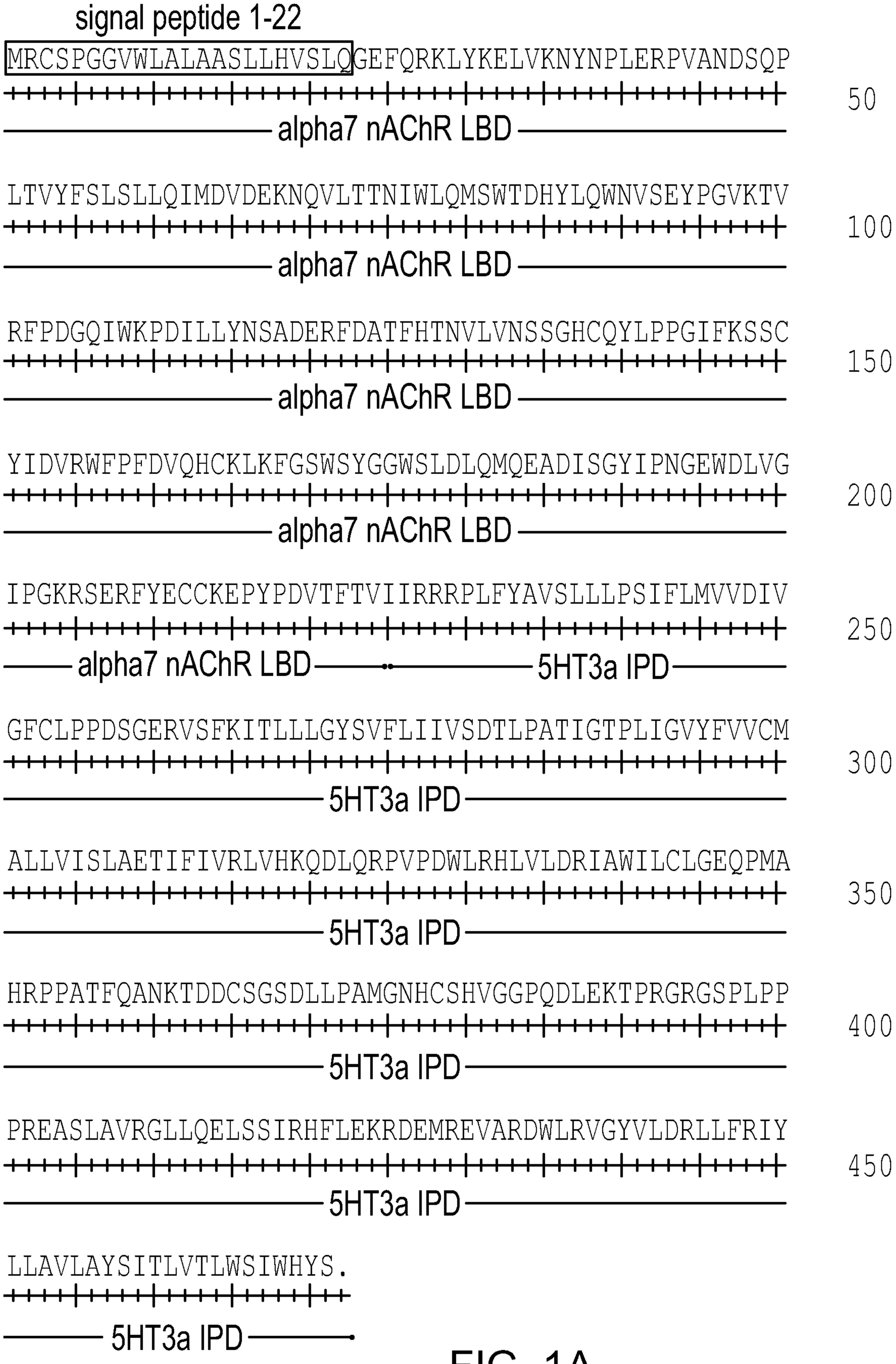

signal peptide 1-22
MRCSPGGVWLALAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQP
alpha7 nAChR LBD
50
LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTV
alpha7 nAChR LBD
100
RFPDGQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSC
alpha7 nAChR LBD
150
YIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVG
alpha7 nAChR LBD
200
IPGKRSERFYECCKEPYPDVTFTVIIRRRPLFYAVSLLLPSIFLMVVDIV
alpha7 nAChR LBD
5HT3a IPD
250
GFCLPPDSGERVSFKITLLLGYSVFLIIVSDTLPATIGTPLIGVYFVVCM
5HT3a IPD
300
ALLVISLAETIFIVRLVHKQDLQRPVPDWLRHLVLDRIAWILCLGEQPMA
5HT3a IPD
350
HRPPATFQANKTDDCSGSDLLPAMGNHCSHVGGPQDLEKTPRGRGSPLPP
5HT3a IPD
400
PREASLAVRGLLQELSSIRHFLEKRDEMREVARDWLRVGYVLDRLLFRIY
5HT3a IPD
450
LLAVLAYSITLVTLWSIWHYS.
5HT3a IPD

FIG. 1A

signal peptide 1-22
MRCSPGGVWLALAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQP
alpha7 nAChR LBD
50
LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTV
alpha7 nAChR LBD
100
RFPDGQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSC
alpha7 nAChR LBD
150
YIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVG
alpha7 nAChR LBD
200
IPGKRSERFYECCKEPYPDVTFTVTMRRRMGYYLIQMYIPSLLIVILSWI
alpha7 nAChR LBD
GlyR IPD
250
SFWINMDAAPARVGLGITTVLTMTTQSSGSRASLPKVSYVKAIDIWMAVC
GlyR IPD
300
LLFVFSALLEYAAVNFVSRQHKELLRFRRKRRHHKEDEAGEGRFNFSAYG
GlyR IPD
350
MGPACLQAKDGISVKGANNSNTTNPPPAPSKSPEEMRKLFIQRAKKIDKI
GlyR IPD
400
SRIGFPMAFLIFNMFYWIIYKIVRREDVHNQ.
GlyR IPD

FIG. 1B

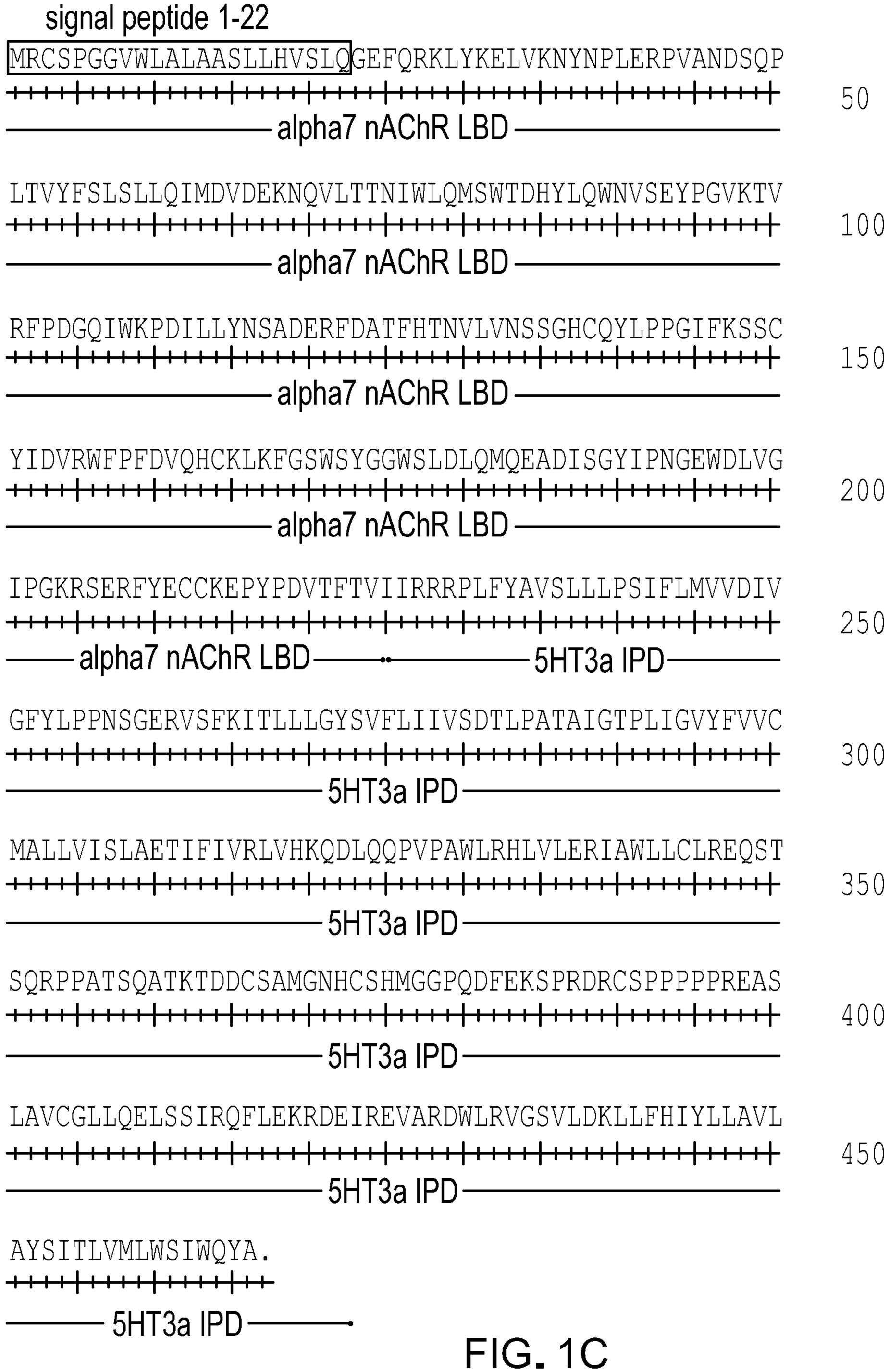

signal peptide 1-22
MRCSPGGVWLALAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQP
alpha7 nAChR LBD
50
LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTV
alpha7 nAChR LBD
100
RFPDGQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSC
alpha7 nAChR LBD
150
YIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVG
alpha7 nAChR LBD
200
IPGKRSERFYECCKEPYPDVTFTVIIRRRPLFYAVSLLLPSIFLMVVDIV
alpha7 nAChR LBD
5HT3a IPD
250
GFYLPPNSGERVSFKITLLLGYSVFLIIVSDTLPATAIGTPLIGVYFVVC
5HT3a IPD
300
MALLVISLAETIFIVRLVHKQDLQQPVPAWLRHLVLERIAWLLCLREQST
5HT3a IPD
350
SQRPPATSQATKTDDCSAMGNHCSHMGGPQDFEKSPRDRCSPPPPPREAS
5HT3a IPD
400
LAVCGLLQELSSIRQFLEKRDEIREVARDWLRVGSVLDKLLFHIYLLAVL
5HT3a IPD
450
AYSITLVMLWSIWQYA.
5HT3a IPD

FIG. 1C

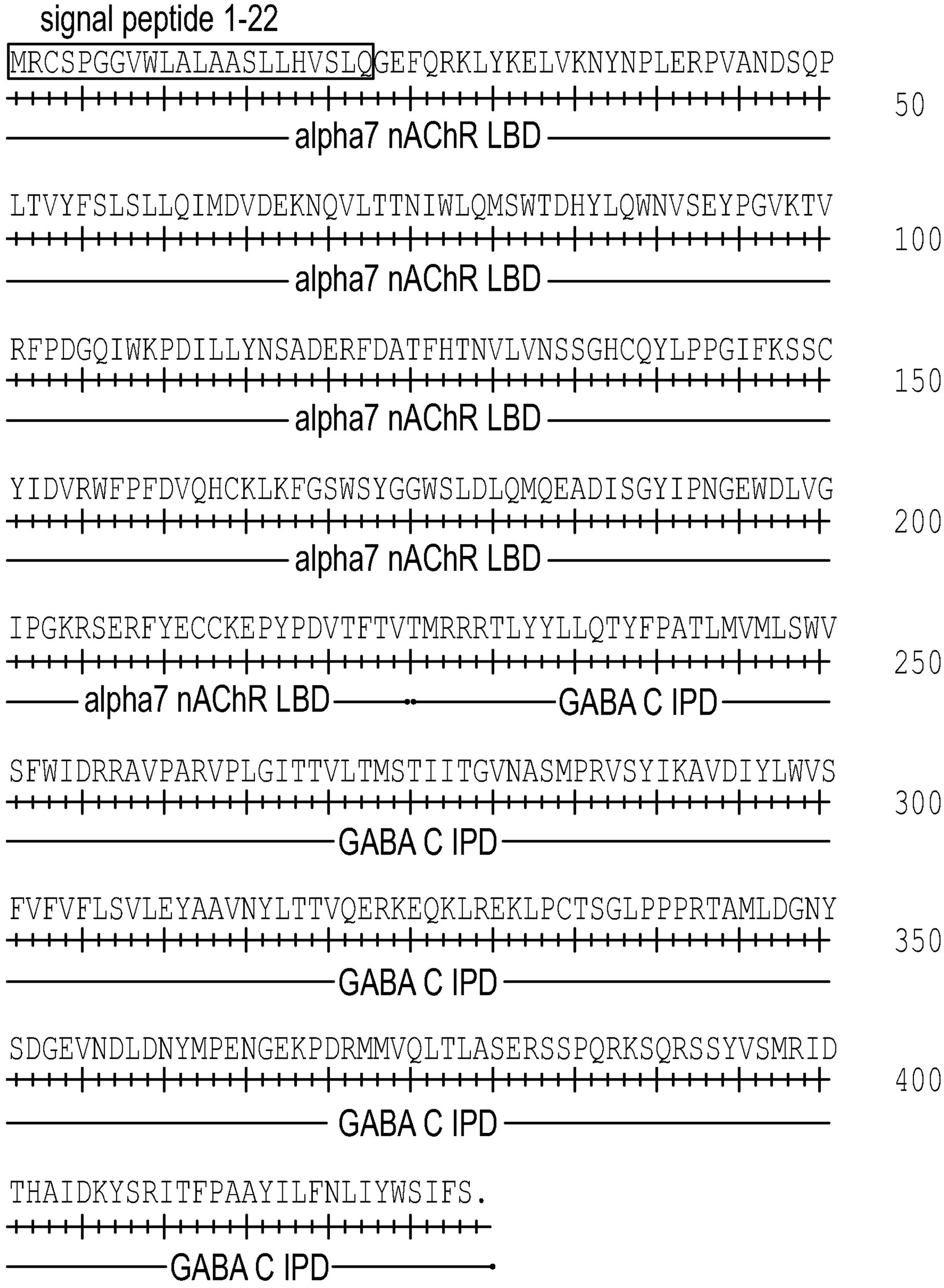

signal peptide 1-22
MRCSPGGVWLALAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQP
alpha7 nAChR LBD
50
LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTV
alpha7 nAChR LBD
100
RFPDGQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSC
alpha7 nAChR LBD
150
YIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVG
alpha7 nAChR LBD
200
IPGKRSERFYECCKEPYPDVTFTVTMRRRTLYYLLQTYFPATLMVMLSWV
alpha7 nAChR LBD
GABA C IPD
250
SFWIDRRAVPARVPLGITTVLTMSTIITGVNASMPRVSYIKAVDIYLWVS
GABA C IPD
300
FVFVFLSVLEYAAVNYLTTVQERKEQKLREKLPCTSGLPPPRTAMLDGNY
GABA C IPD
350
SDGEVNDLDNYMPENGEKPDRMMVQLTLASERSSPQRKSQRSSYVSMRID
GABA C IPD
400
THAIDKYSRITFPAAYILFNLIYWSIFS.
GABA C IPD

FIG. 1D

signal peptide 1-22

MGGGRGGIWLALAAALLHVSLQGEFQRRLYKELVKNYNPLERPVANDSQP

50

LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNMSEYPGVKNV

100

RFPDGQIWKPDILLYNSADERFDATFHTNVGVNASGHCQYLPPGIFKSSC

150

YIDVRWFPFDVQQCKLKFGSWSYGGWSLDLQMQEADISSYIPNGEWDLMG

200

IPGKRNEKFYECCKEPYPDVTYTVTMRRRTLYYGLNLLIPCVLISALALL

250

VFLLPADSGEKISLGITVLLSLTTFMLLVAEIMPATSDSVPLIAQYFAST

300

MIIVGLSVVVTVIVLRYHHHDPDGGKMPKWTRIILLNWCAWFLRMKRPGE

350

DKVRPACQHKPRRCSLASVELSAGAGPPTSNGNLLYIGFRGLEGMHCAPT

400

PDSGVVCGRLACSPTHDEHLMHGAHPSDGDPDLAKILEEVRYIANRNRCQ

450

DESEVICSEWKFAACVVDPLCLMAFSVFTIICTIGILMSAPNFVEAVSKD

500

FA.

FIG. 1E

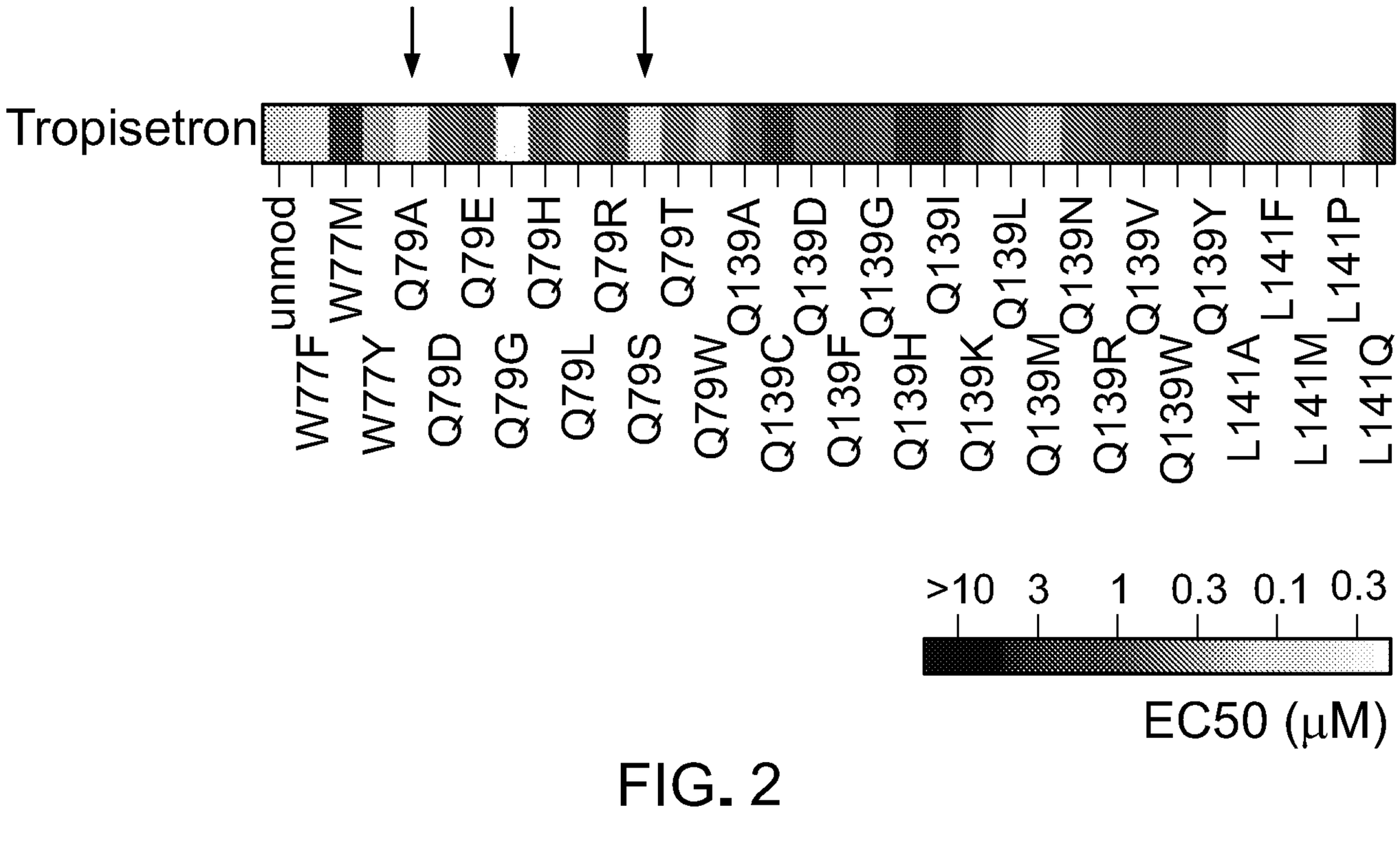

Tropisetron
unmodified
W77F
W77M
W77Y
Q79A
Q79D
Q79E
Q79G
Q79H
Q79L
Q79R
Q79S
Q79T
Q79W
Q139A
Q139C
Q139D
Q139F
Q139G
Q139H
Q139I
Q139K
Q139L
Q139M
Q139N
Q139R
Q139V
Q139W
Q139Y
L141A
L141F
L141M
L141P
L141Q
>10
3
1
0.3
0.1
0.3
EC50 (μM)

