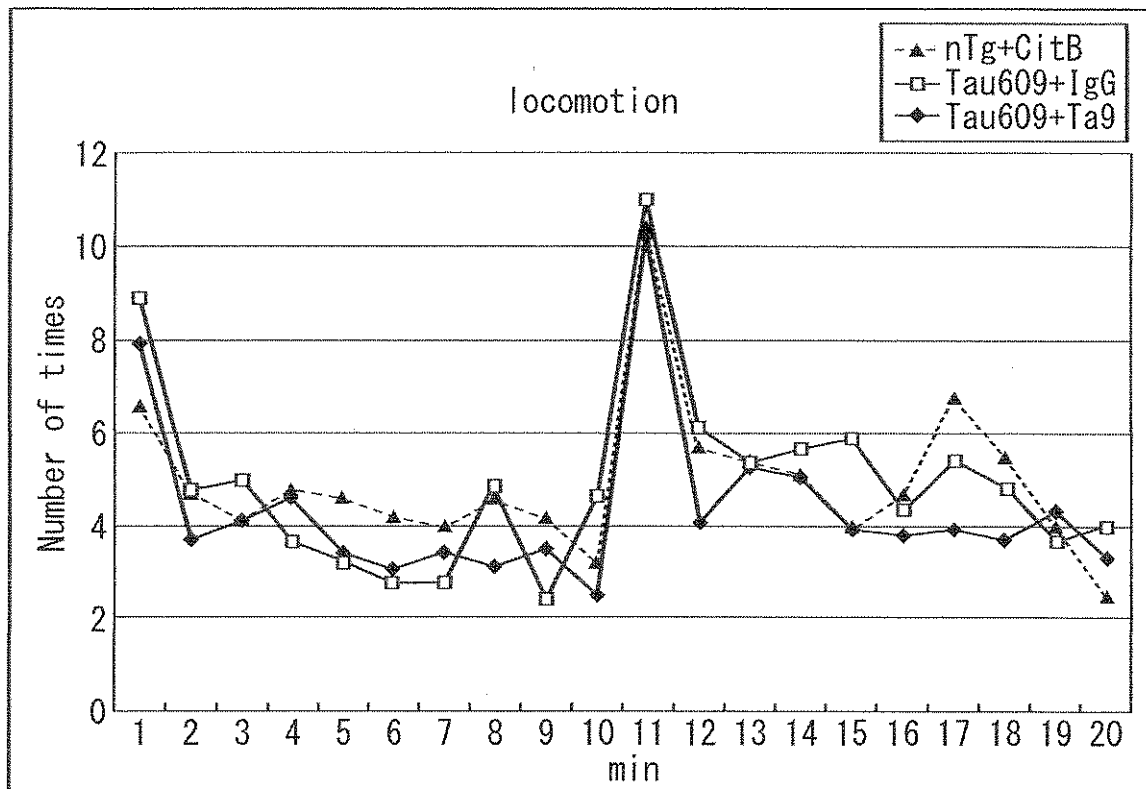


FIG. 15

(3-3) Open Field test

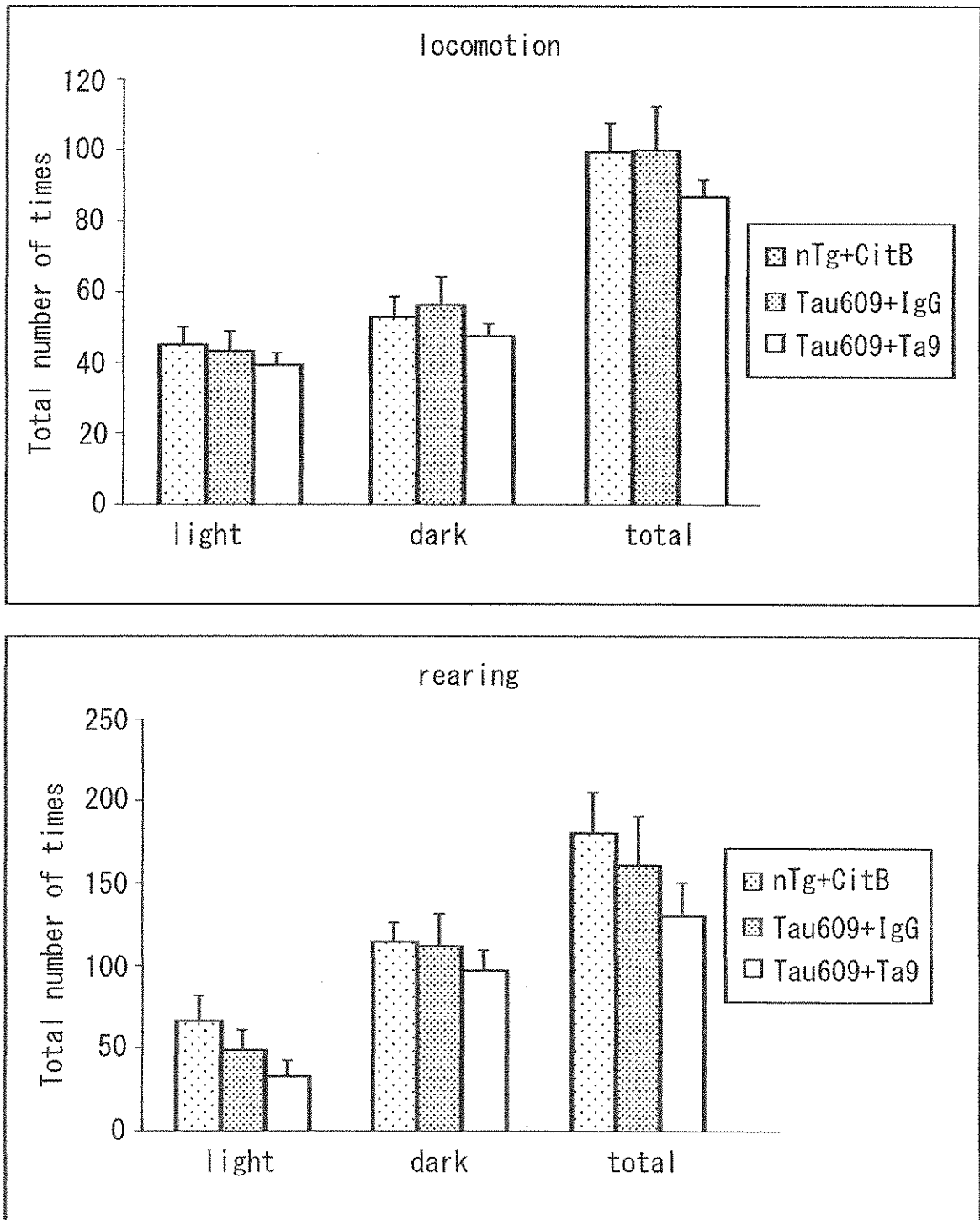
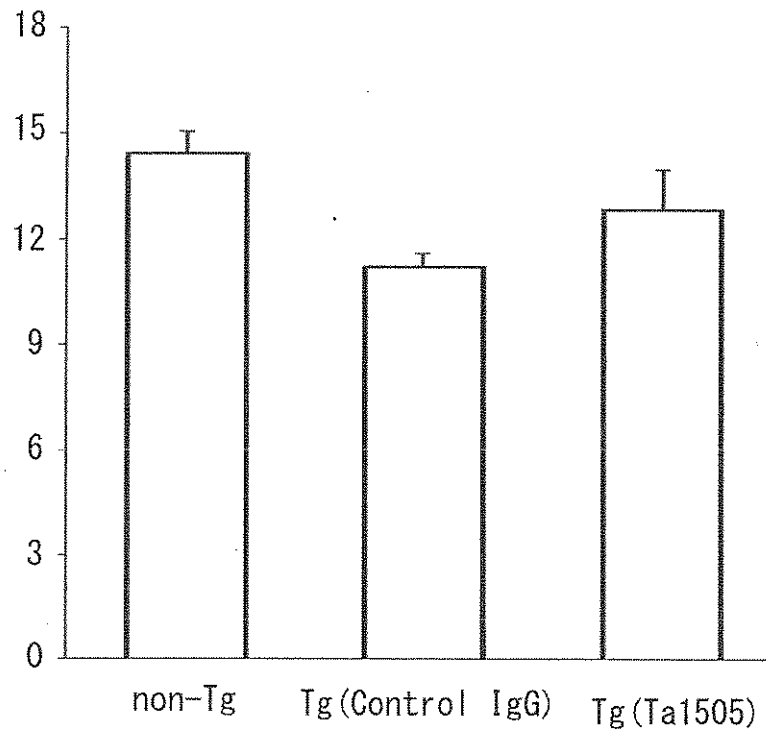