FIG. 2

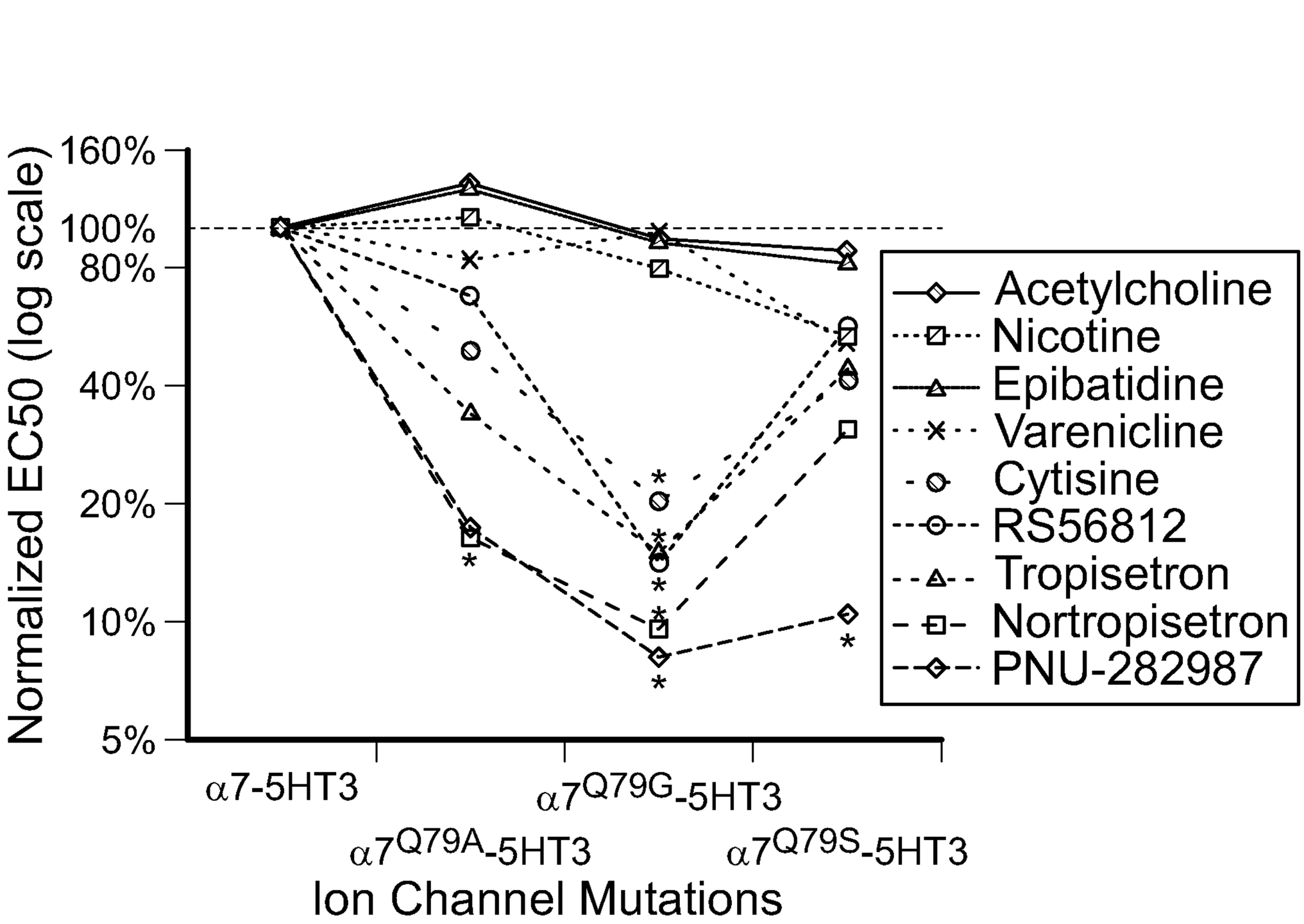

Normalized EC50 (log scale)
160%
100%
80%
40%
20%
10%
5%
α7-5HT3
α7Q79A-5HT3
α7Q79G-5HT3
α7Q79S-5HT3
Ion Channel Mutations
Acetylcholine
Nicotine
Epibatidine
Varenicline
Cytisine
RS56812
Tropisetron
Nortropisetron
PNU-282987

FIG. 3A

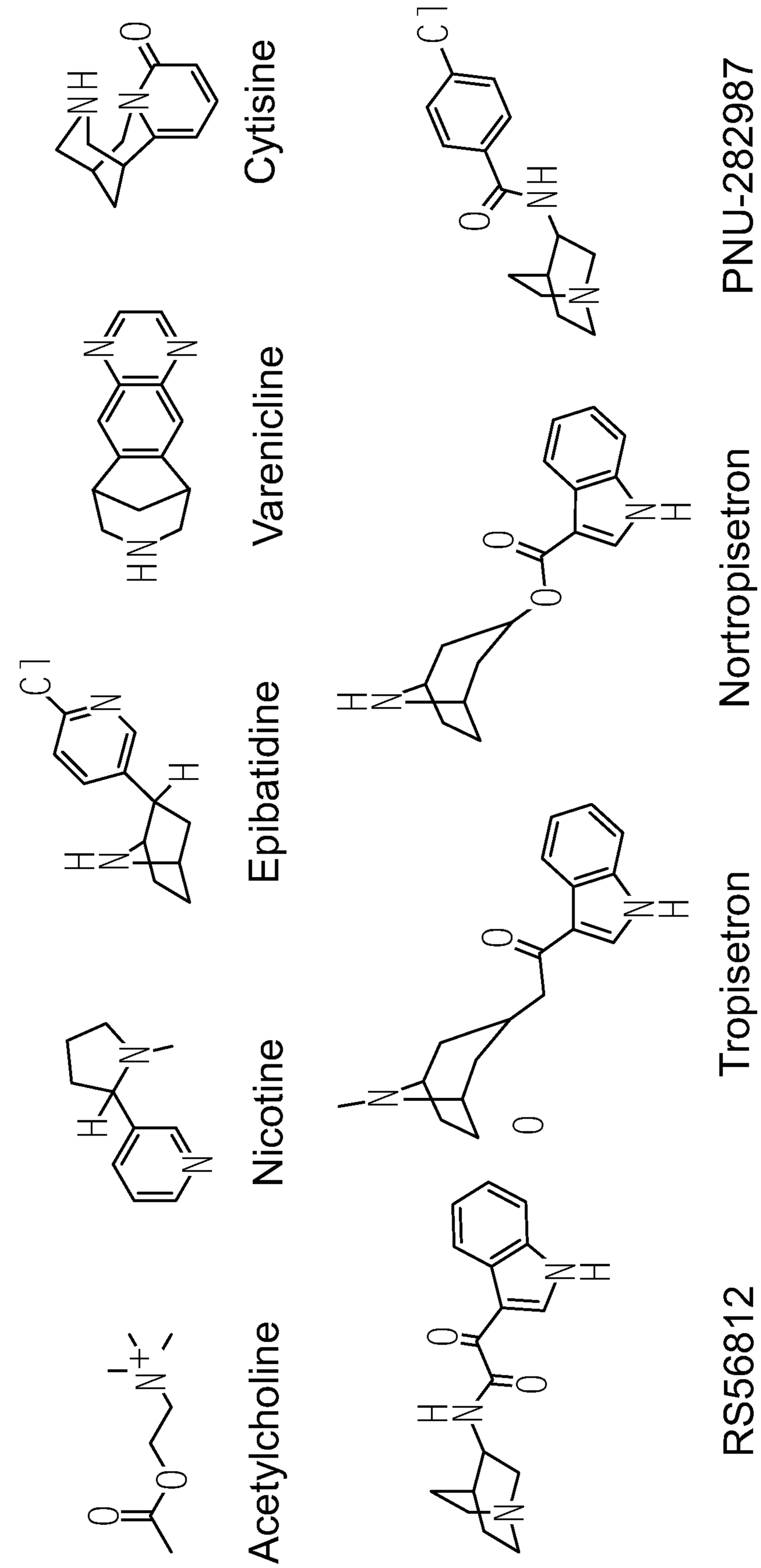

Cytisine
Varenicline
Epibatidine
Nicotine
Acetylcholine
PNU-282987
Nortropisetron
Tropisetron
RS56812

FIG. 3B

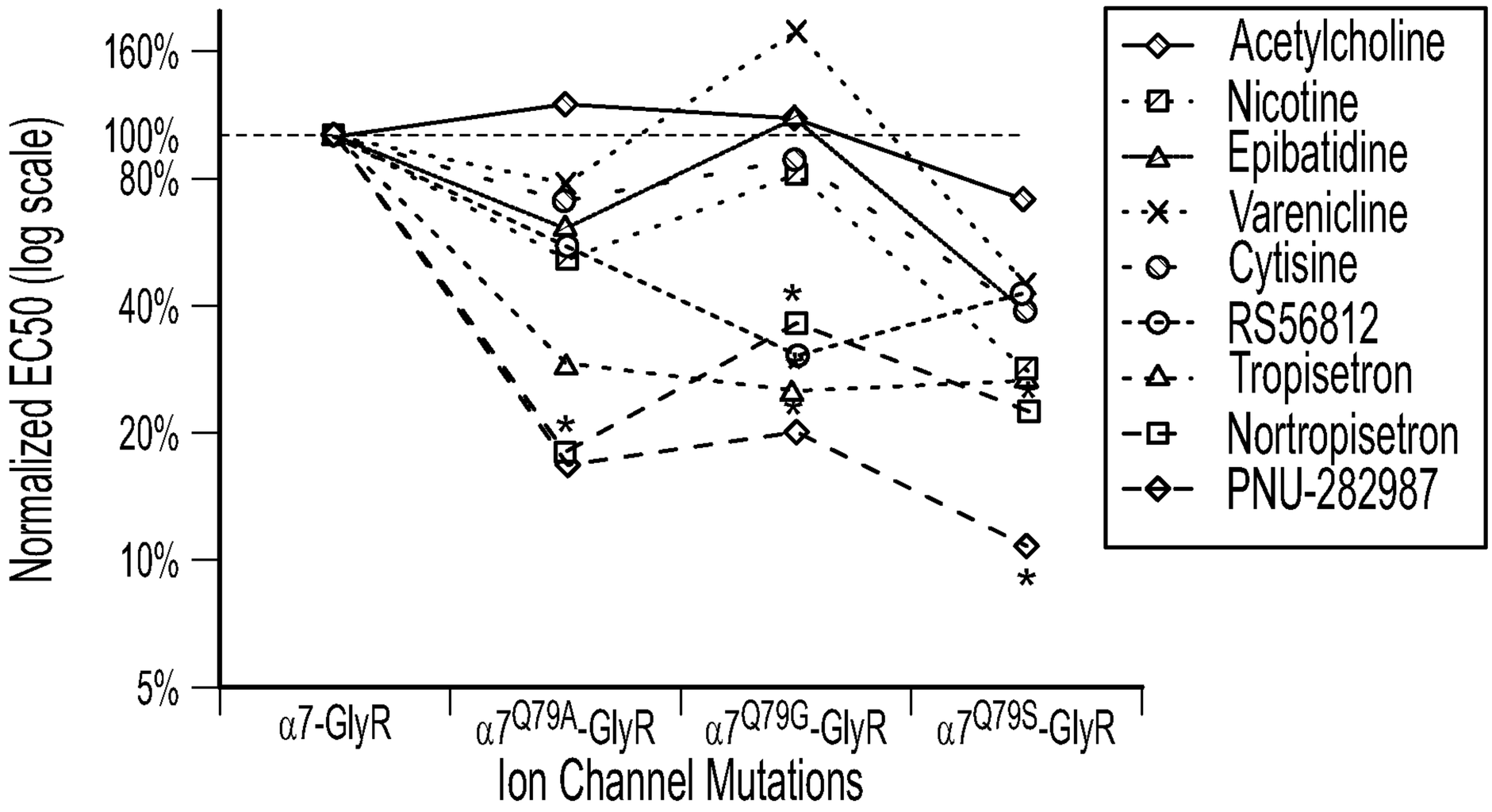


FIG. 4A

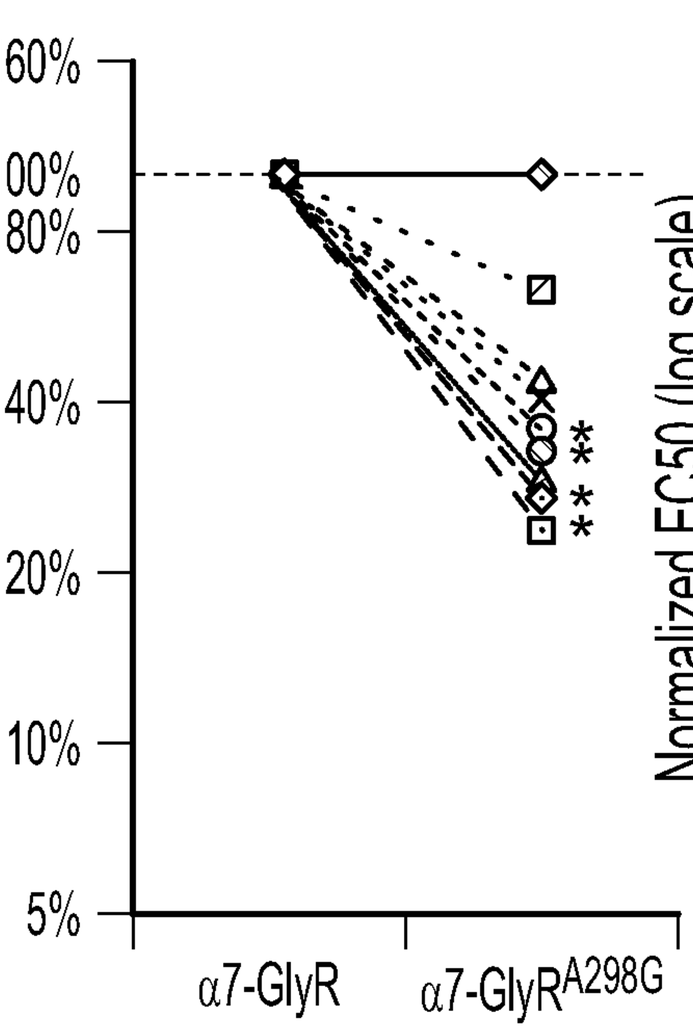


FIG. 4B

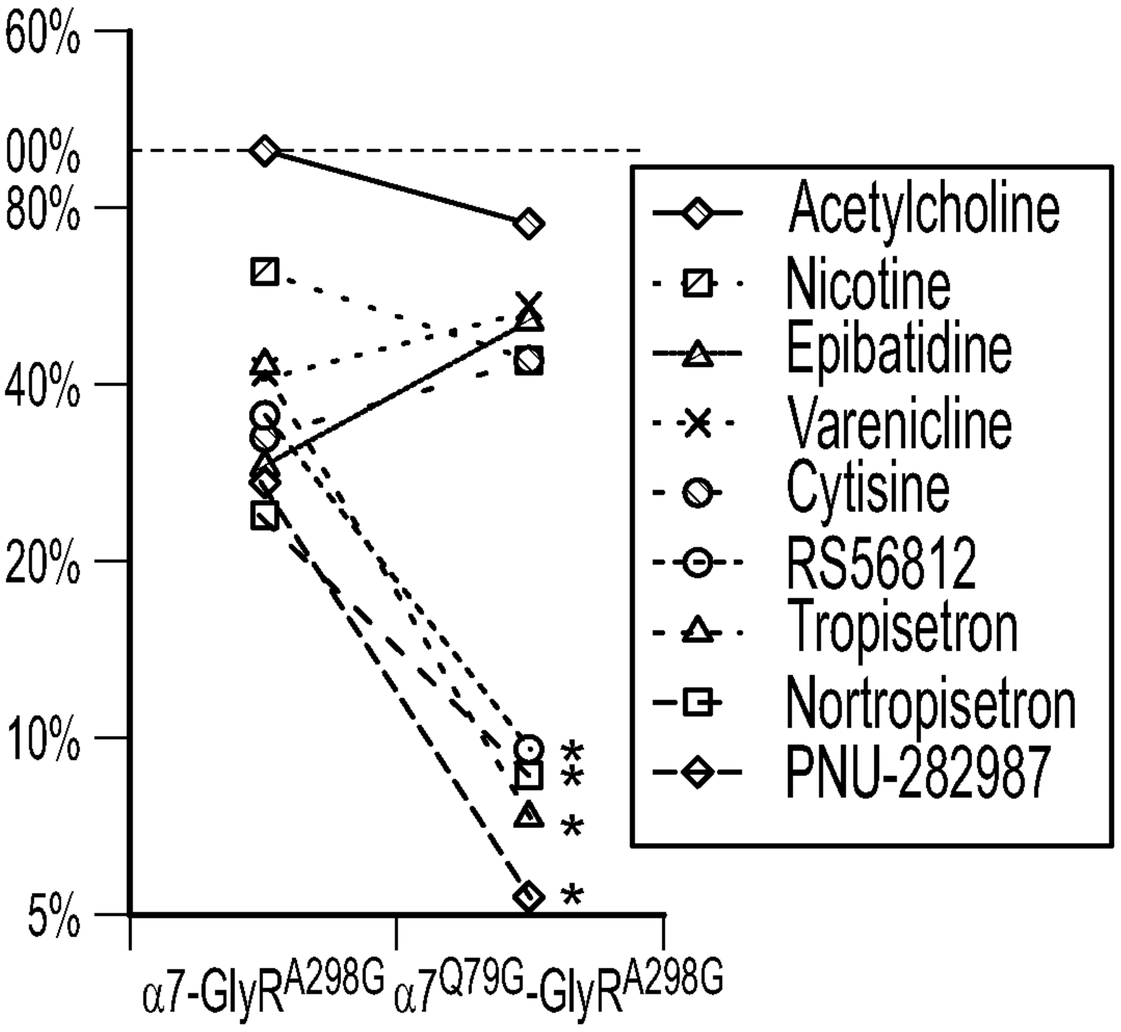
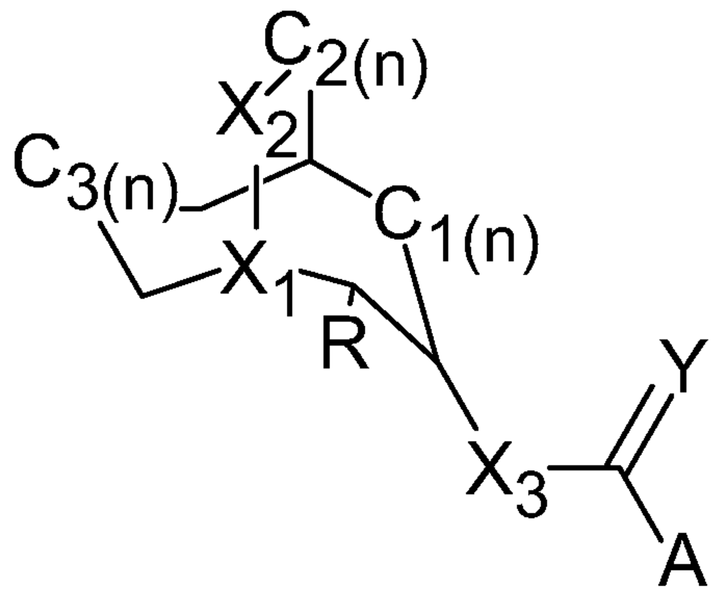
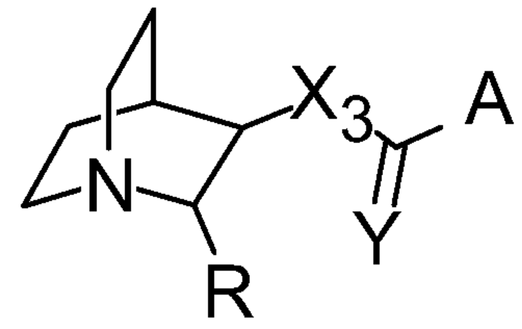


FIG. 4C

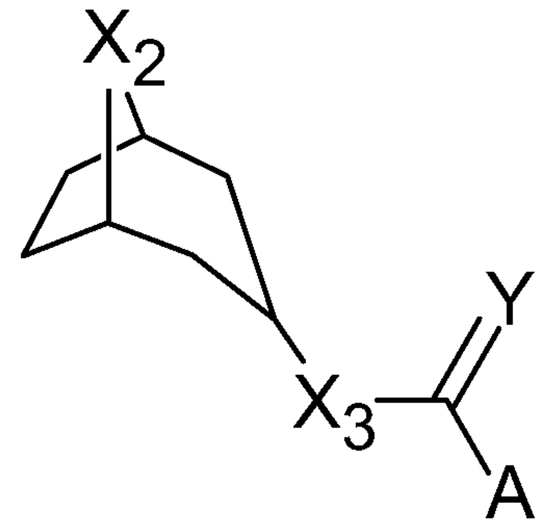


X = CH, CH2, O, NH, NMe
n = 0 or 1
Y = O, S
A = Aromatic
R = Pyridinylmethylene

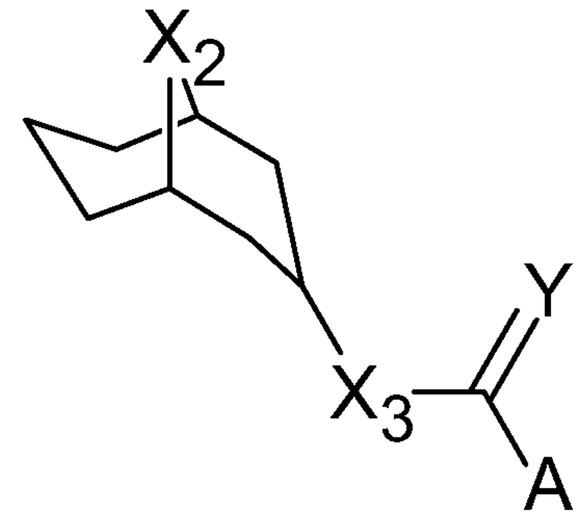
FIG. 5A



Pharmacophore:
Quinuclidine
$C_{1(n)}$ = 0
$C_{2(n)}$ = 1
$C_{3(n)}$ = 0
X_1 = N
X_2 = CH_2
X_3 = O, NH,CH_2
Y = O, S
A = Aromatic
R = Pyridinylmethylene