FIG. 16



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

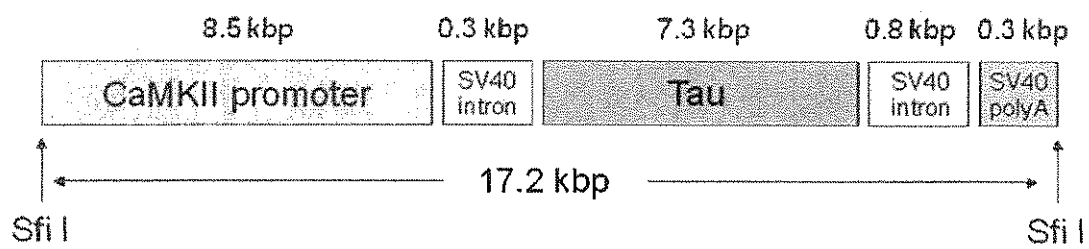
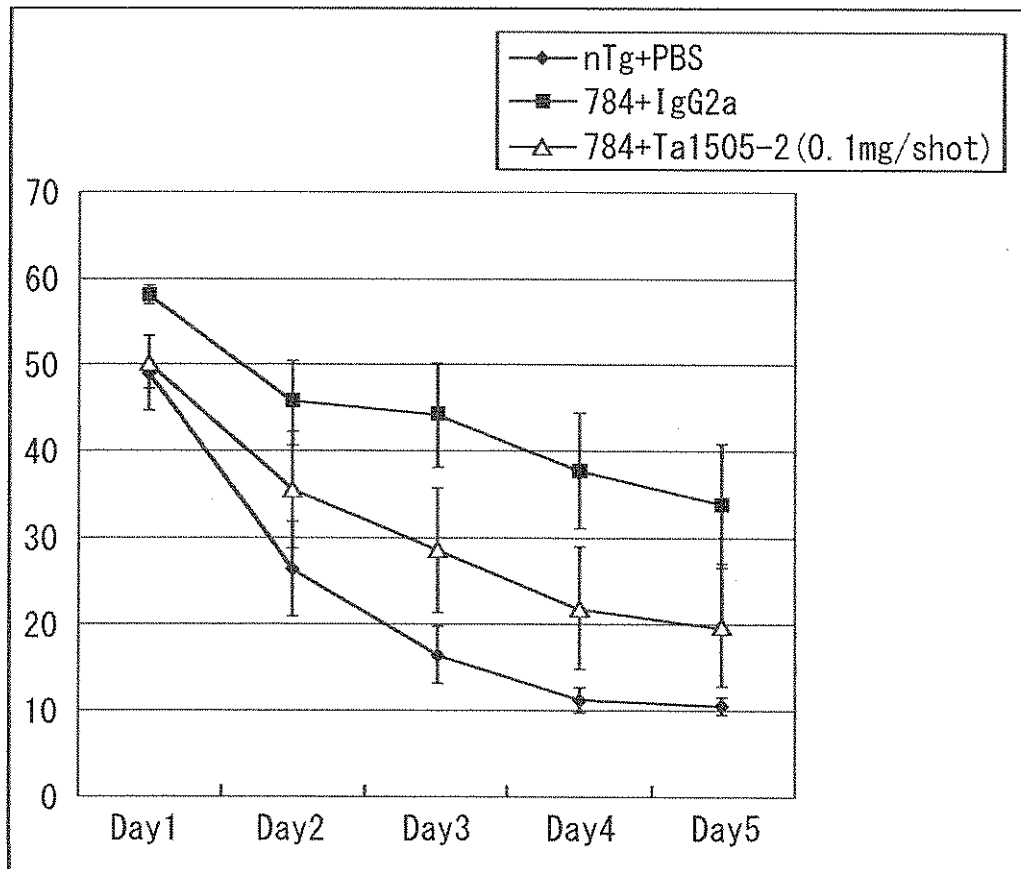


FIG. 18

(4-1) Trial test



nonTg vs Tg(Control IgG)

p=0.0025

nonTg vs Tg(Ta1505)

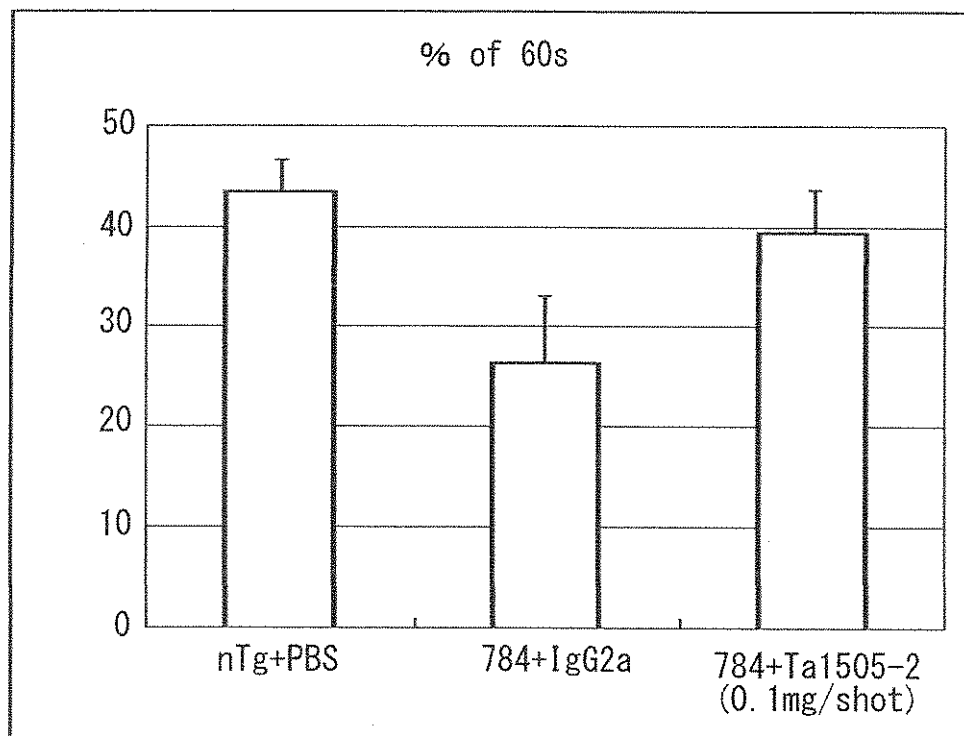
p=0.1926 (No significant difference)

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

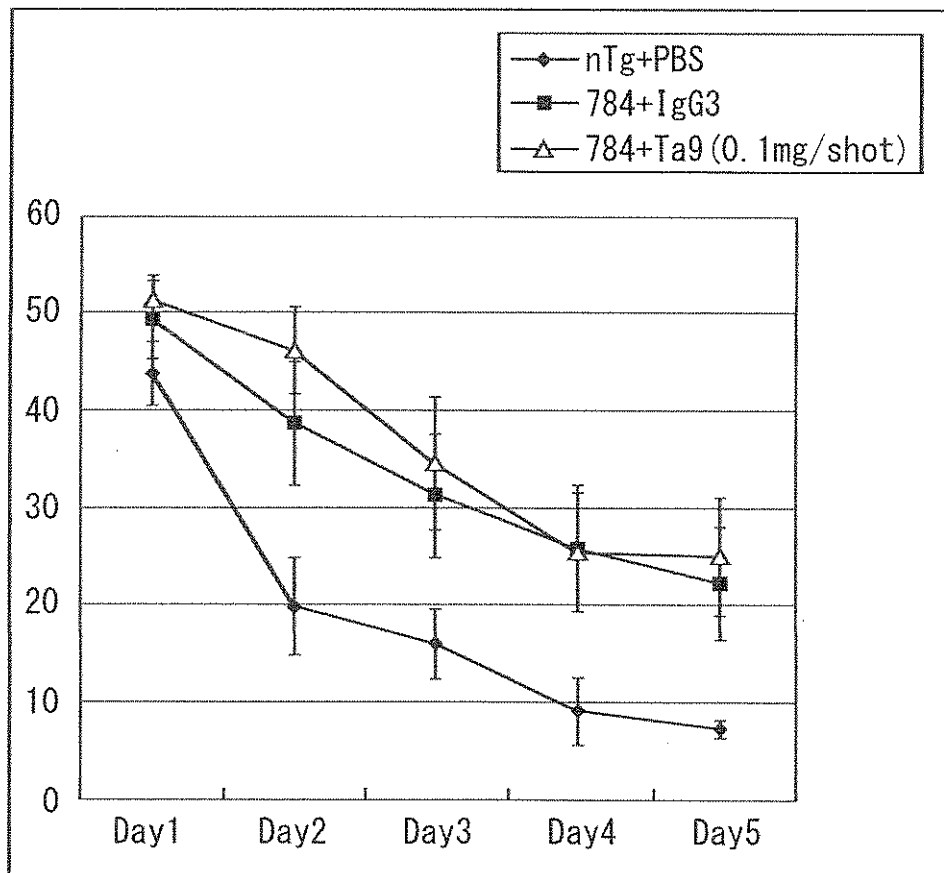
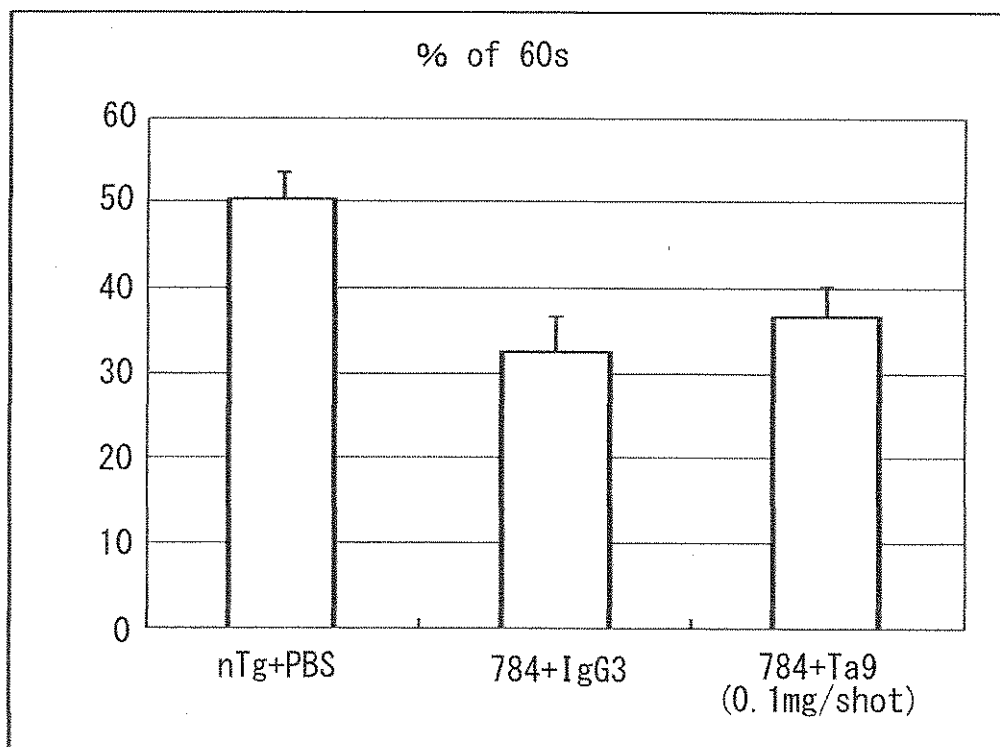
nonTg vs Tg(Control IgG) $p=0.0065$ nonTg vs Tg(Ta9) $p=0.0044$ Tg(Ta9) vs Tg(Control IgG) $p=0.8635$ (No significant difference)