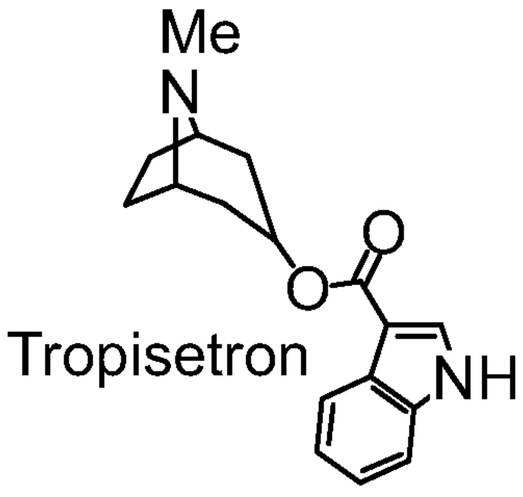


Pharmacophore:
Tropane
$C_{1(n)}$ = 1
$C_{2(n)}$ = 0
$C_{3(n)}$ = 0
X_1 = CH
X_2 = NH, NMe
X_3 = O, NH,CH_2
Y = O, S
A = Aromatic

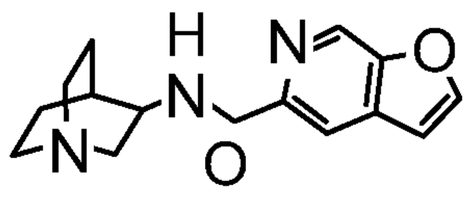


Pharmacophore:
9-azabicyclo[3.3.1]nonane
$C_{1(n)}$ = 1
$C_{2(n)}$ = 0
$C_{3(n)}$ = 1
X_1 = CH
X_2 = NH, NMe
X_3 = O, NH,CH_2
Y = O, S
A = Aromatic

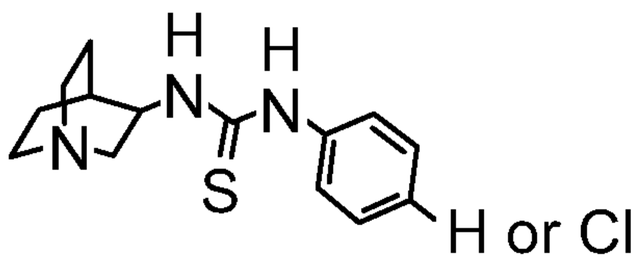
FIG. 5B



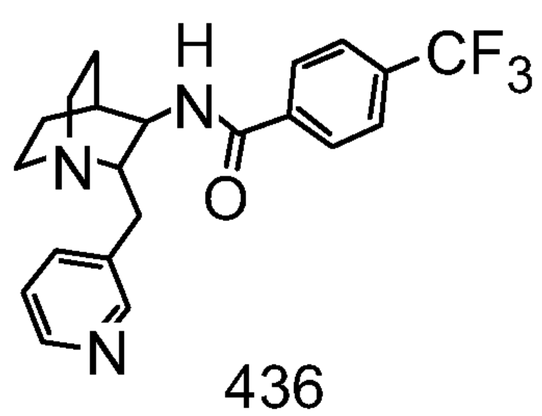
Tropisetron



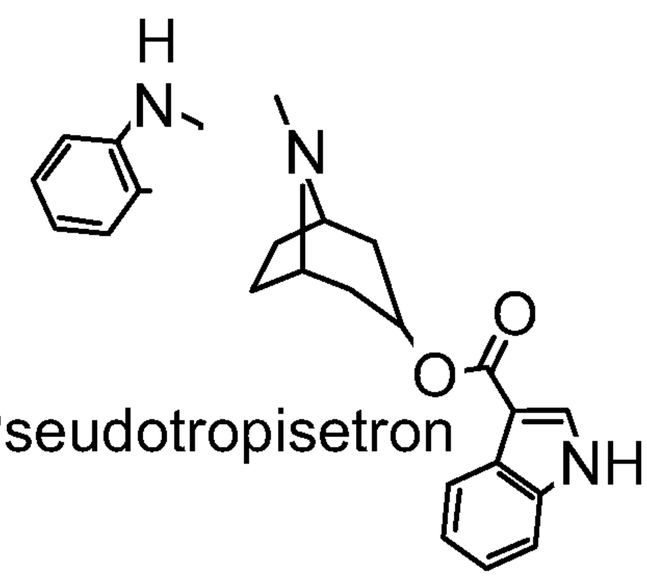
PHA-543613



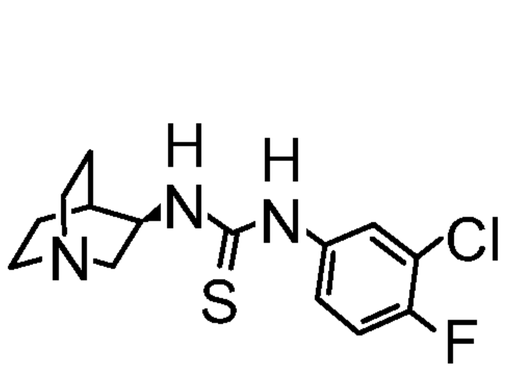
353 and 354



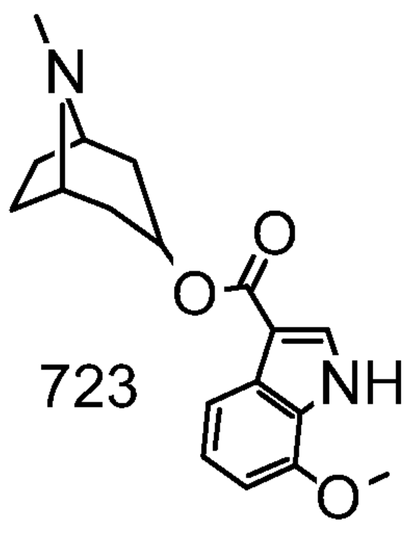
436



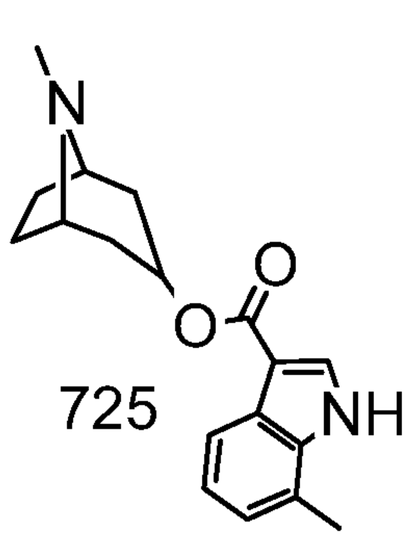
Pseudotropisetron



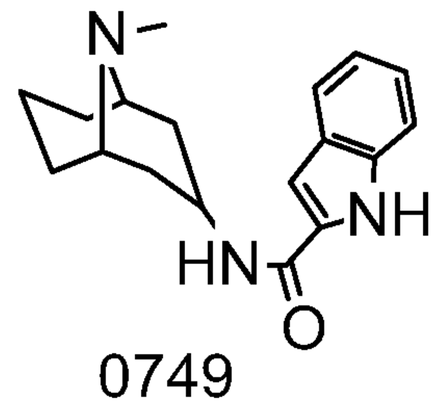
702



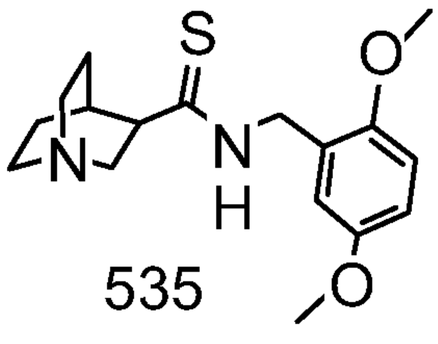
723



725



0749



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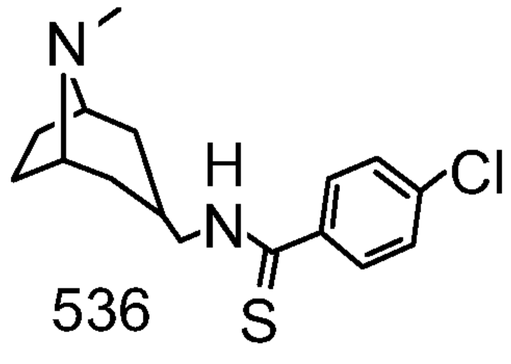

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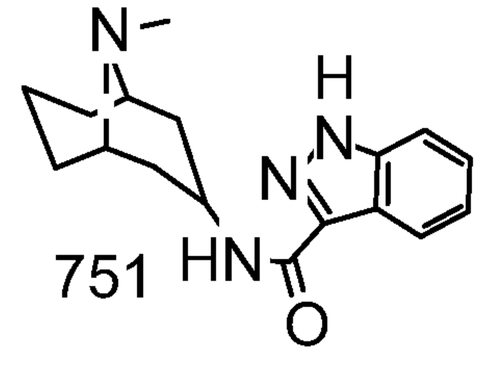

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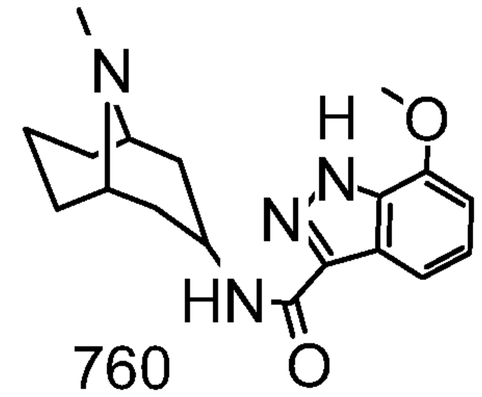
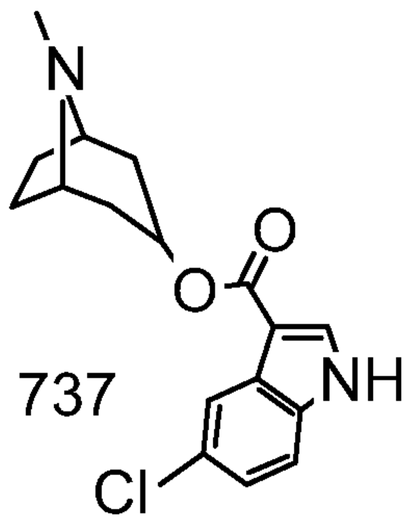
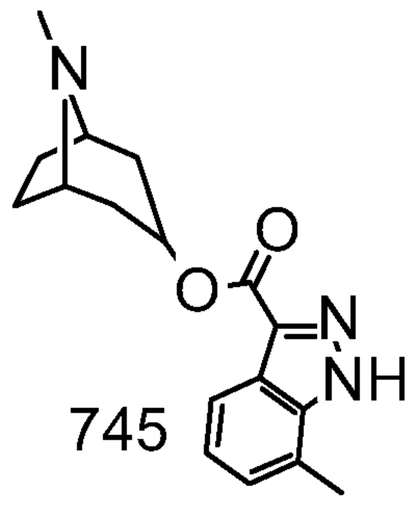


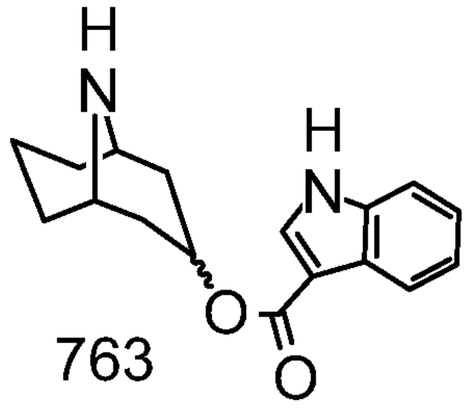
760



737



745



763

FIG. 5C

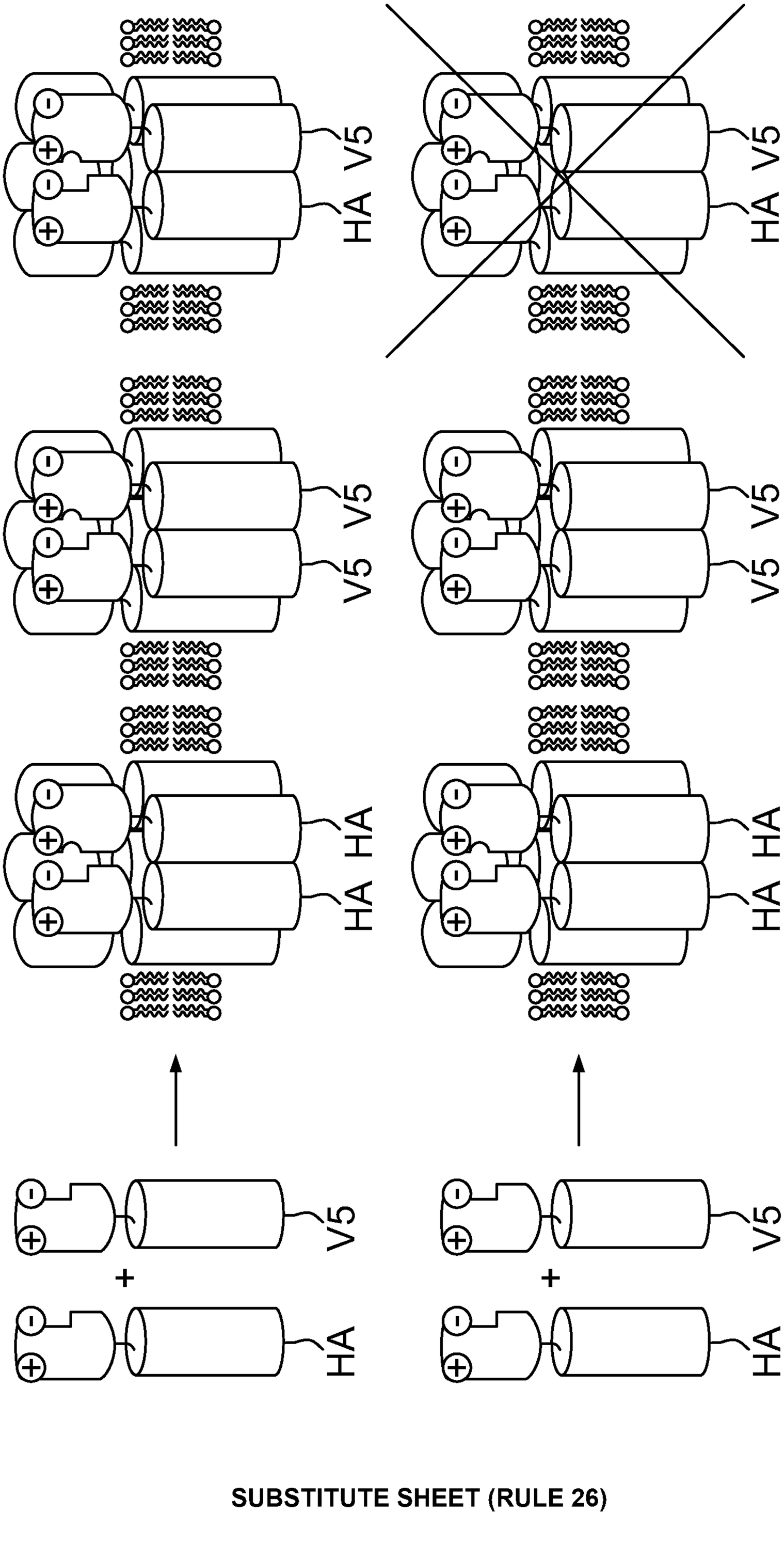


FIG. 6A

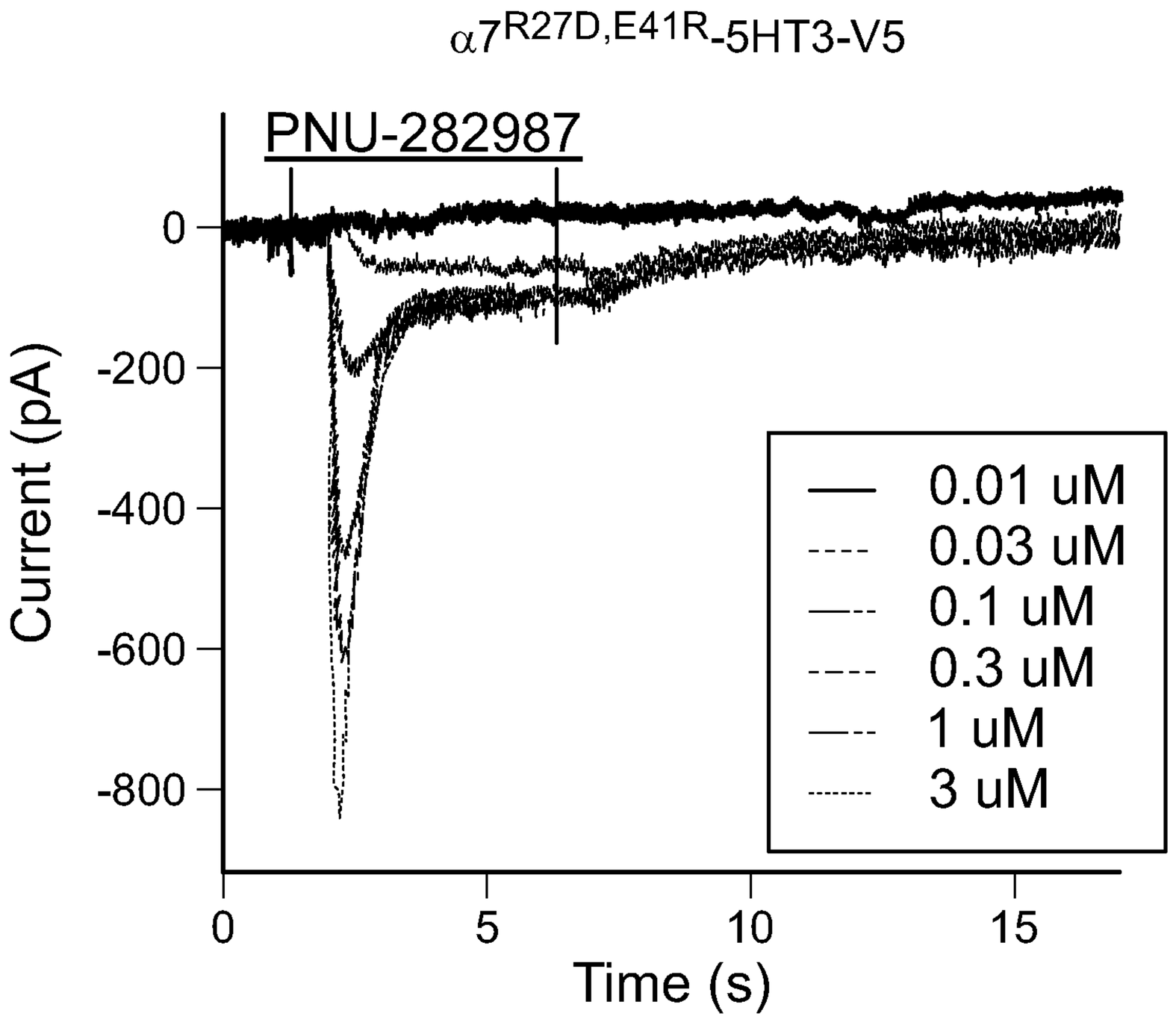
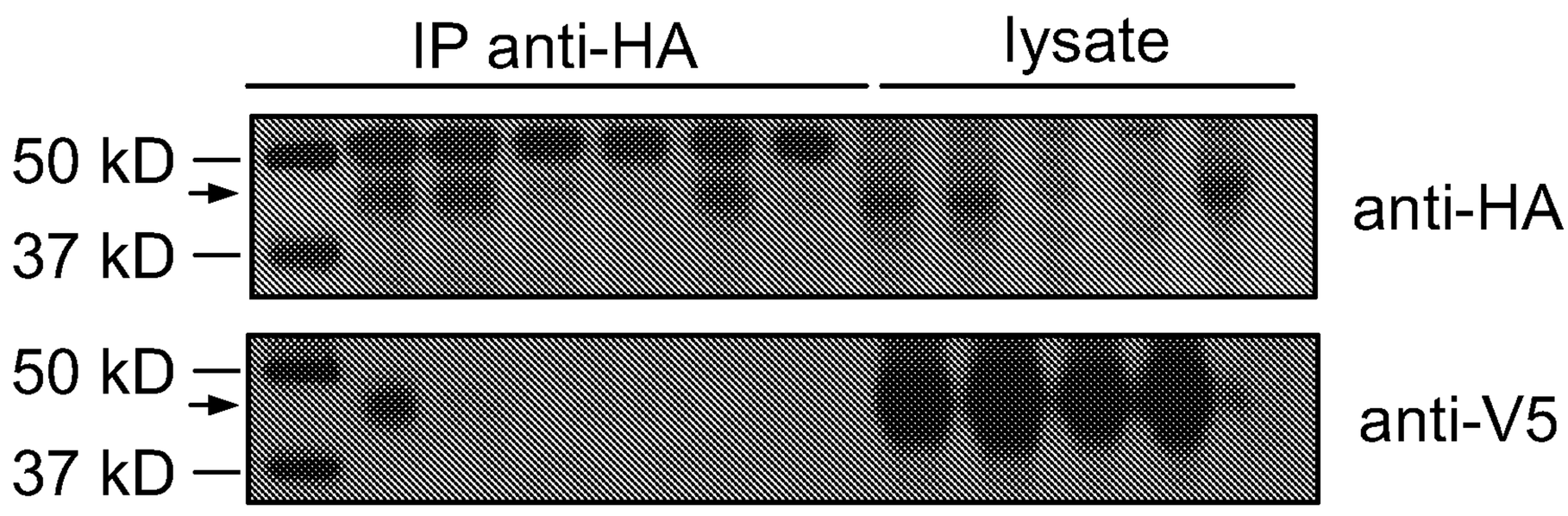


FIG. 6B



α7-5HT3-HA/α7-5HT3-V5
α7-5HT3-HA/
α7R27D,E41R-5HT3-V5
α7-5HT3-V5
α7R27D,E41R-5HT3-V5
α7-5HT3-HA
vector
α7-5HT3-HA/α7-5HT3-V5
α7-5HT3-HA/
α7R27D,E41R-5HT3-V5
α7-5HT3-V5
α7R27D,E41R-5HT3-V5
α7-5HT3-HA

FIG. 6C

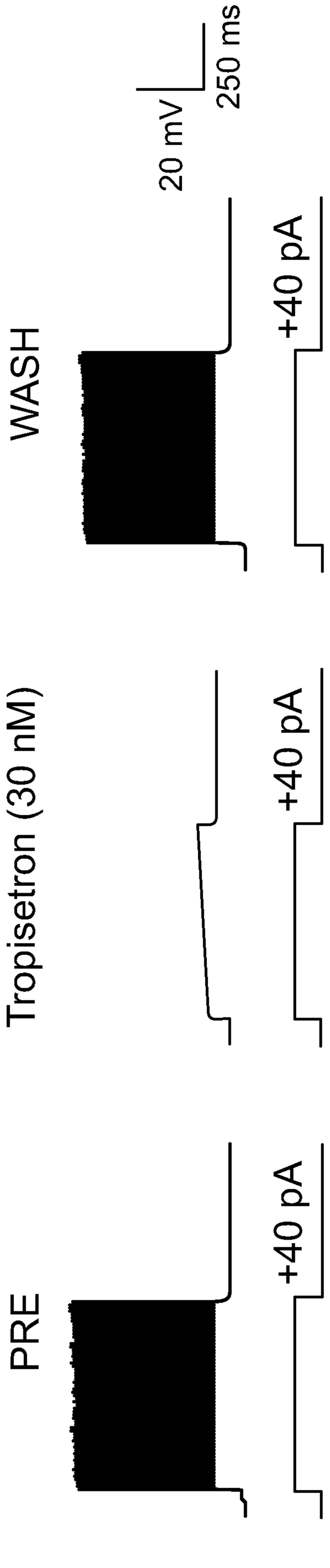


FIG. 7

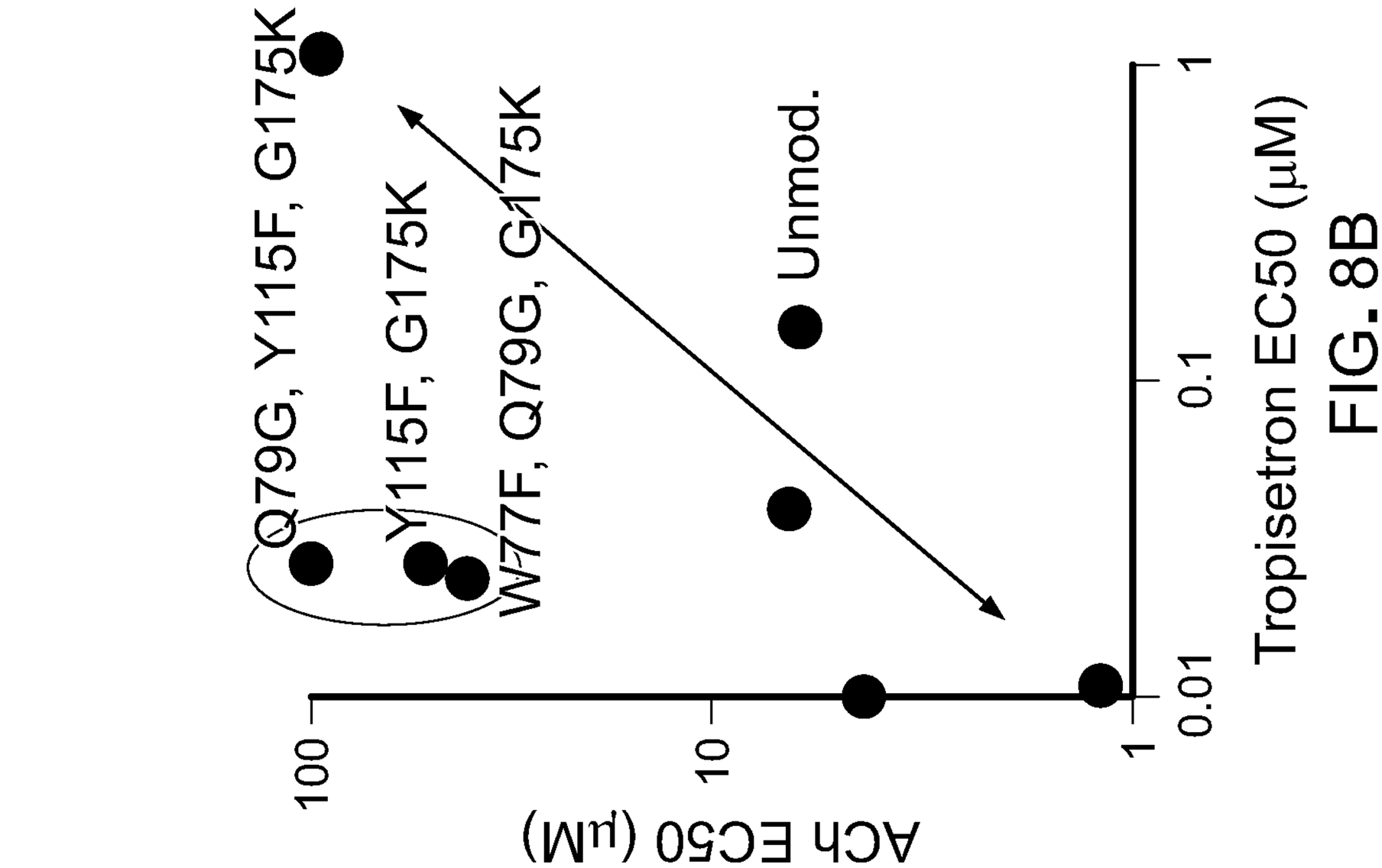

Q79G, Y115F, G175K
Y115F, G175K
W77F, Q79G, G175K
Unmod.
ACh EC50 (μM)
100
10
1
0.01
0.1
1
Tropisetron EC50 (μM)

FIG. 8B

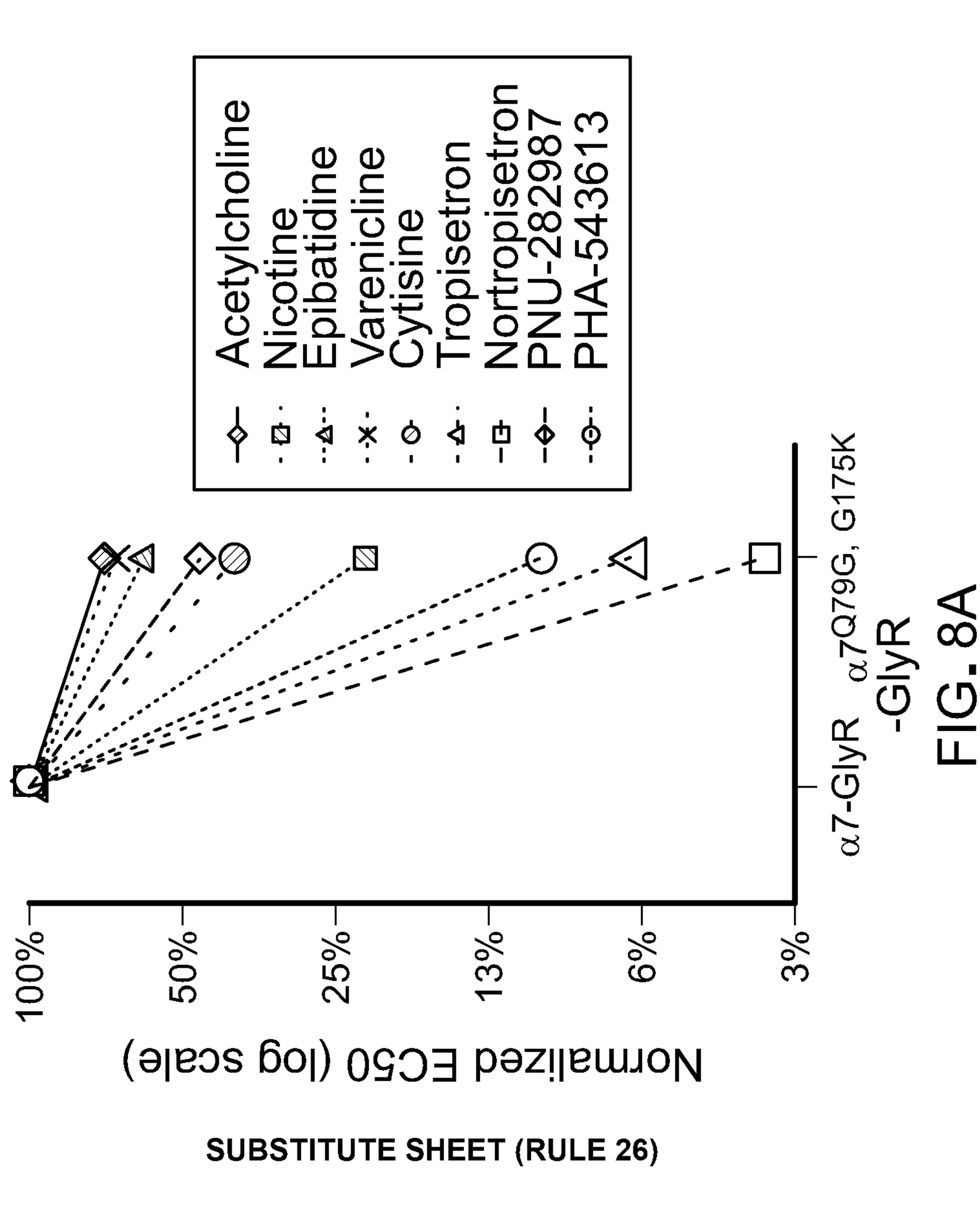

Acetylcholine
Nicotine
Epibatidine
Varenicline
Cytisine
Tropisetron
Nortropisetron
PNU-282987
PHA-543613
α7-GlyR
α7Q79G, G175K -GlyR
100%
50%
25%
13%
6%
3%
Normalized EC50 (log scale)

FIG. 8A

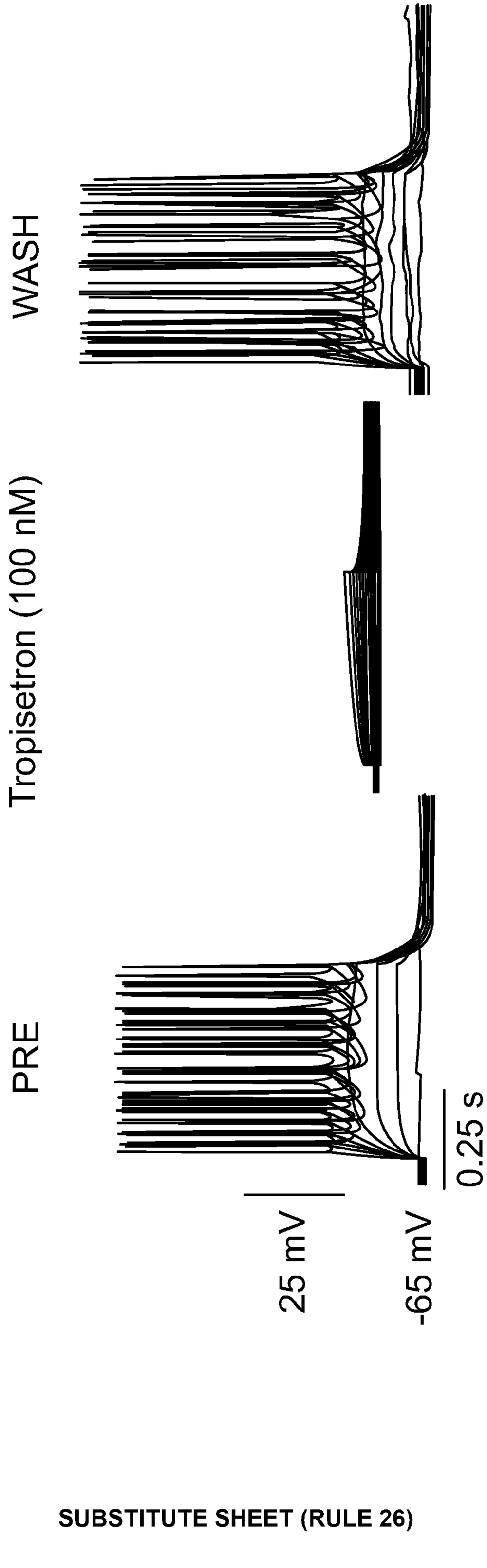


FIG. 8C

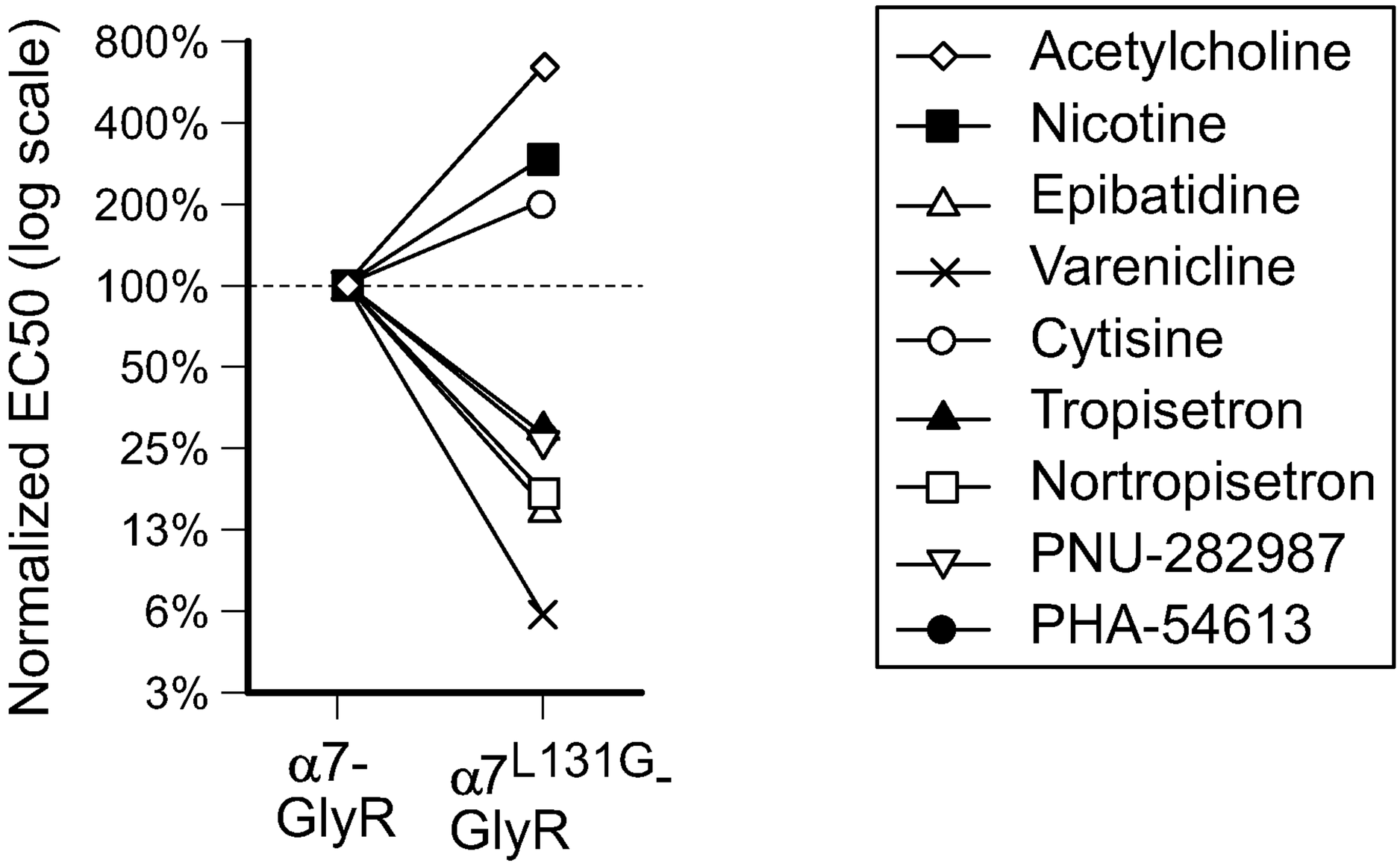

Normalized EC50 (log scale)
800%
400%
200%
100%
50%
25%
13%
6%
3%
α7-GlyR
α7L131G-GlyR
Acetylcholine
Nicotine
Epibatidine
Varenicline
Cytisine
Tropisetron
Nortropisetron
PNU-282987
PHA-54613

FIG. 9A

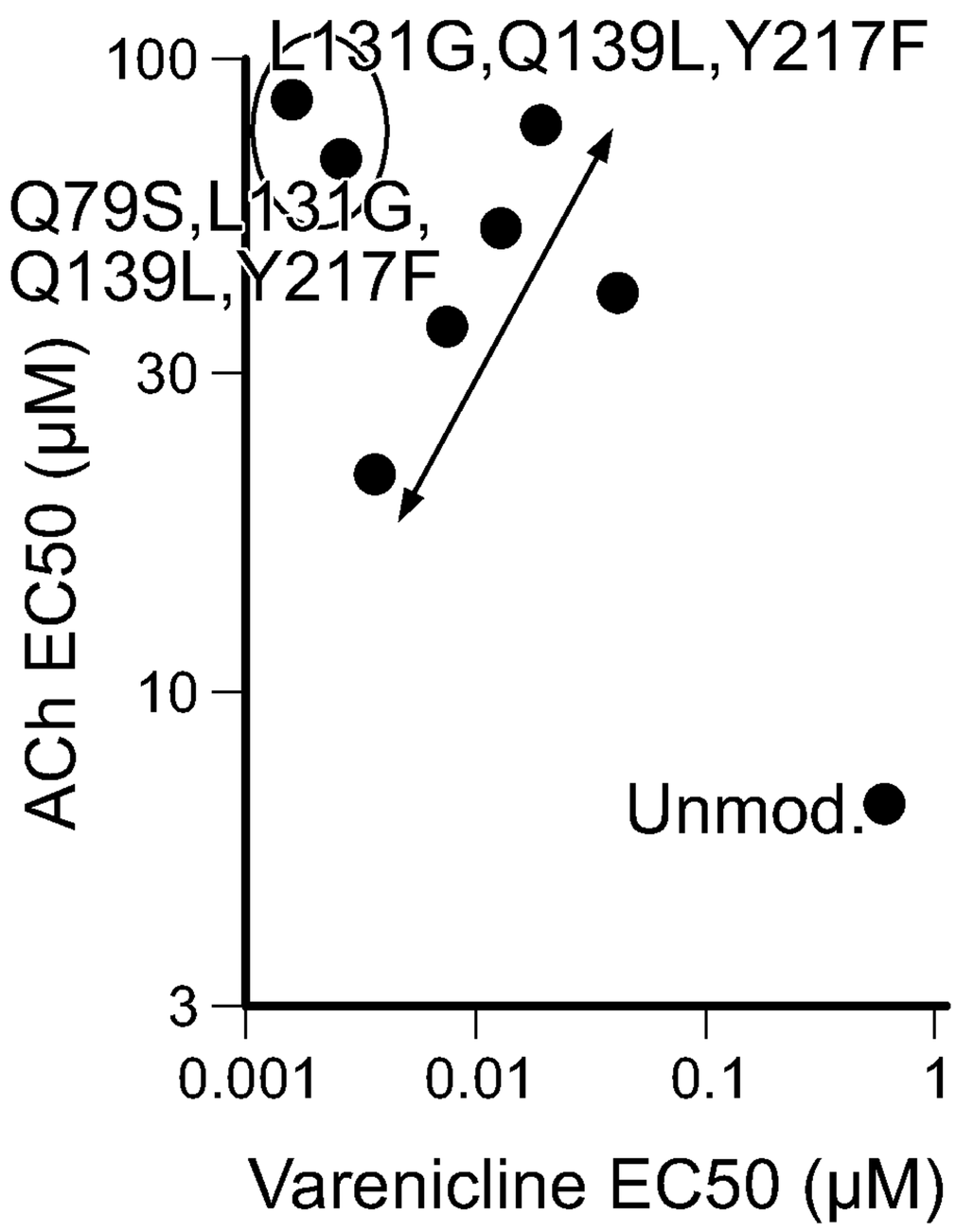

L131G,Q139L,Y217F
Q79S,L131G,
Q139L,Y217F
Unmod.
ACh EC50 (μM)
100
30
10
3
0.001
0.01
0.1
1
Varenicline EC50 (μM)