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)

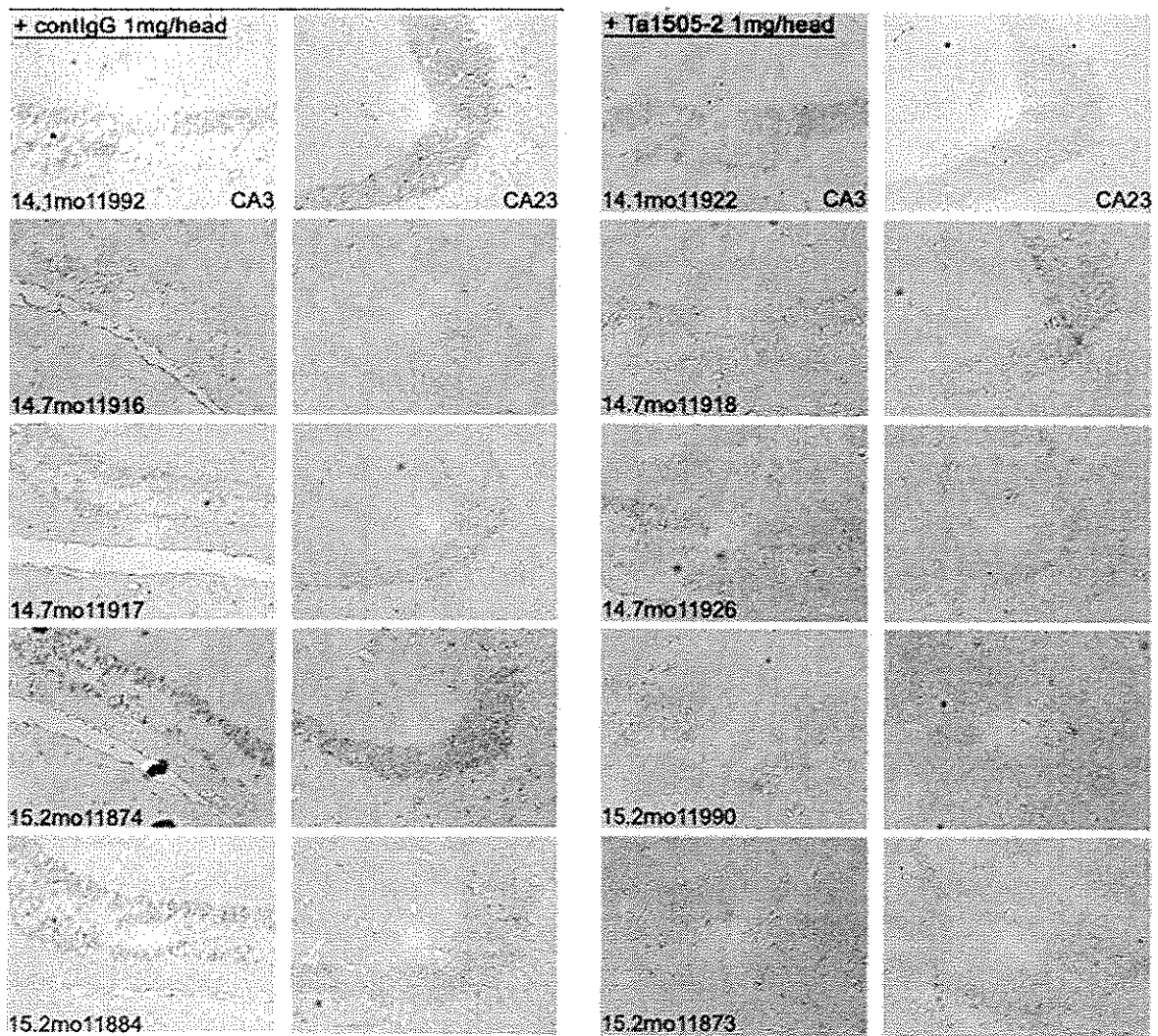


FIG. 23

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