FIG. 9B

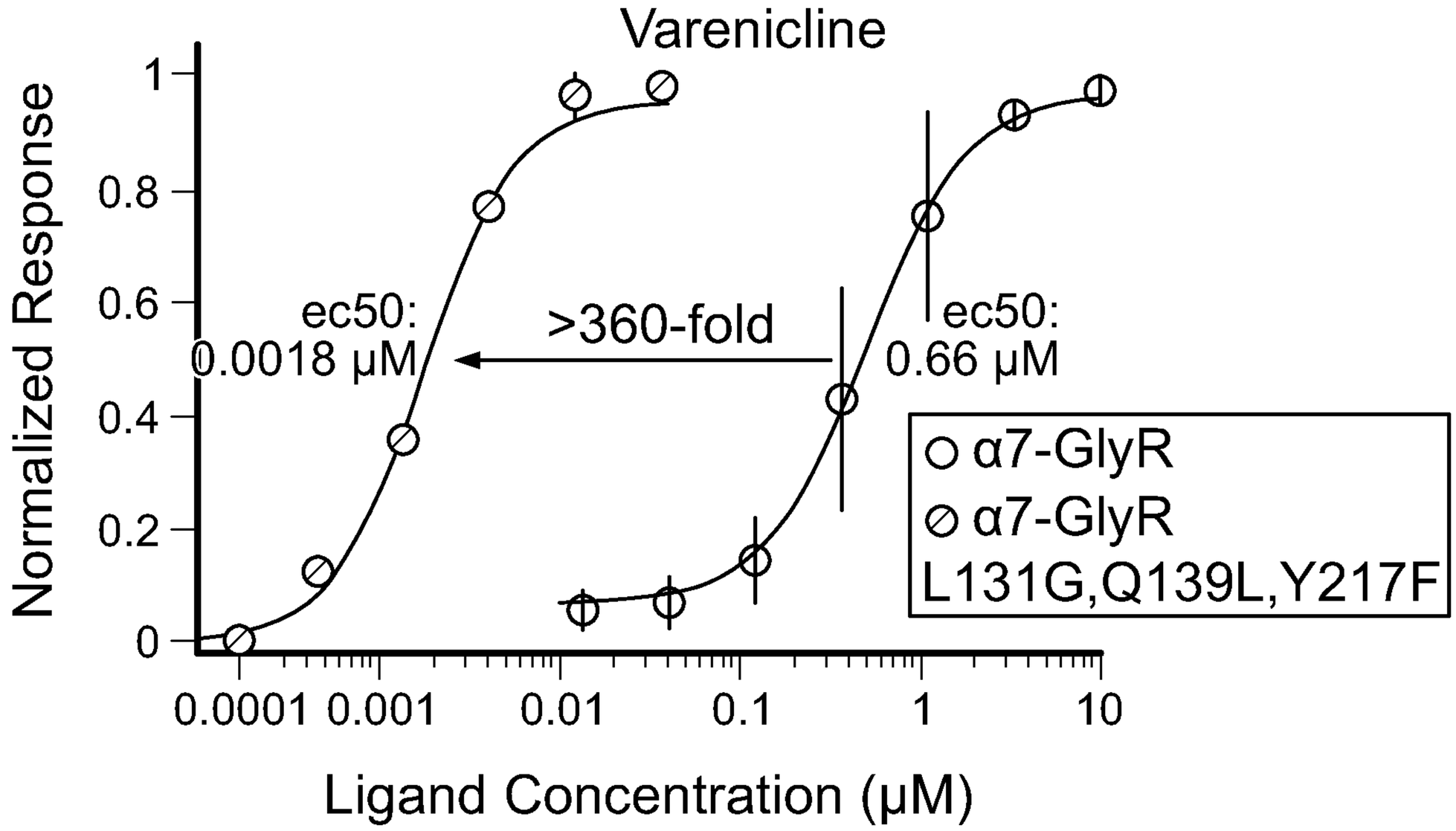

Varenicline
Normalized Response
1
0.8
0.6
0.4
0.2
0
ec50:
0.0018 μM
>360-fold
ec50:
0.66 μM
α7-GlyR
α7-GlyR
L131G,Q139L,Y217F
0.0001
0.001
0.01
0.1
1
10
Ligand Concentration (μM)

FIG. 9C

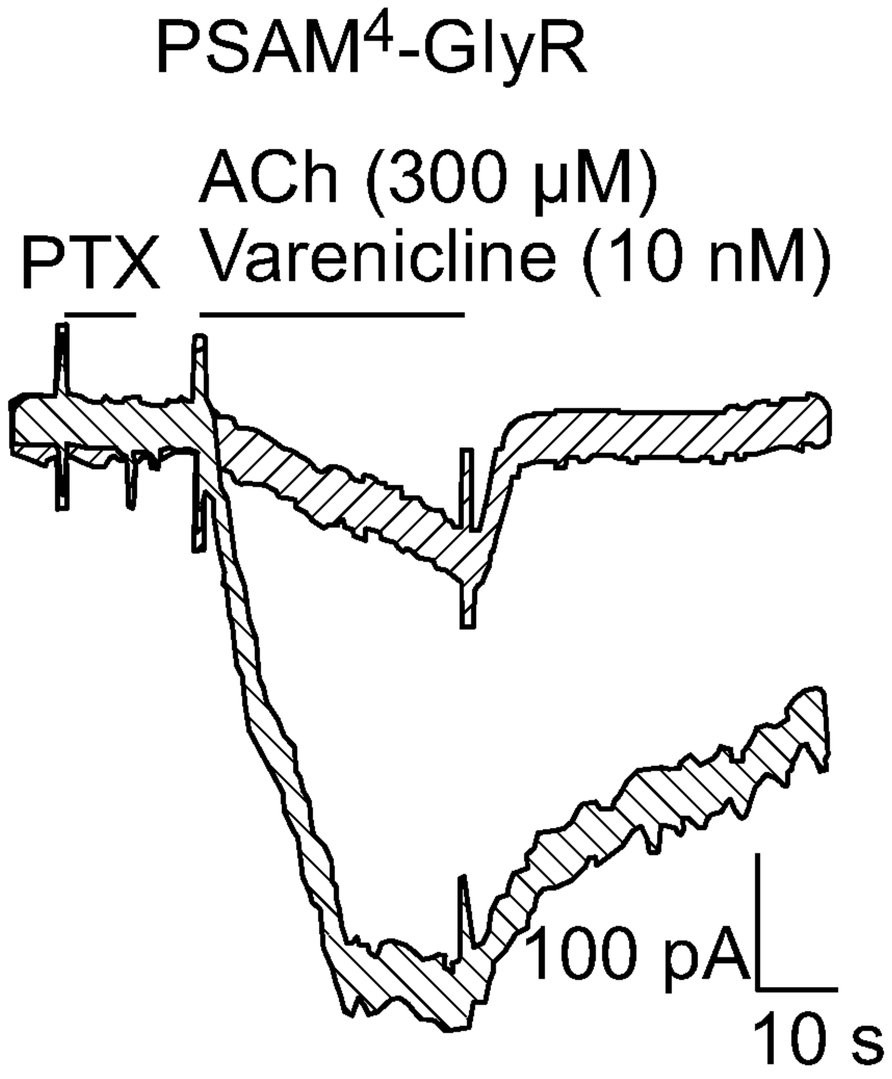

PSAM4-GlyR
ACh (300 μM)
PTX
Varenicline (10 nM)
100 pA
10 s

FIG. 9D

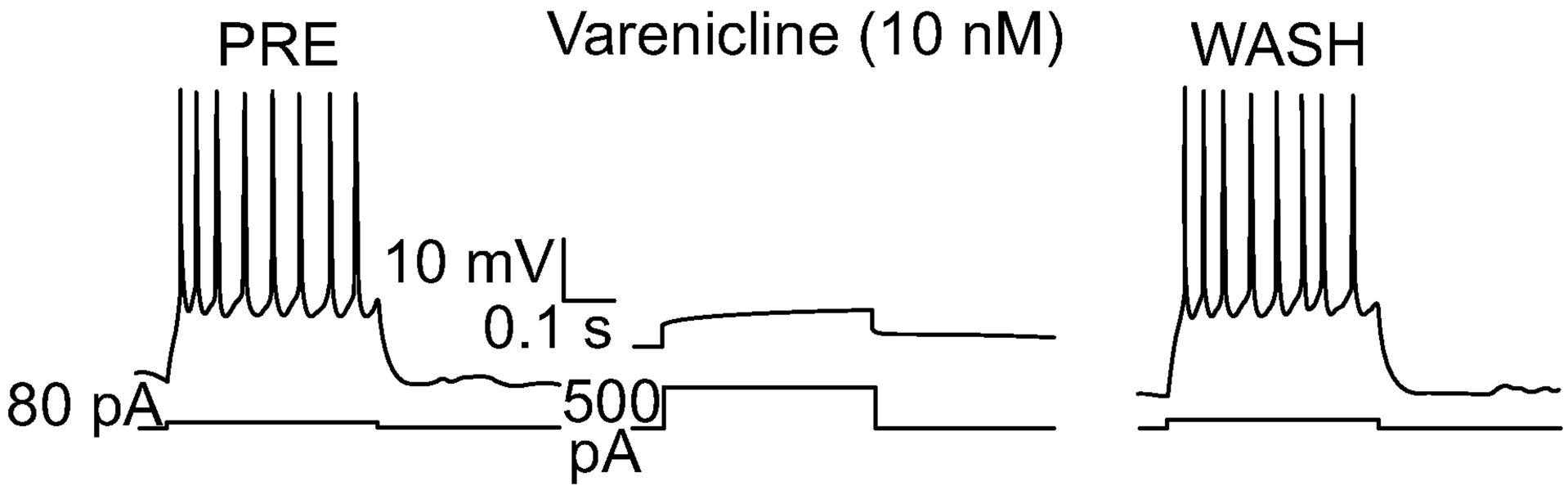

PRE
Varenicline (10 nM)
WASH
10 mV
0.1 s
80 pA
500 pA

FIG. 9E

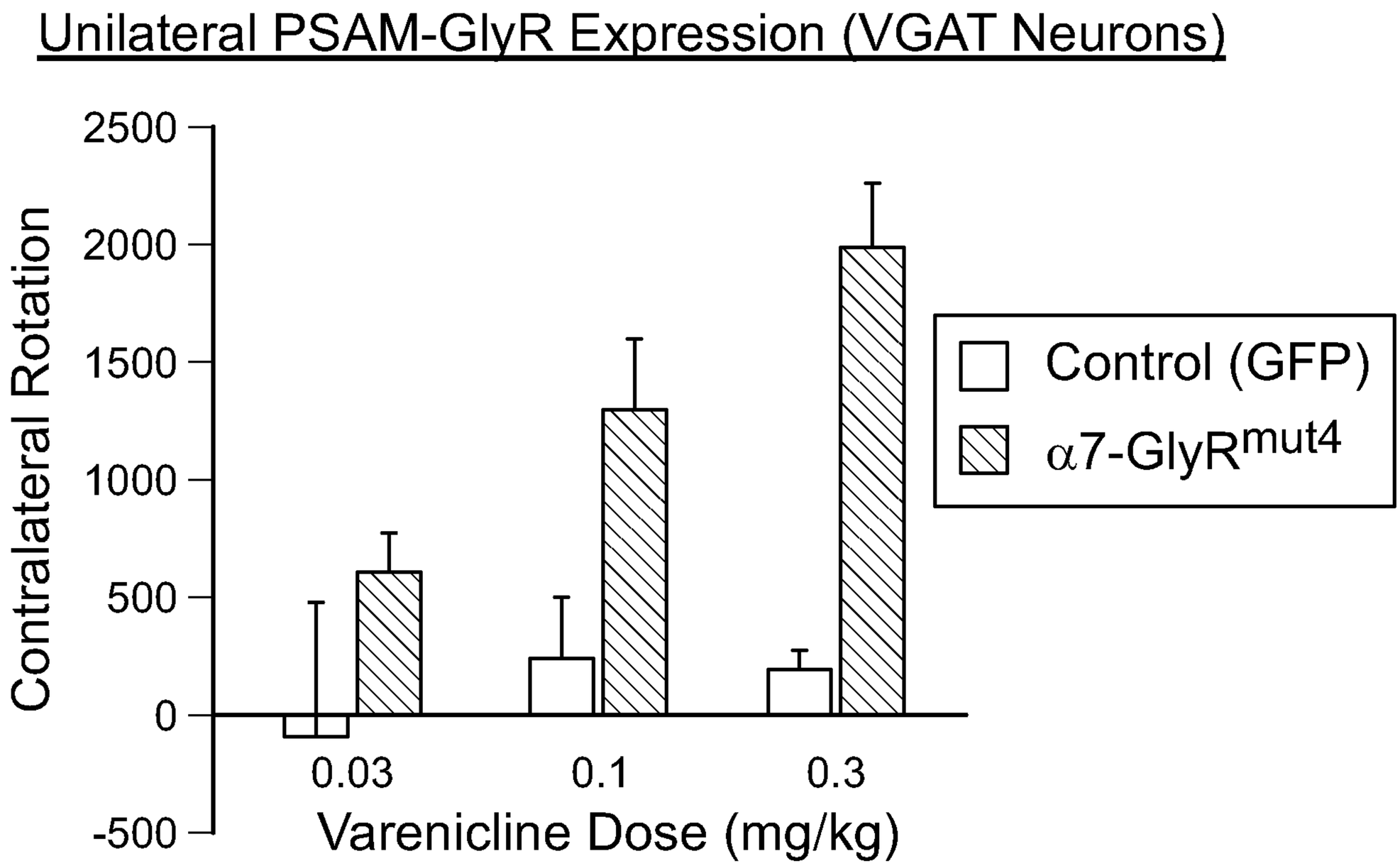
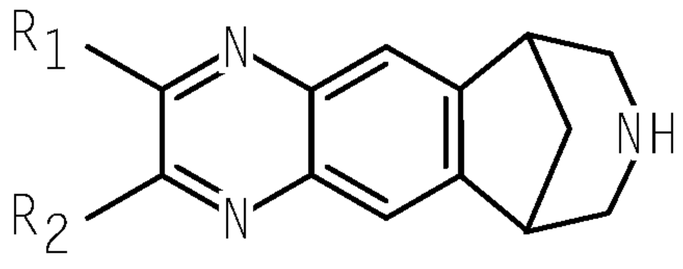
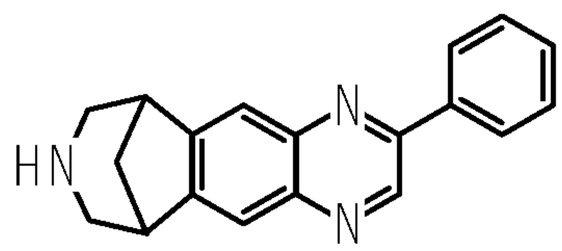

Unilateral PSAM-GlyR Expression (VGAT Neurons)
Contralateral Rotation
2500
2000
1500
1000
500
0
-500
0.03
0.1
0.3
Varenicline Dose (mg/kg)
Control (GFP)
α7-GlyRmut4

FIG. 10

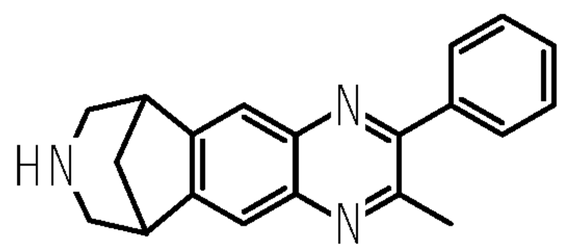


R_1 = H, an aromatic substituent, a methyl containing group, an ethyl containing group, a methoxy containing group, or an amino-containing group

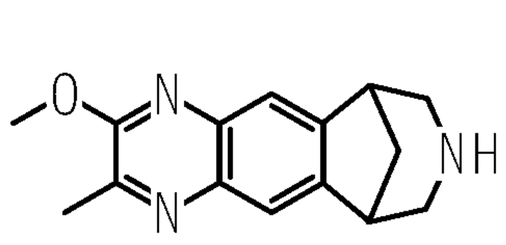
R_2 = H, methyl, or phenyl



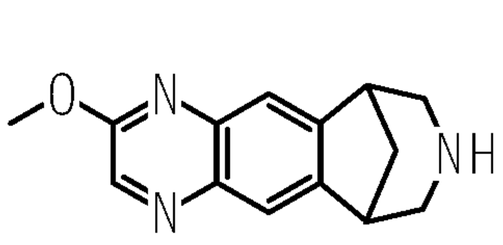
765



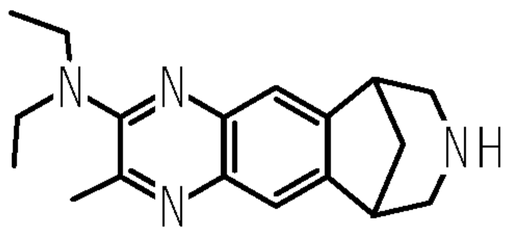
770



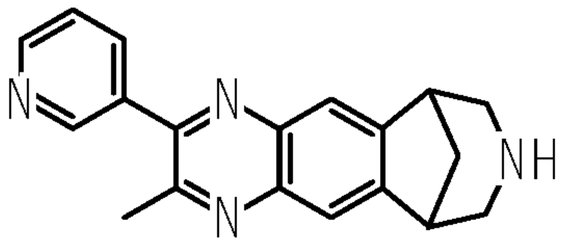
791



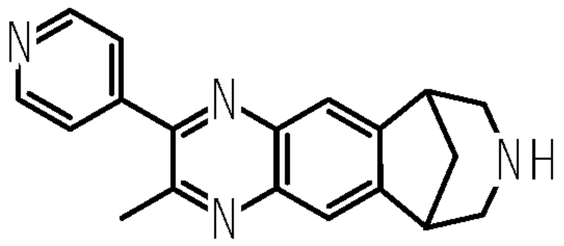
793



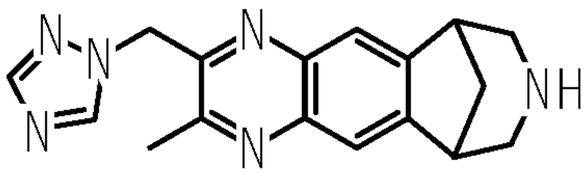
795



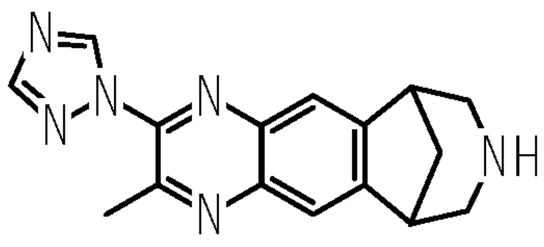
802



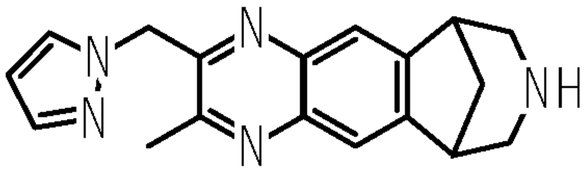
803



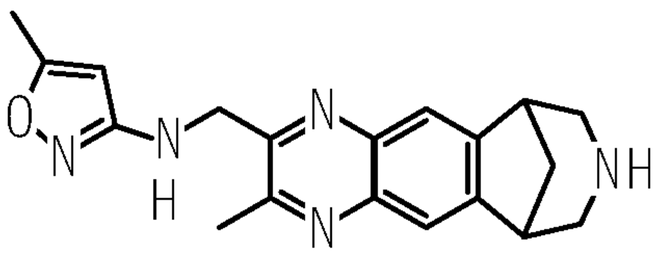
807



808

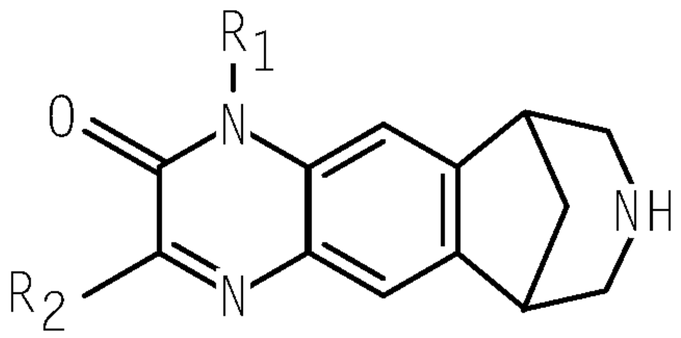


812

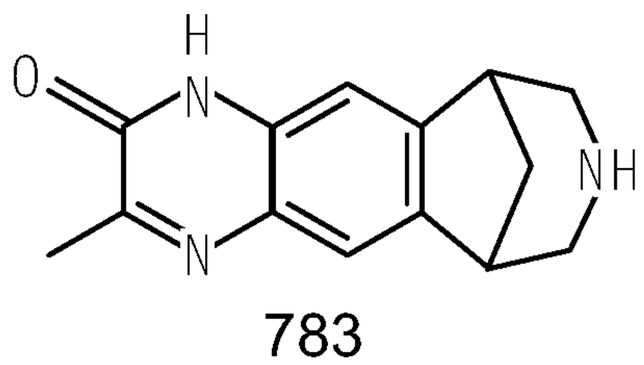


813

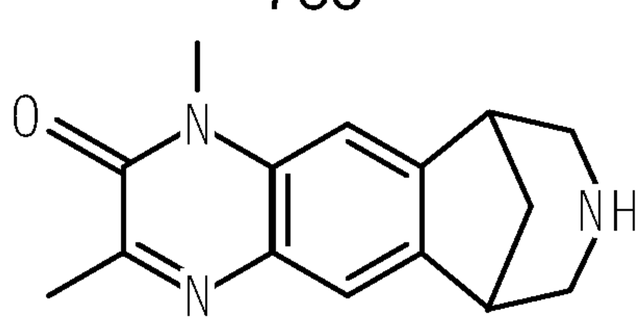
FIG. 11A



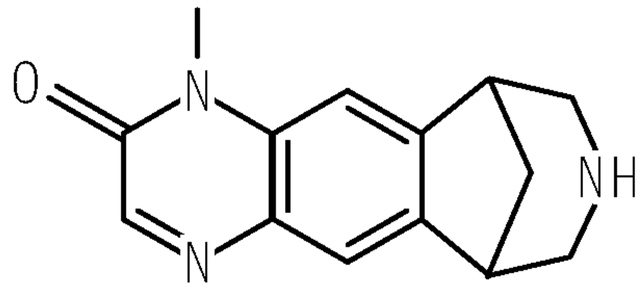
R_1 = H or CH3
R_2 = H, CH3, or an aromatic substituent