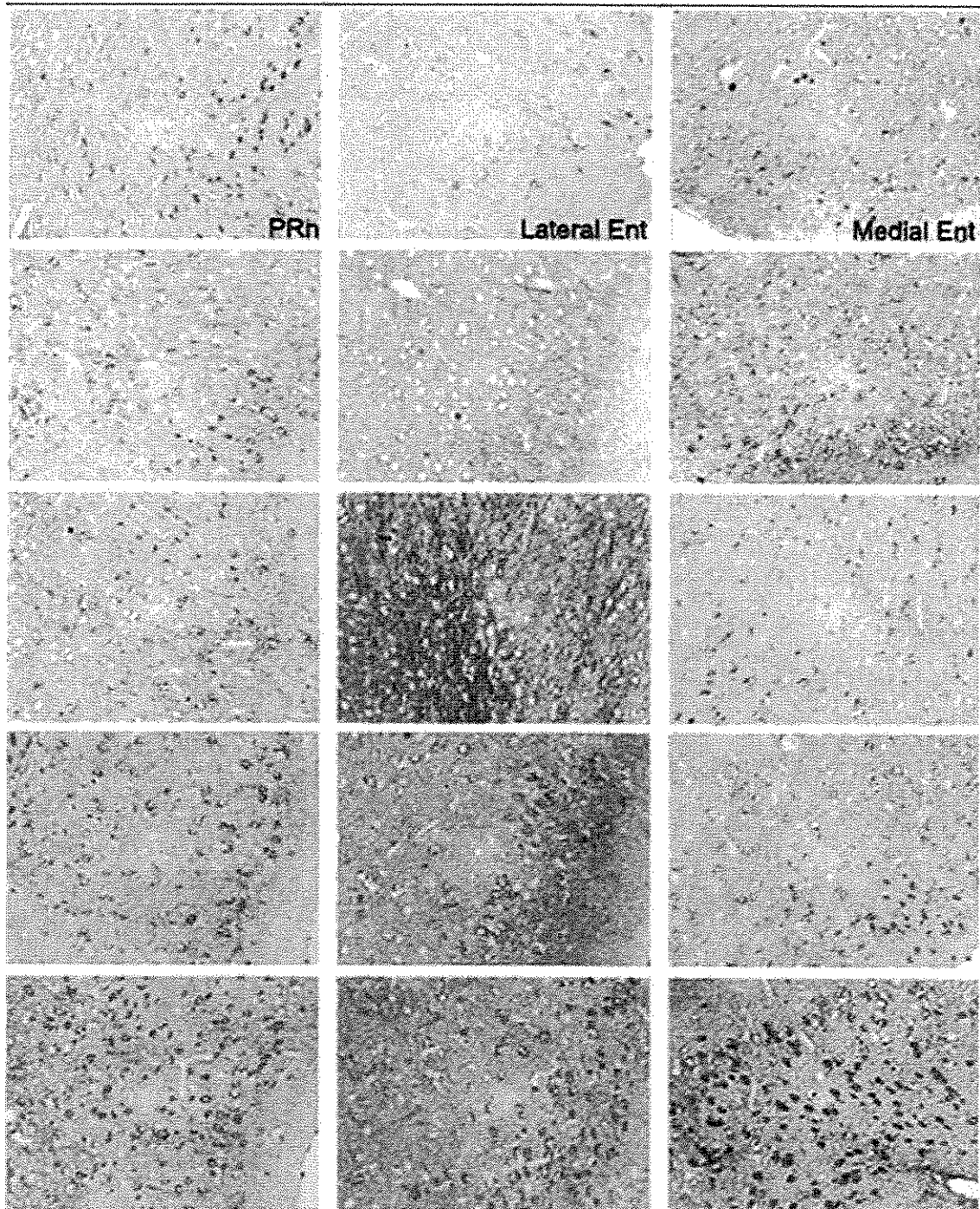


FIG. 24

Ta1505 administration (1mg/head)

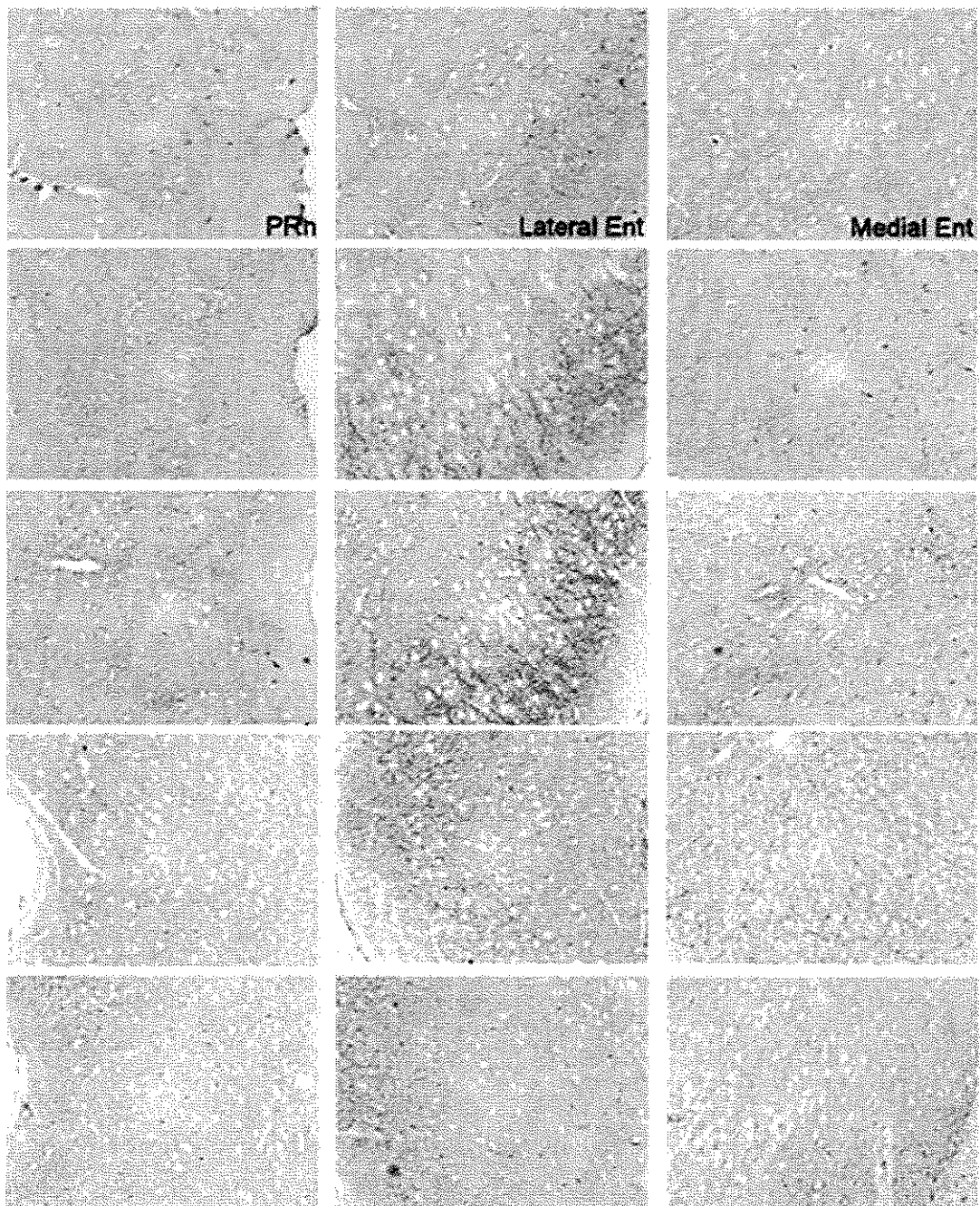


FIG. 25

Immunohistostaining of hippocampal region(AT8 stain)