783



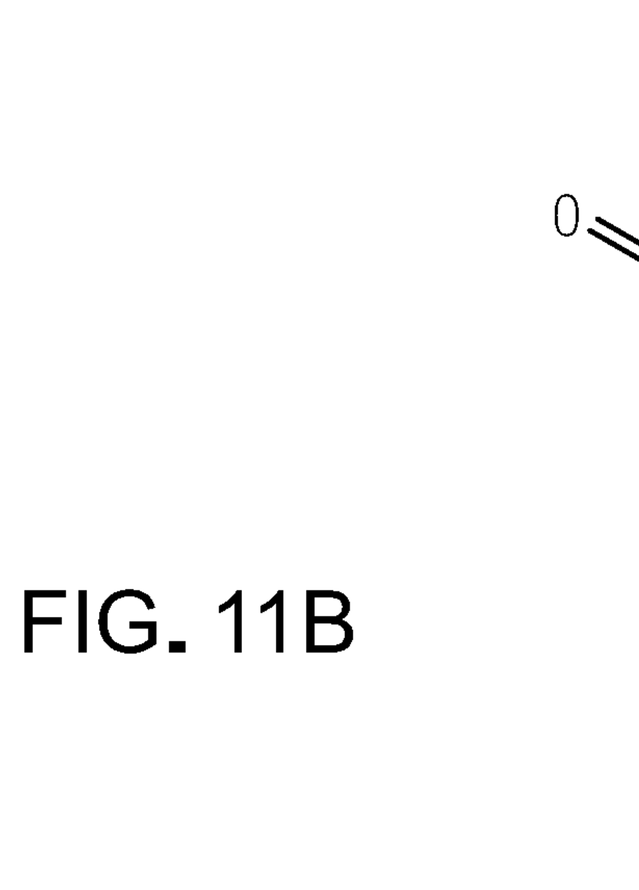
790



792

FIG. 11B

R = H, F, NO2



3-(1,4-diazabicyclo[3.2.2] nonan-4-yl)dibenzo[b,d] thiophene 5,5-dioxide

773

774

FIG. 11C

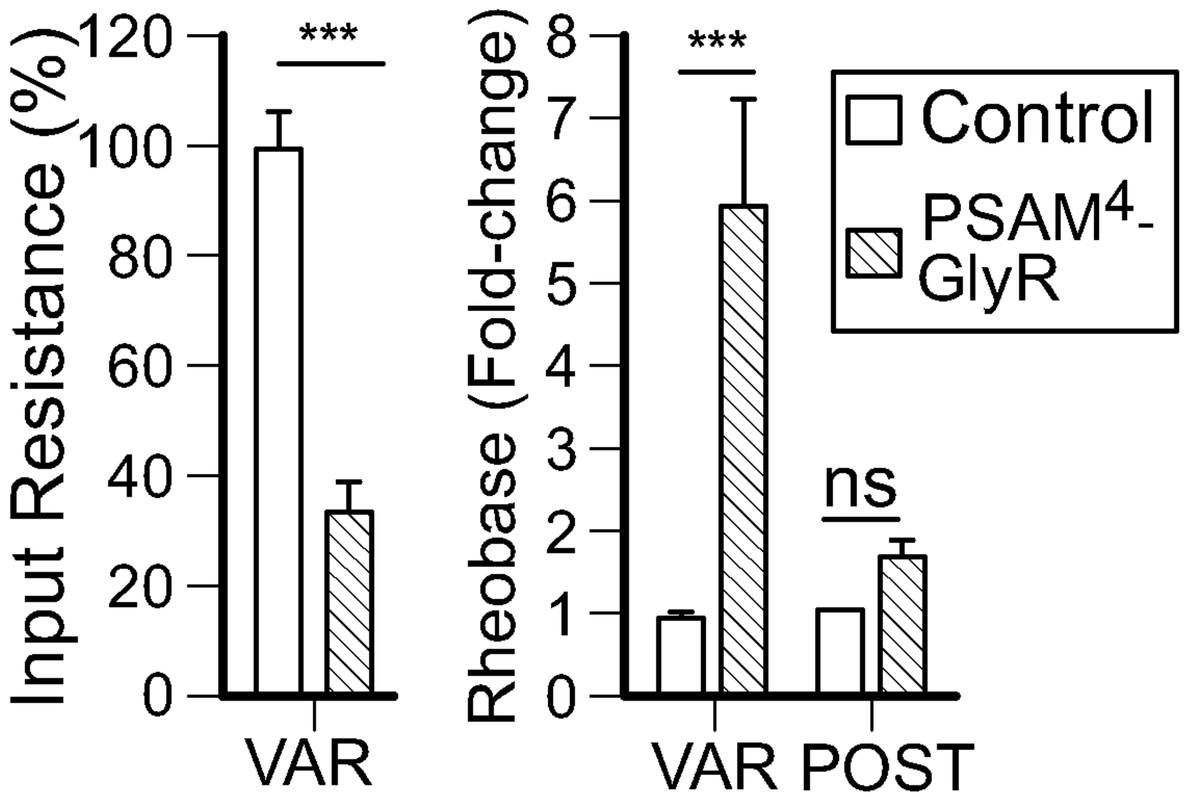


FIG. 12A

FIG. 12B

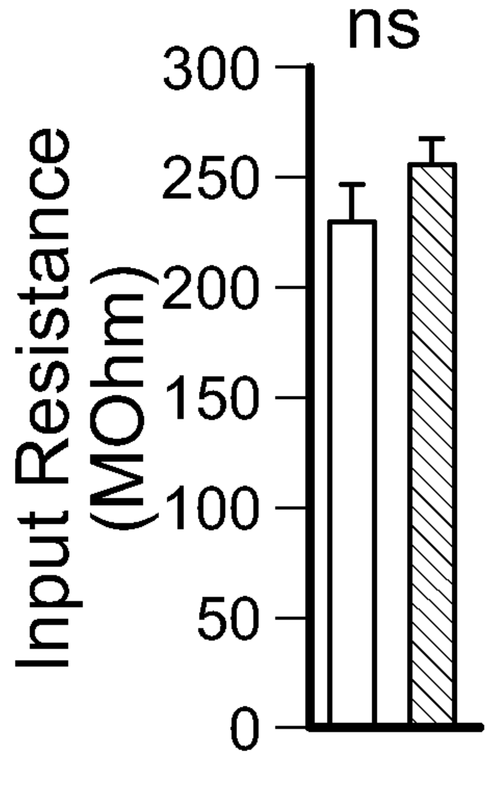
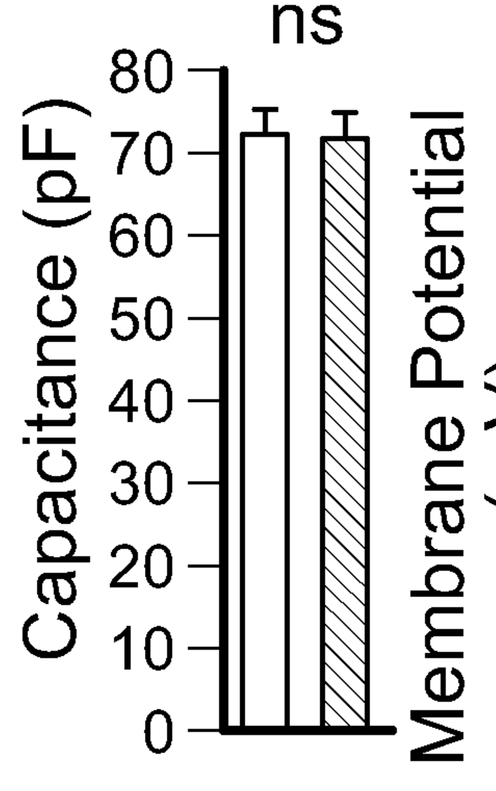
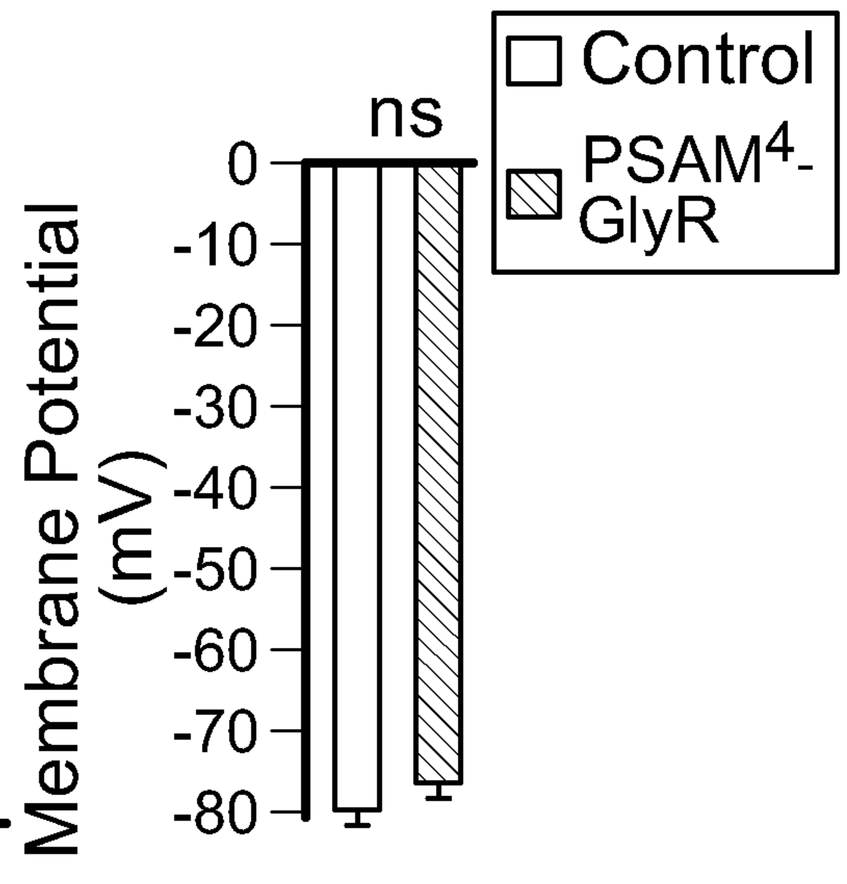


FIG. 12C





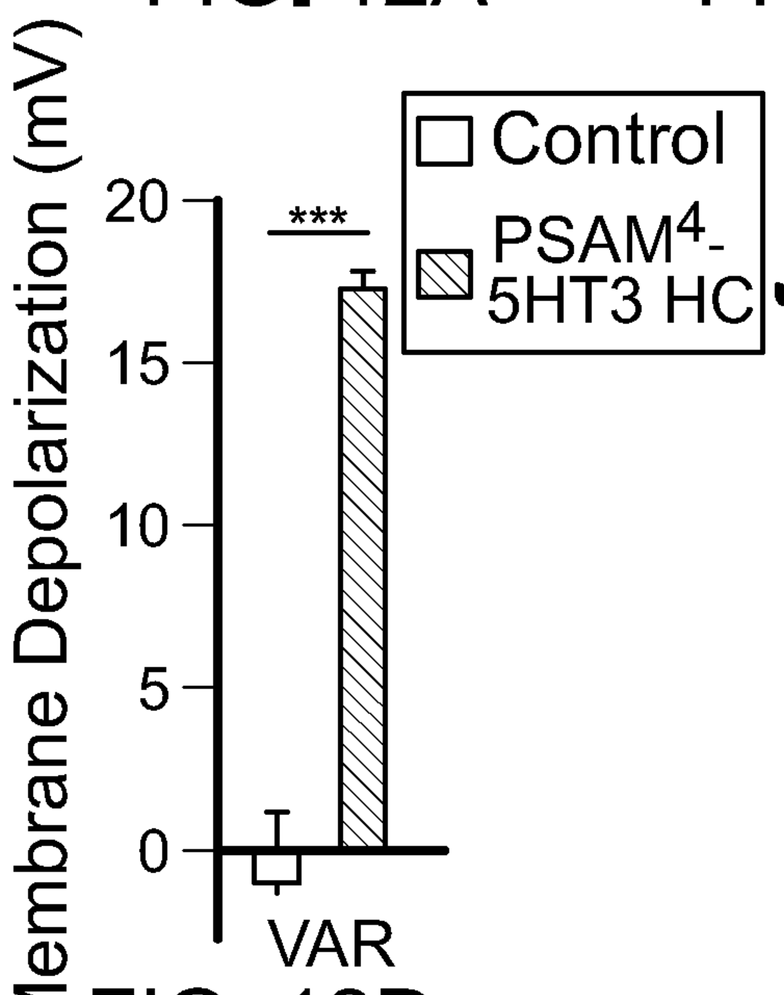


FIG. 12D

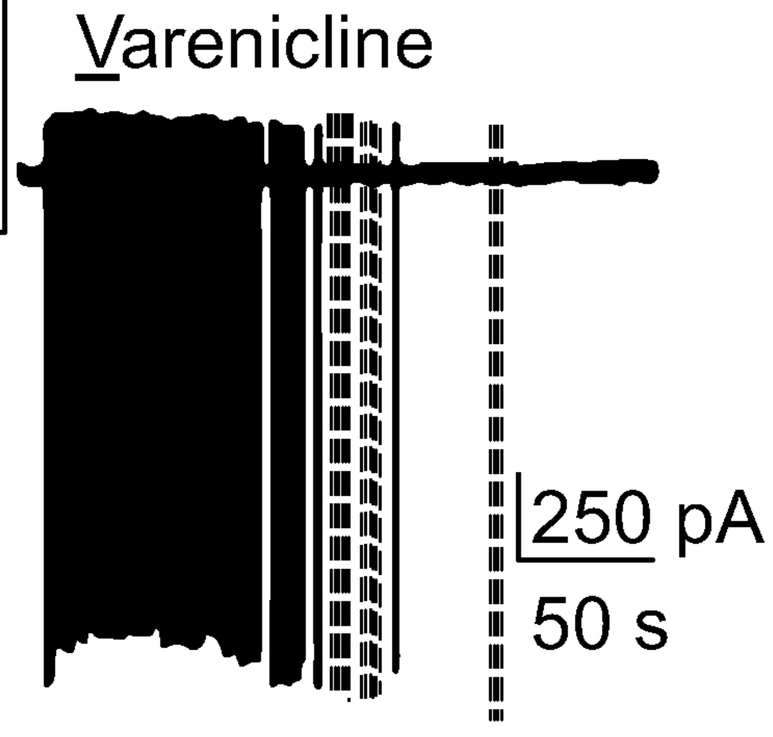
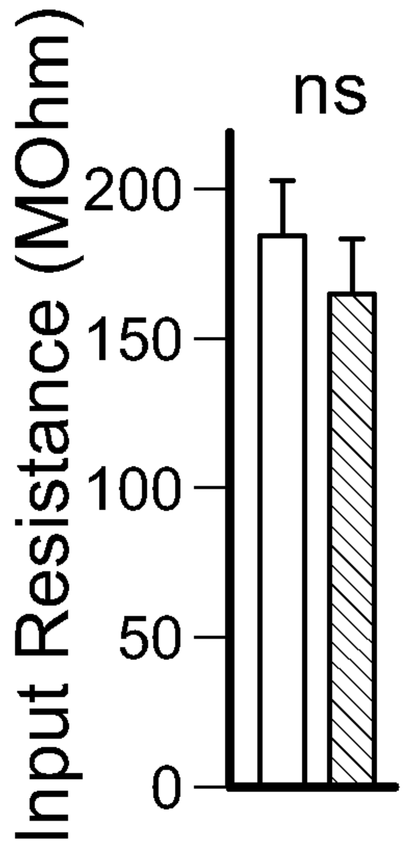
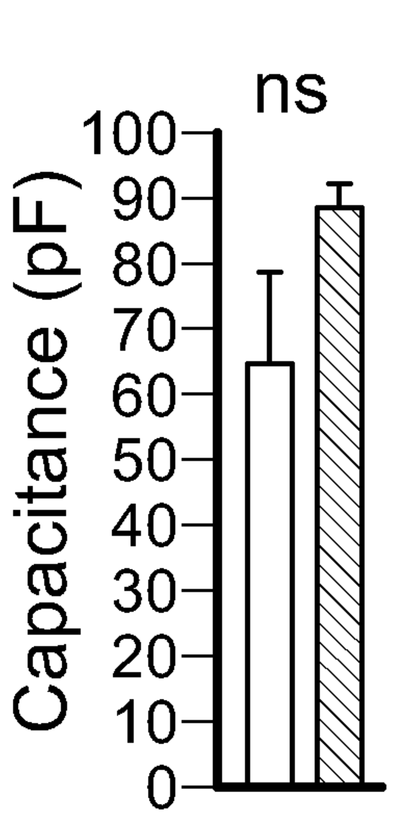


FIG. 12E





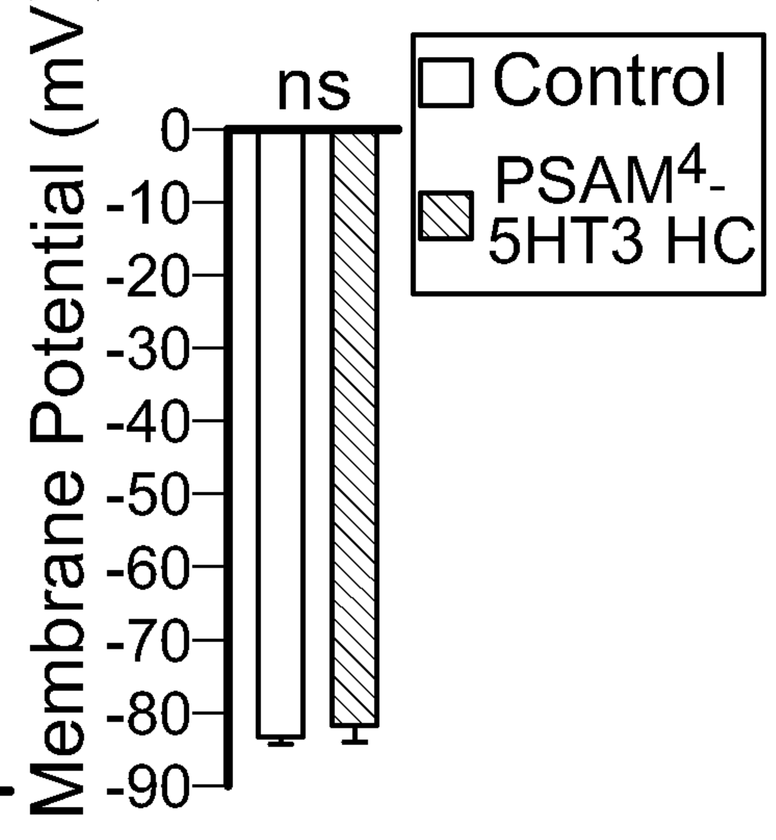


FIG. 12F

WO 2019/094778
PCT/US2018/060109

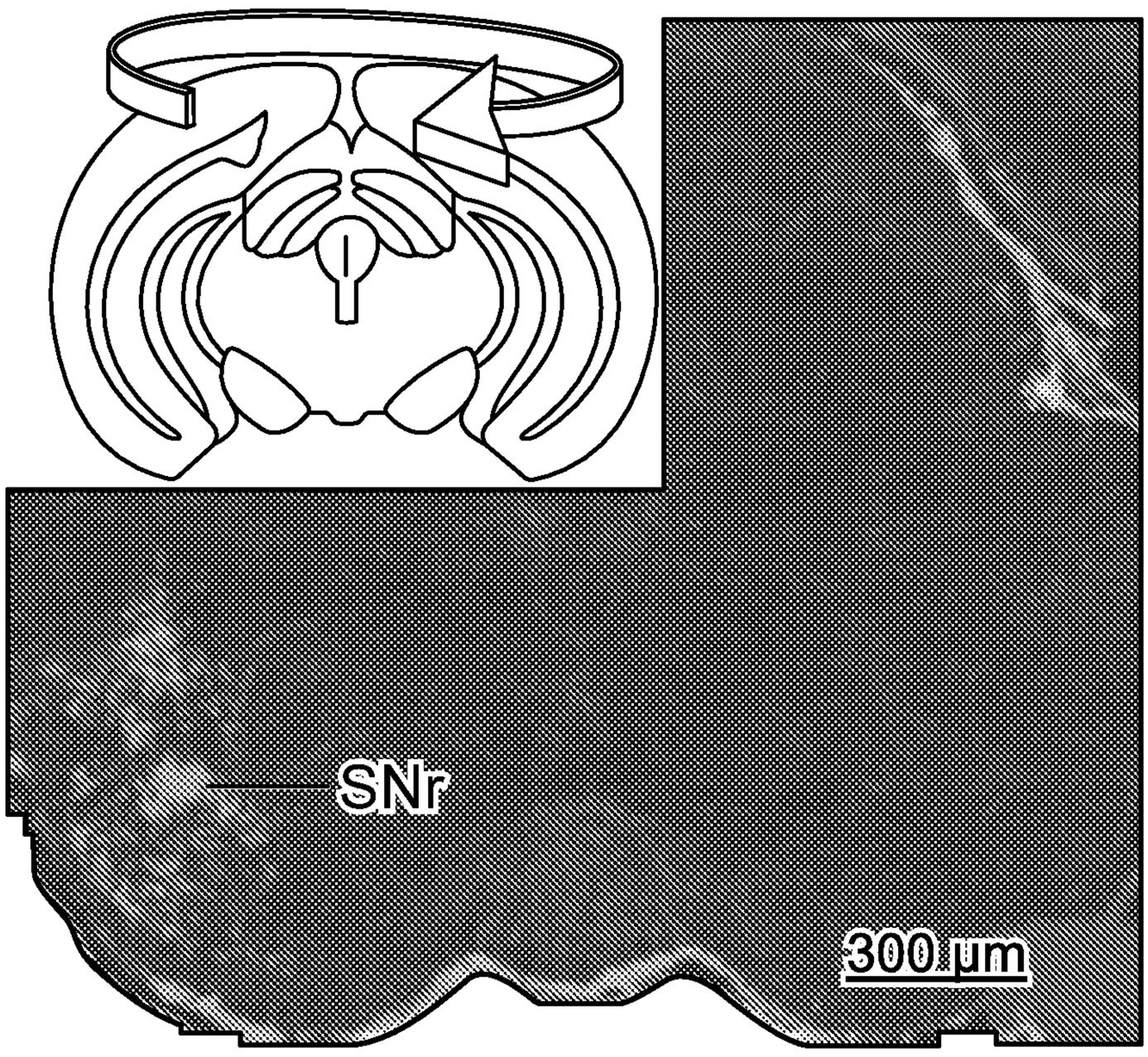


FIG. 13A

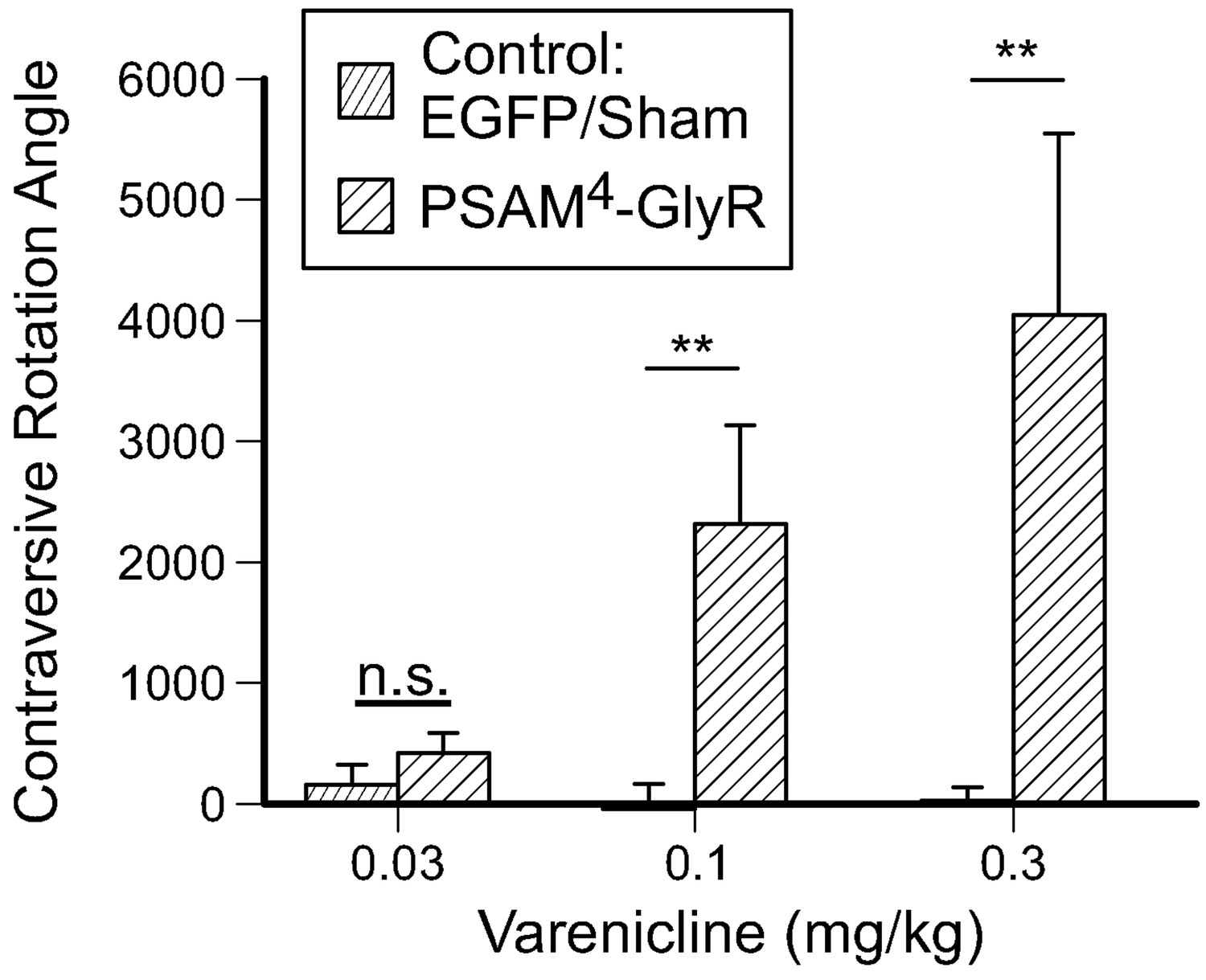


FIG. 13B

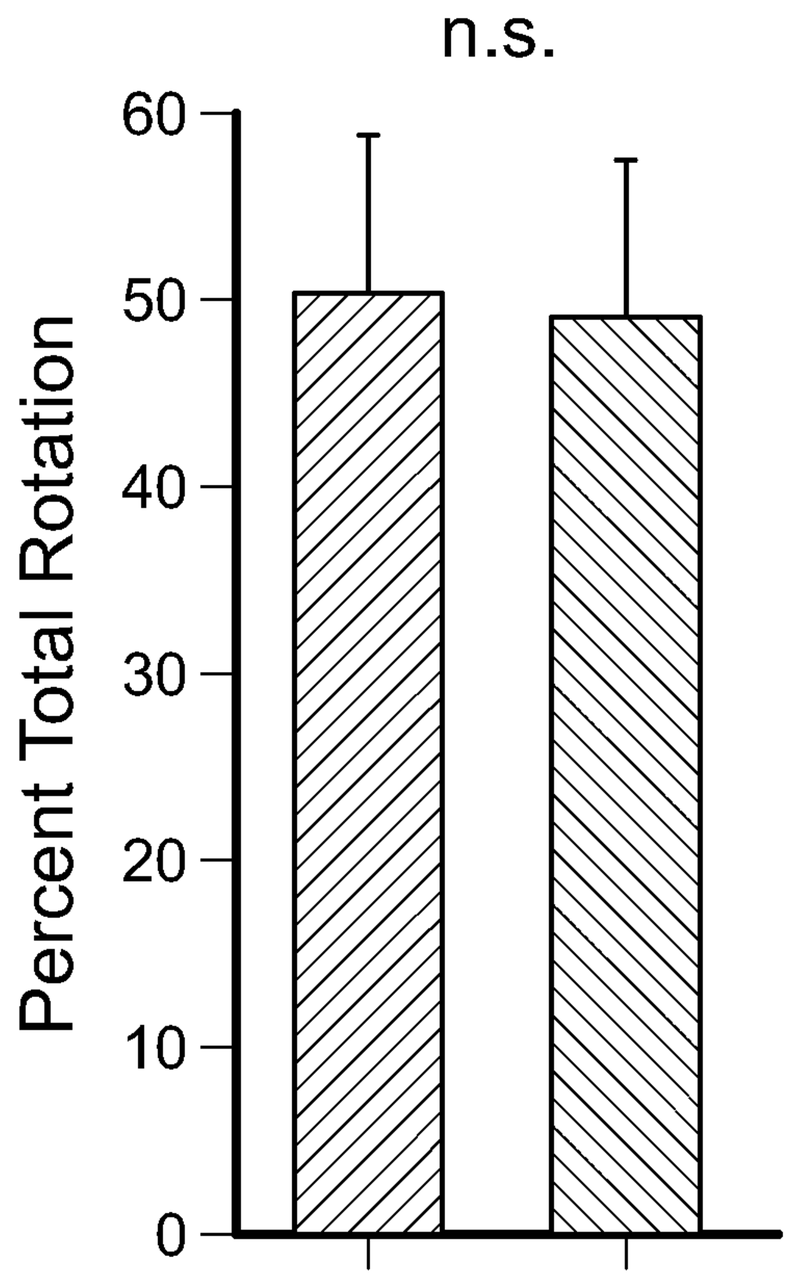


FIG. 13C

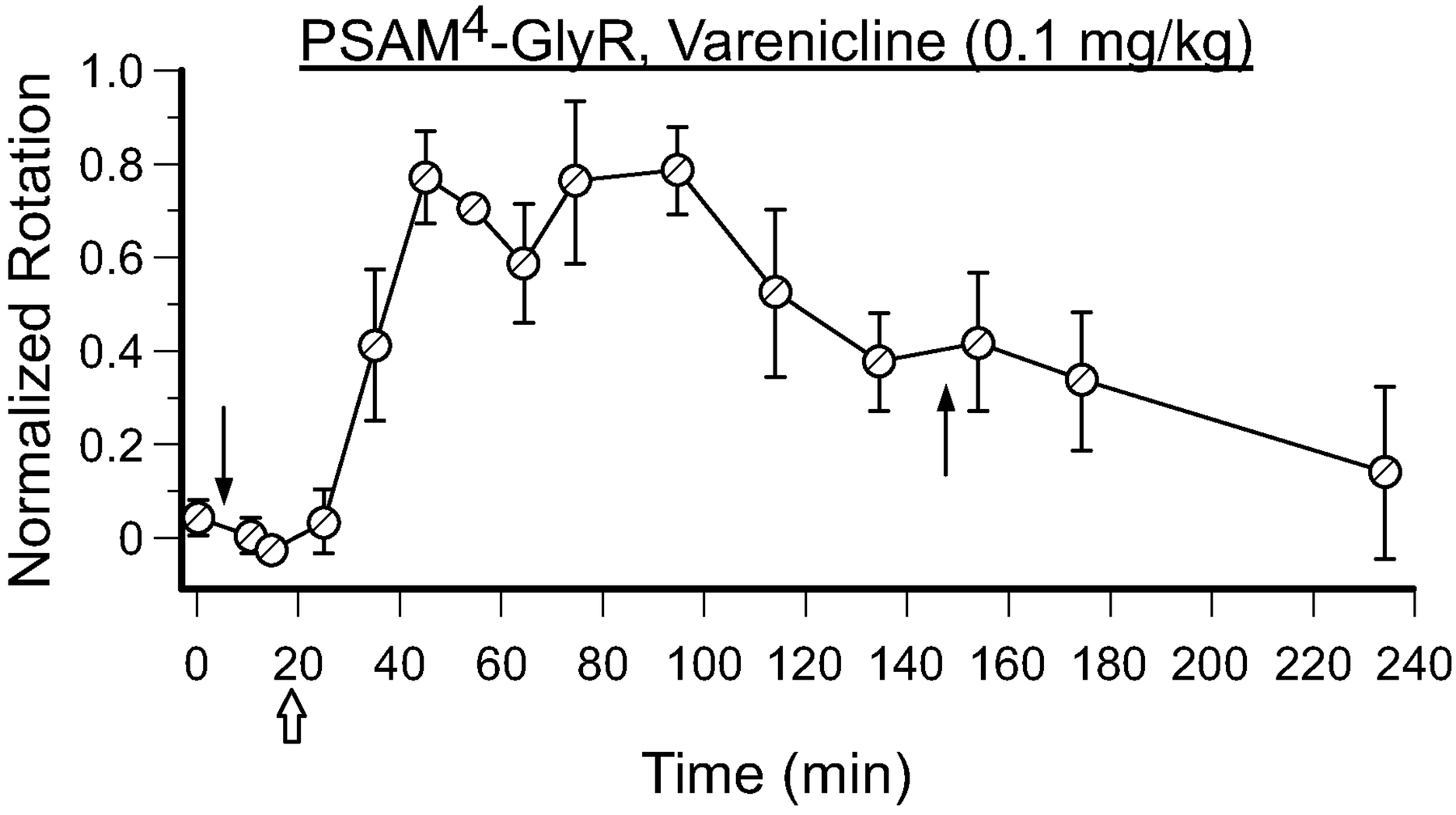


FIG. 13D

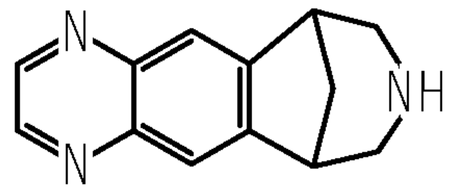
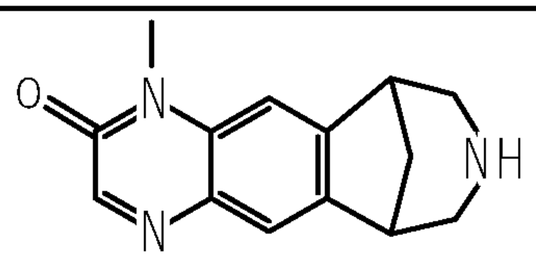
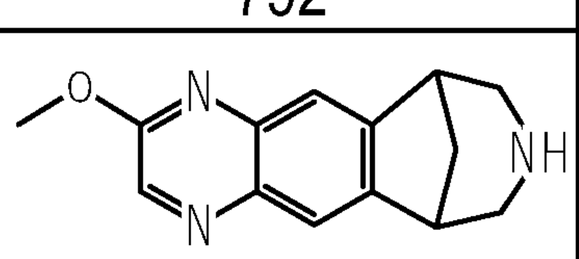
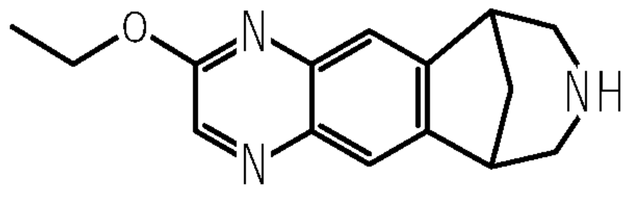
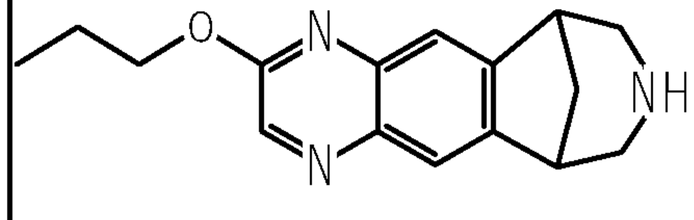
	α7 nAChR	α7-GlyR	α7-5HT3	PSAM^4 - GlyR	PSAM^4 - 5HT3	α4β2 agonist	h5HT3 agonist	α4β2 1 mM ACh	LED in vivo
 varenicline	not determined	620 (200) 390-fold	920 (150) 230-fold	1.6 (0.1)	4 (2)	250 (60) 160-fold	1,400 (400) 880-fold	3 2-fold	0.1 mg/kg
 792	>1,000-fold	>30,000 >10,000-fold	>30,000 >10,000-fold	2.3 (0.3)	1.6 (0.2)	520 (100) 230-fold	40,500 (500) >10,000-fold	(agonist)	1 mg/kg
 793	>1,000-fold	31,000 (17,000) >10,000-fold	26,000 (4,200) >10,000-fold	0.6 (0.4)	0.9 (0.4)	610 (250) 1,000-fold	1,300 (0) 2,200-fold	23 (5) 38-fold	0.03 mg/kg
 815	>1,000-fold	>100,000 >10,000-fold	>100,000 >10,000-fold	0.5 (1)	0.8 (0.4)	>30 >10,000-fold	1,200 (100) 3,000-fold	21 (4) 42-fold	0.1 mg/kg
 817	>1,000-fold	>100,000 >10,000-fold	>100,000 >10,000-fold	0.3 (0.4)	0.5 (0.2)	>30 >10,000-fold	1,500 (100) 5,000-fold	31 (10) 100-fold	0.1 mg/kg