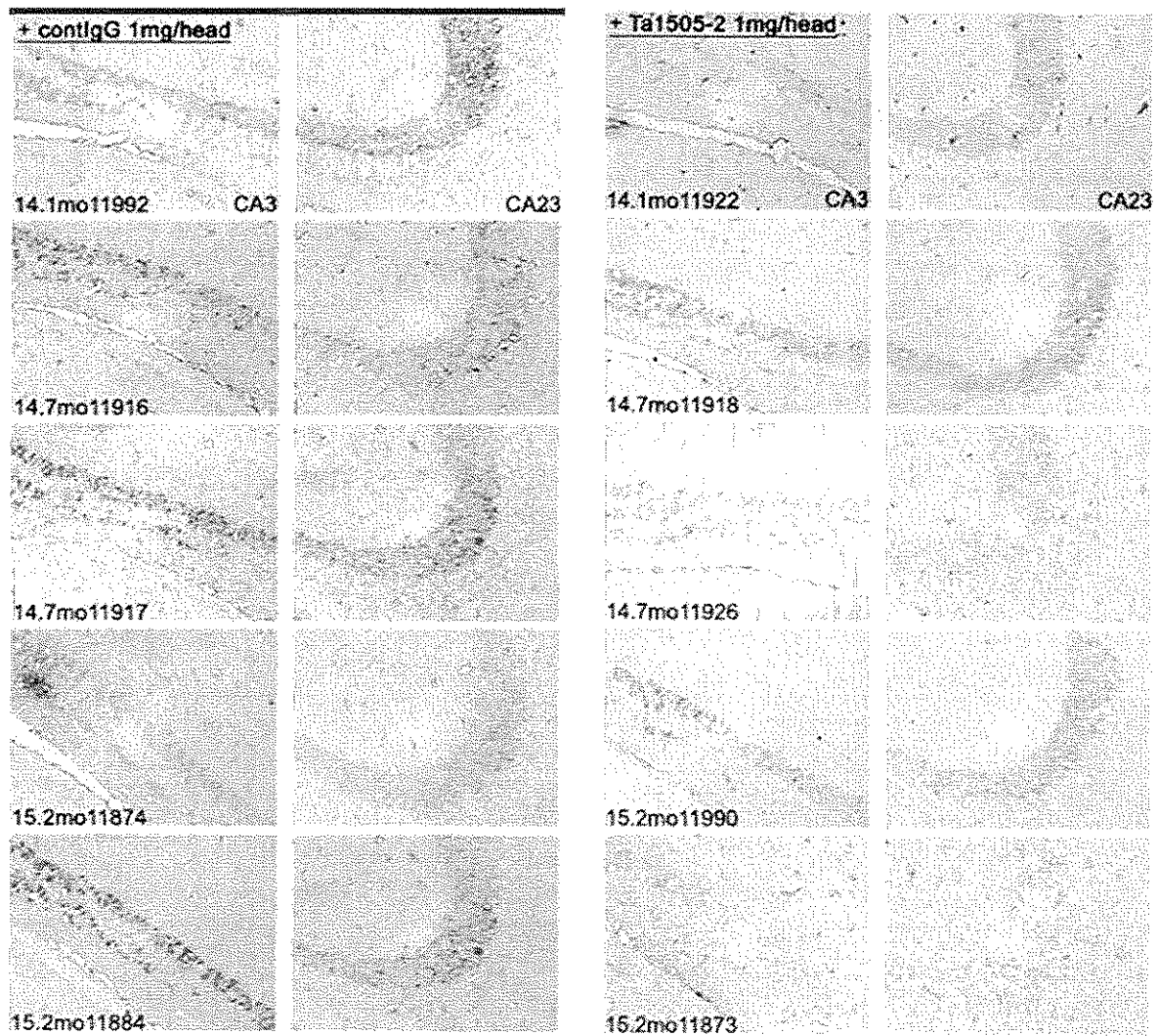


FIG. 26

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

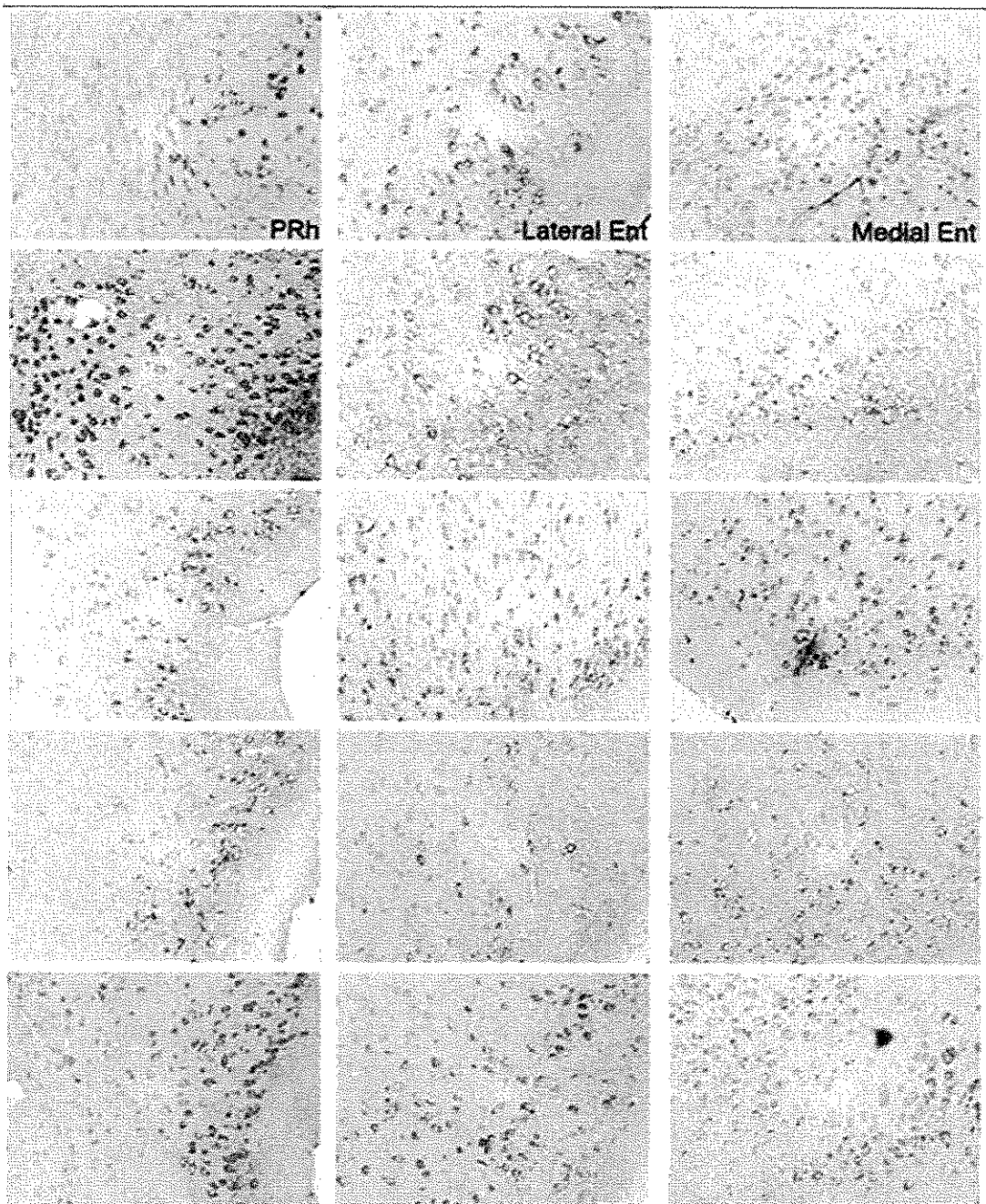


FIG. 27

Ta1505 administration(1mg/head)

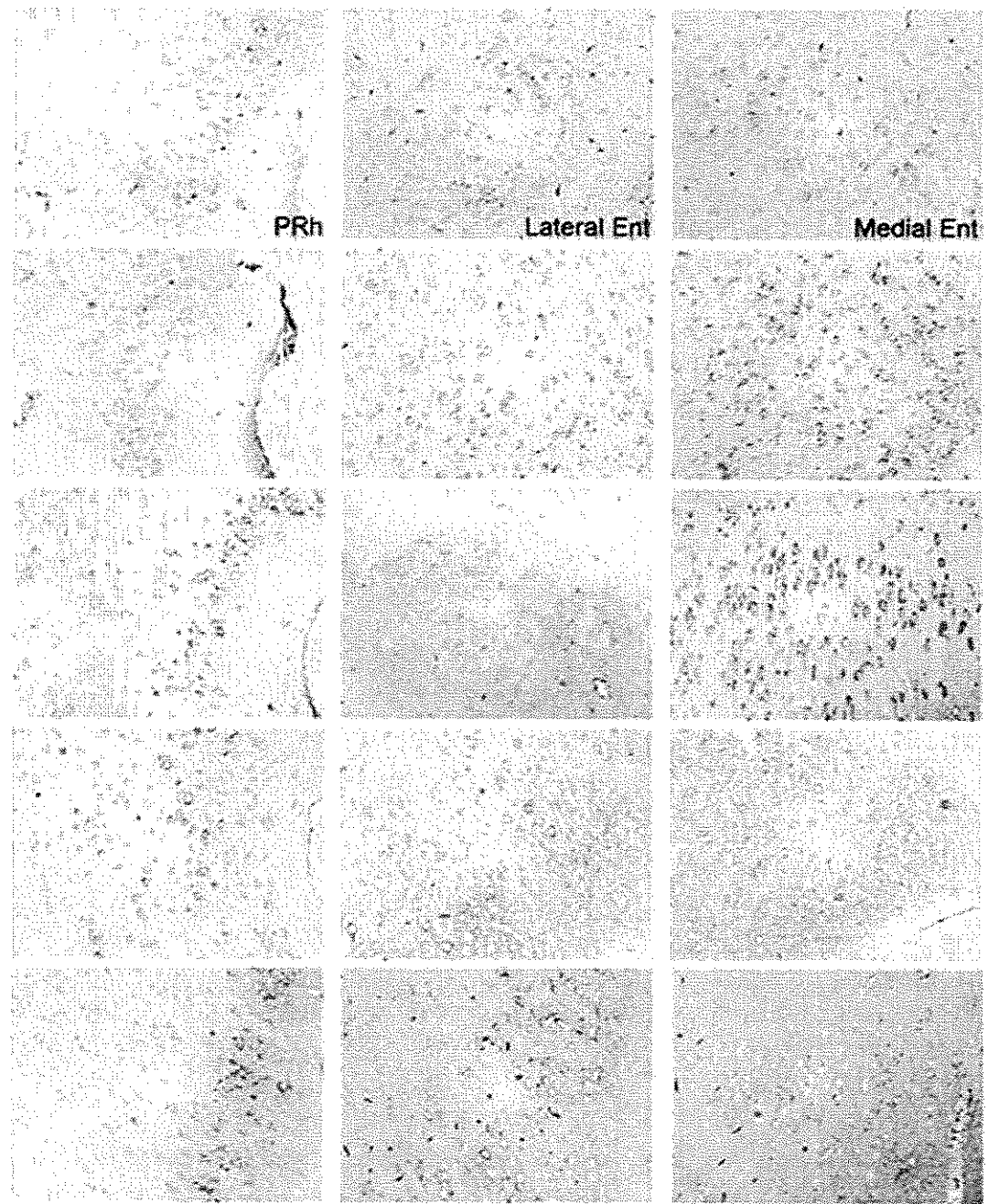
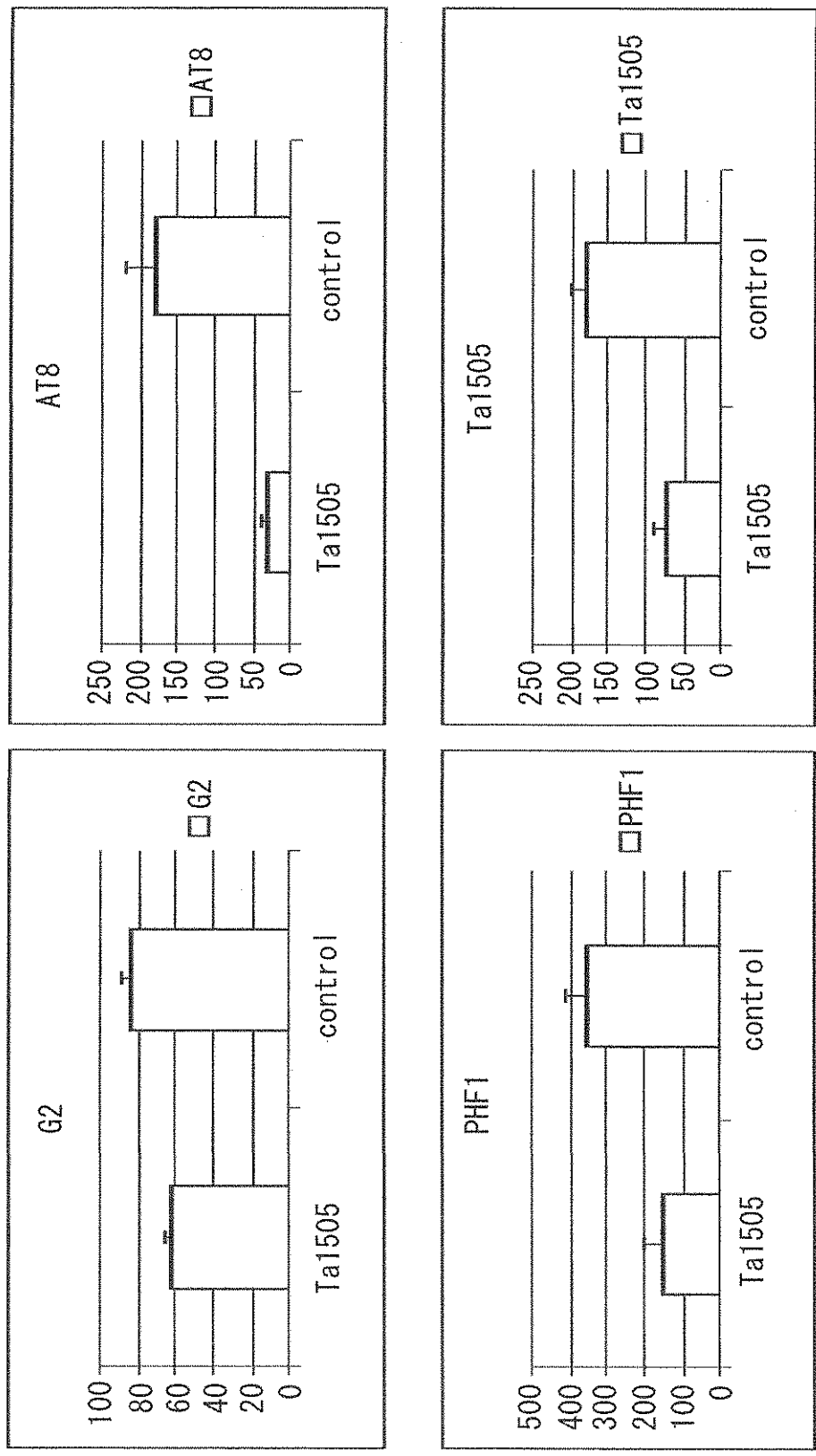


FIG. 28

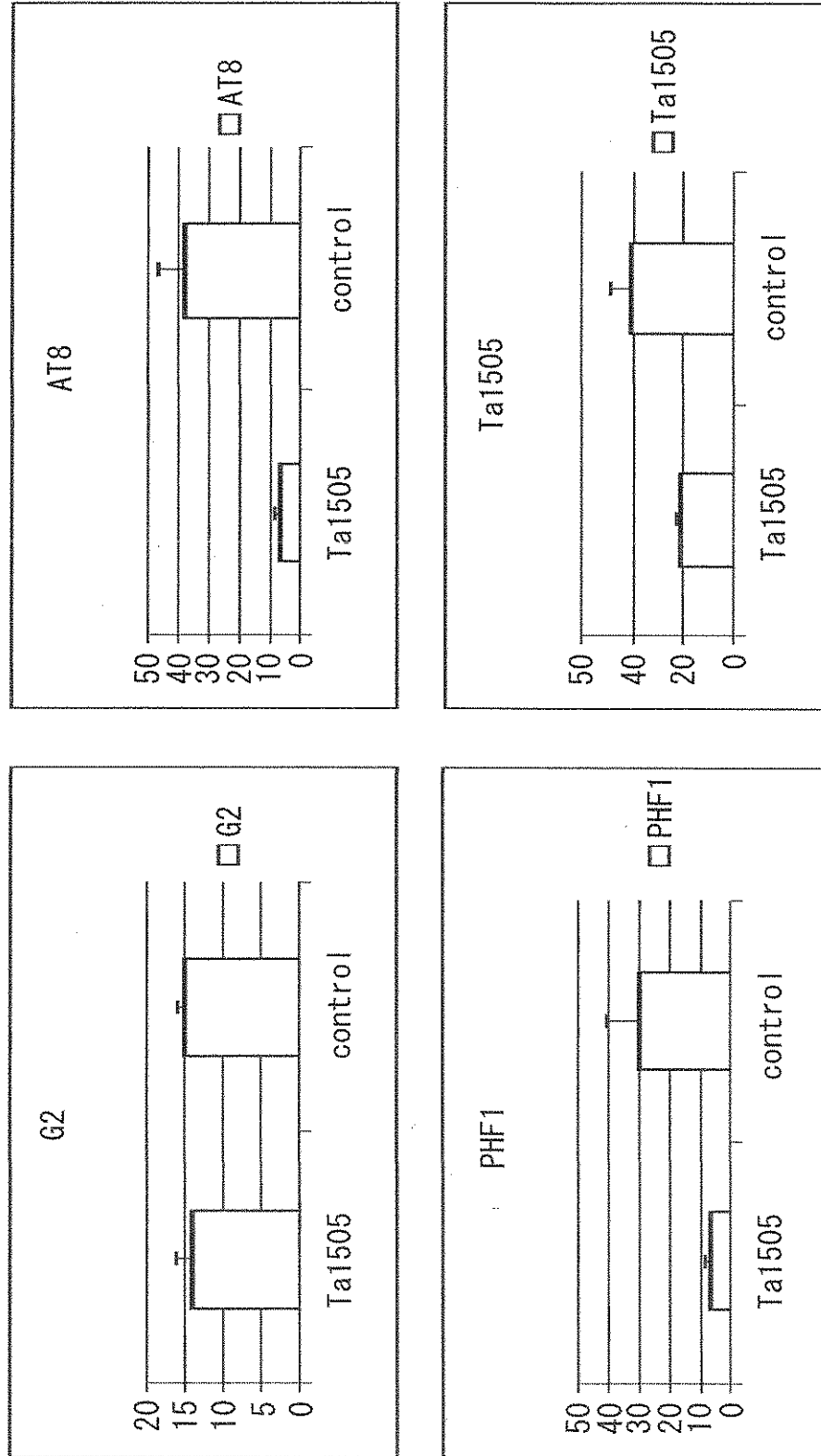
TBS-soluble fraction



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)