FIG. 14A

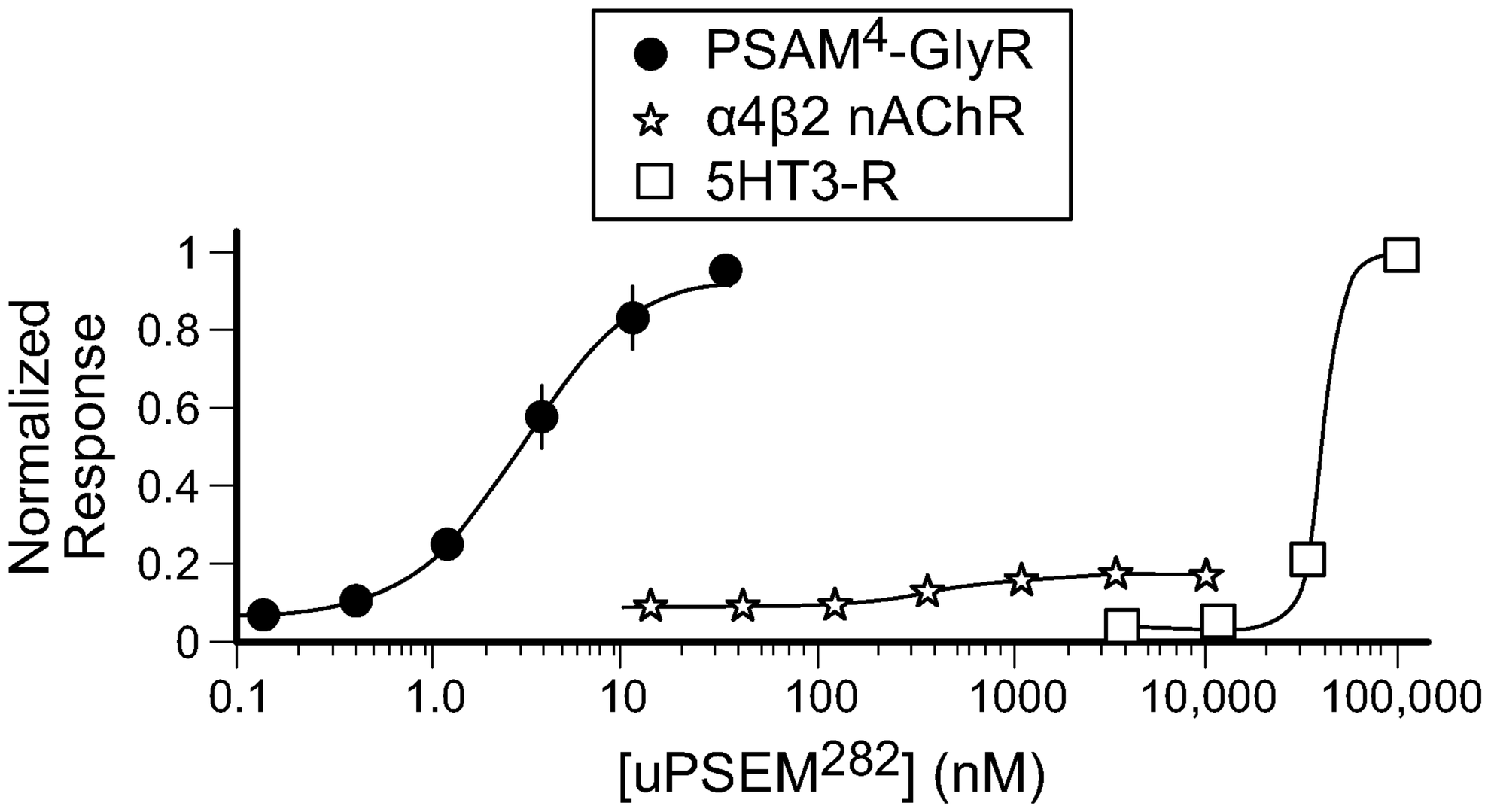


FIG. 14B

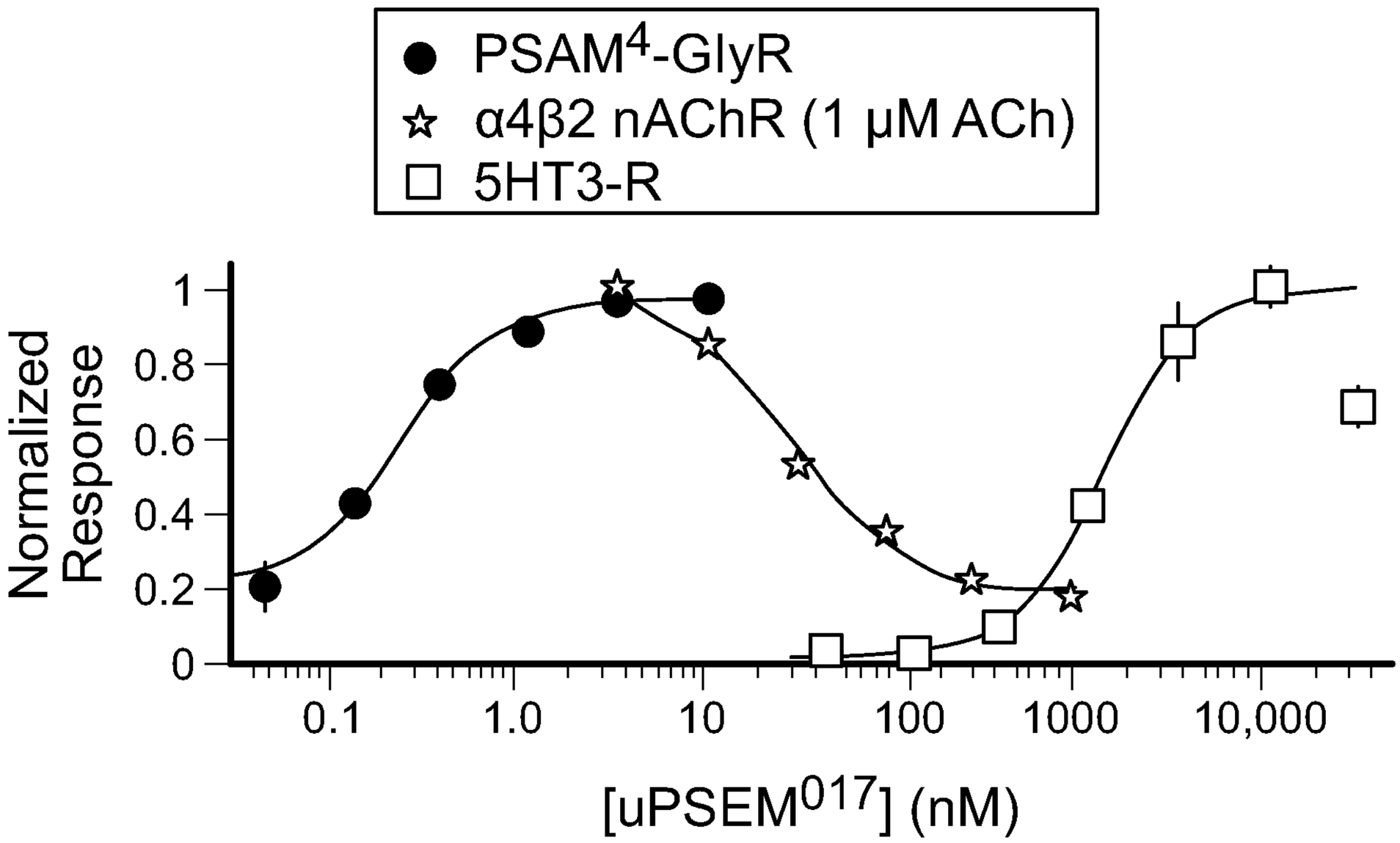


FIG. 14C

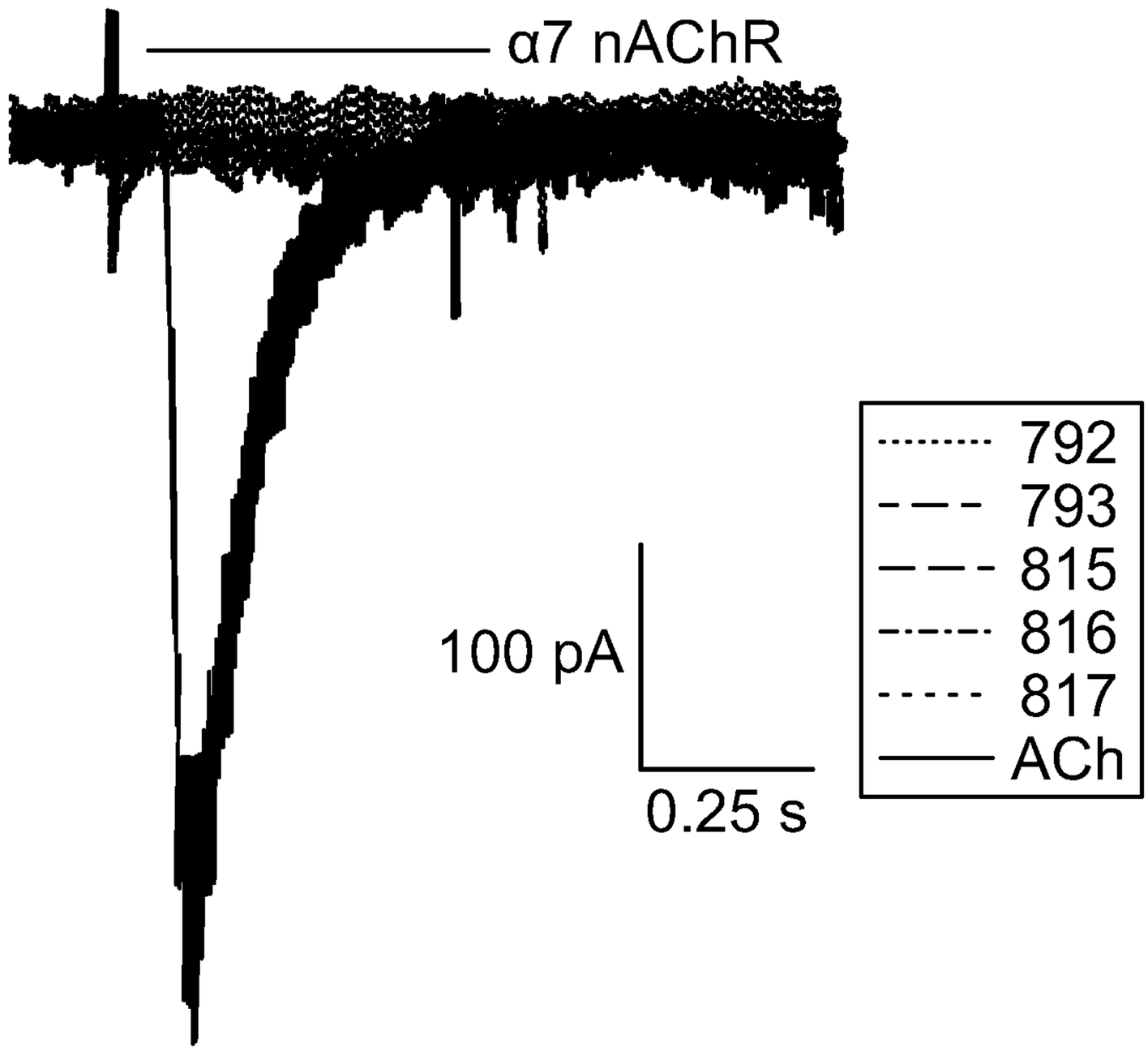


FIG. 14D

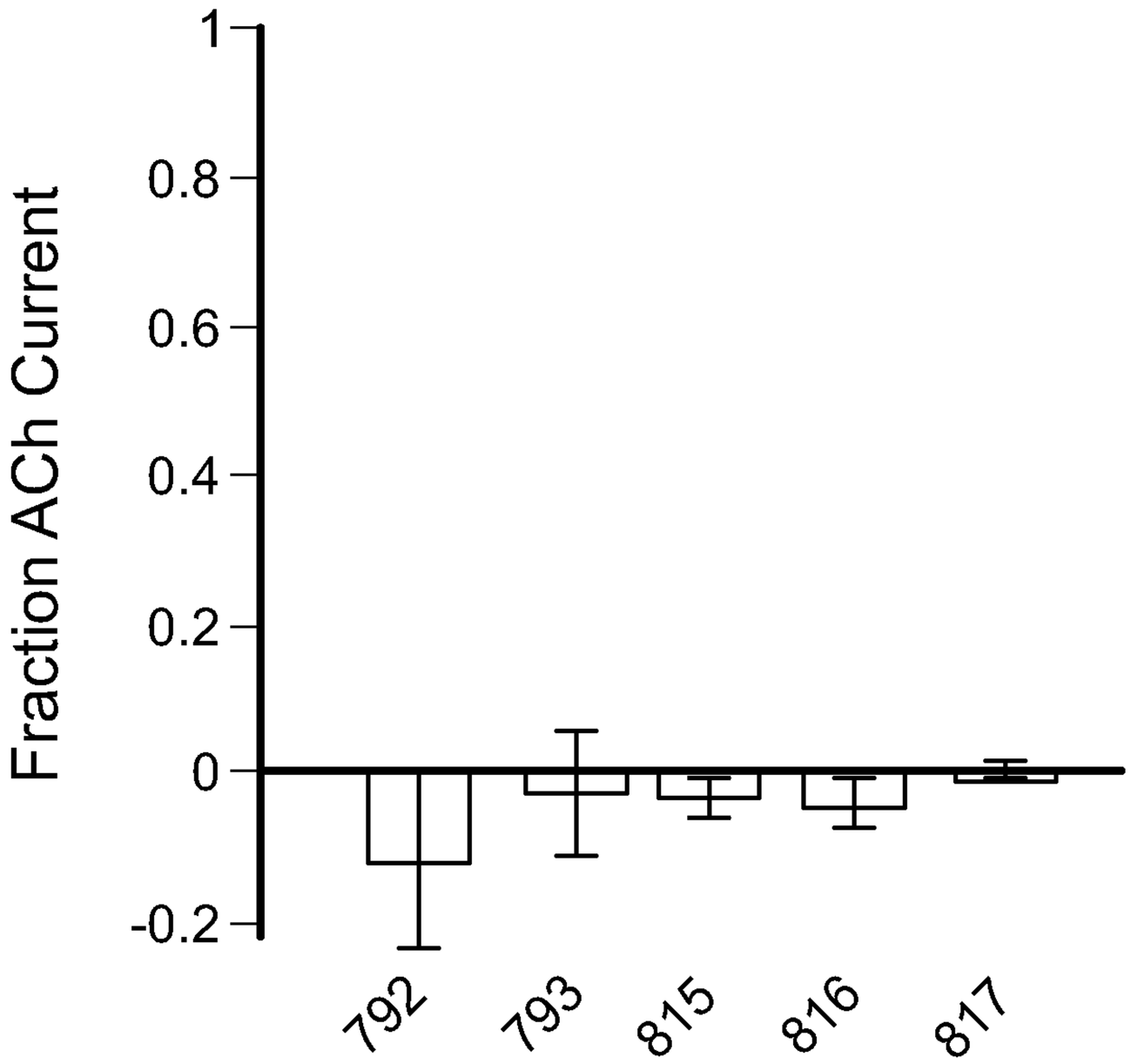


FIG. 14E

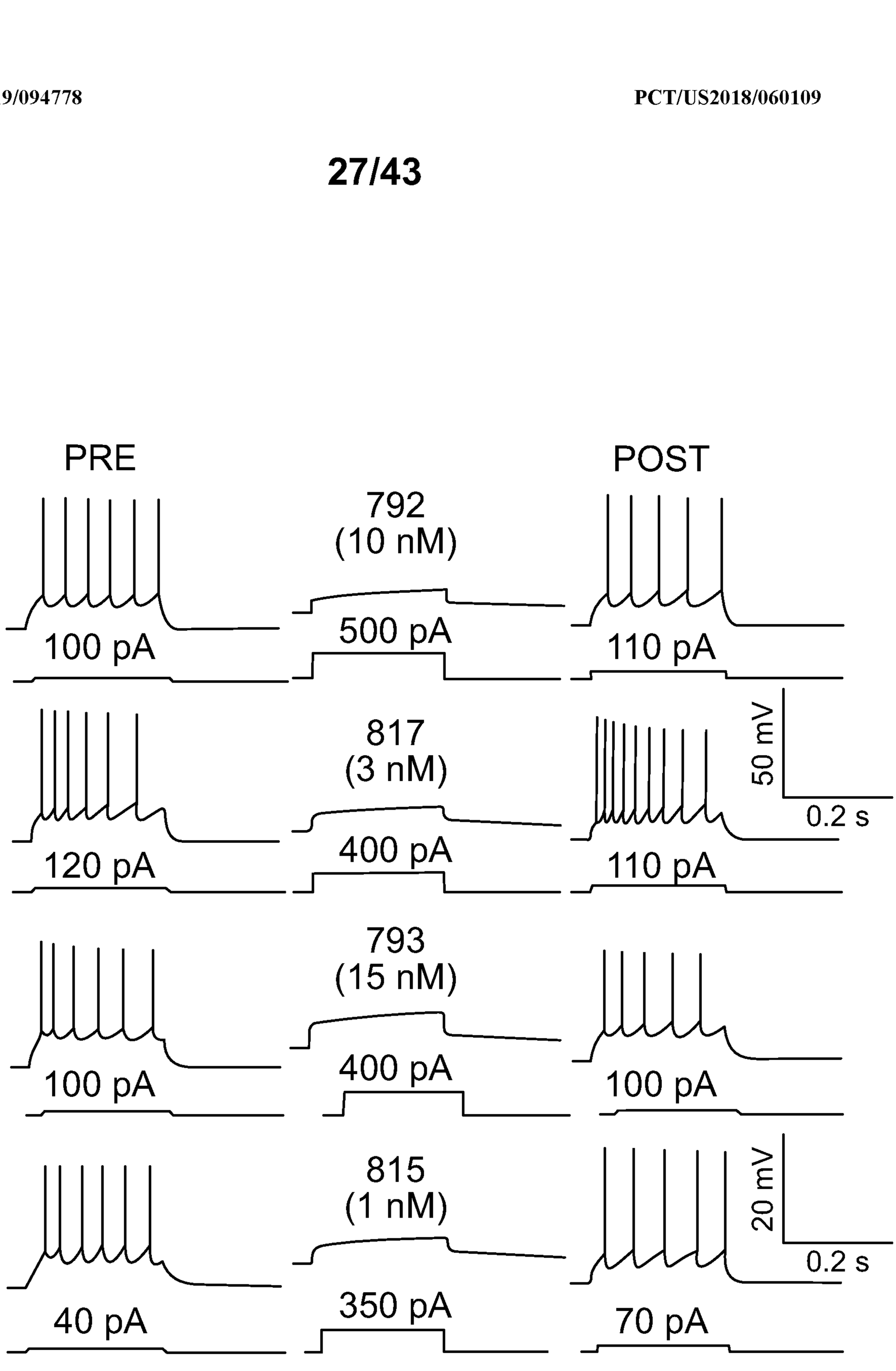

PRE
POST
792
(10 nM)
100 pA
500 pA
110 pA
817
(3 nM)
120 pA
400 pA
110 pA
50 mV
0.2 s
793
(15 nM)
100 pA
400 pA
100 pA
815
(1 nM)
40 pA
350 pA
70 pA
20 mV
0.2 s

FIG. 14F

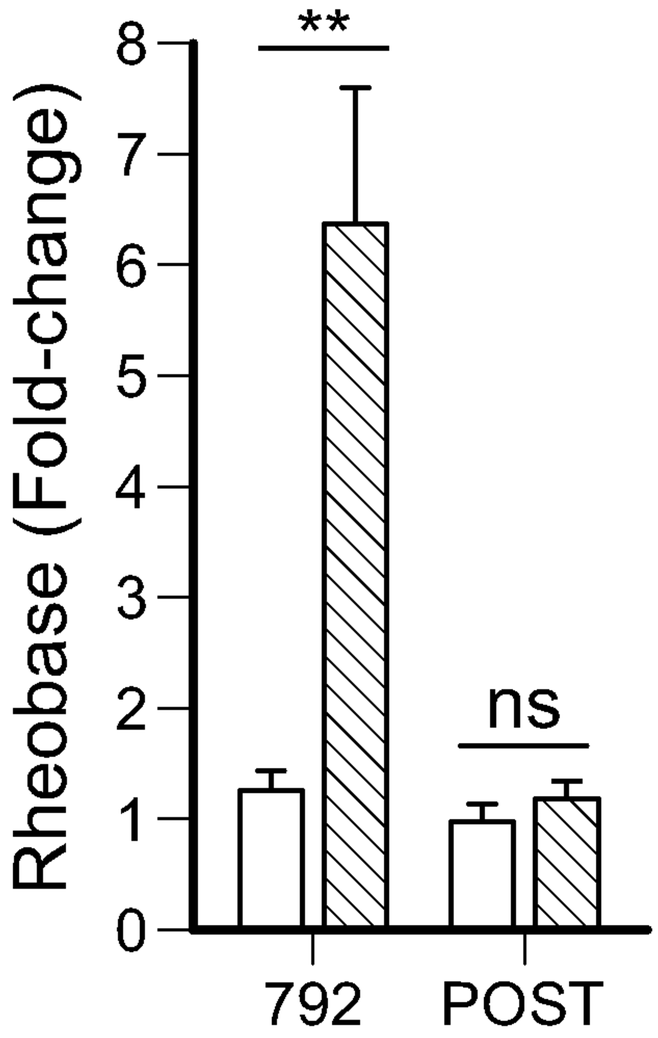


FIG. 14G

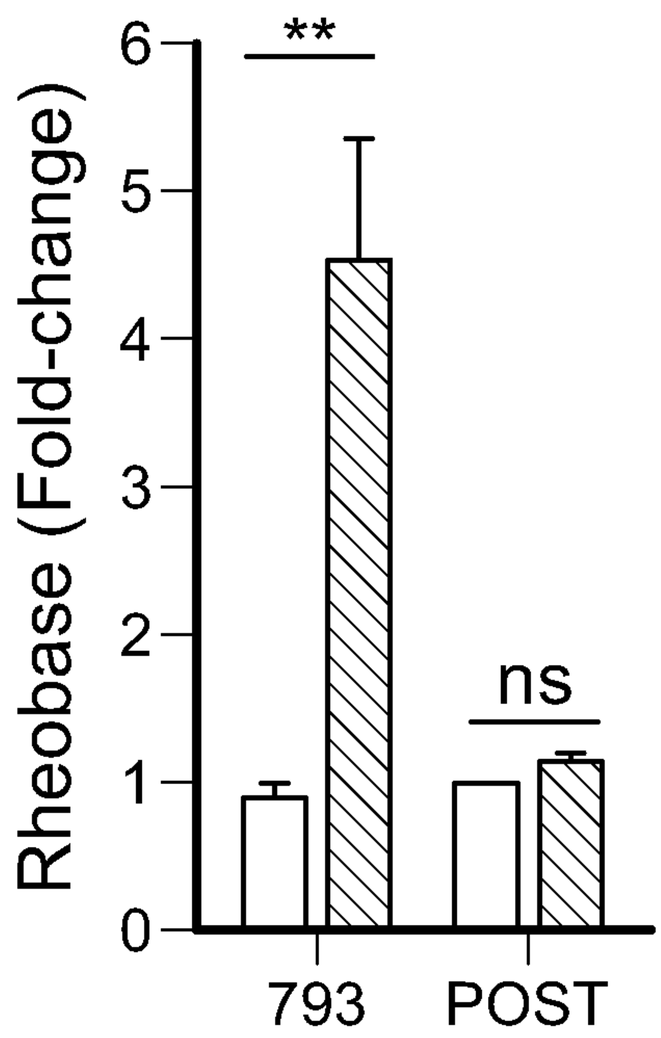


FIG. 14H

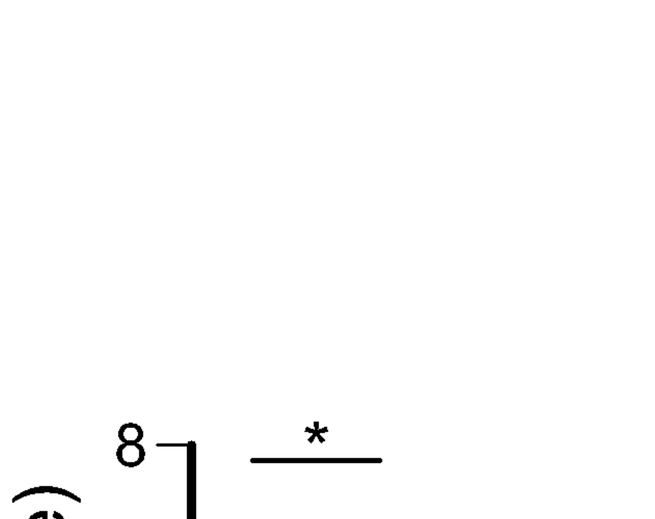


FIG. 14I

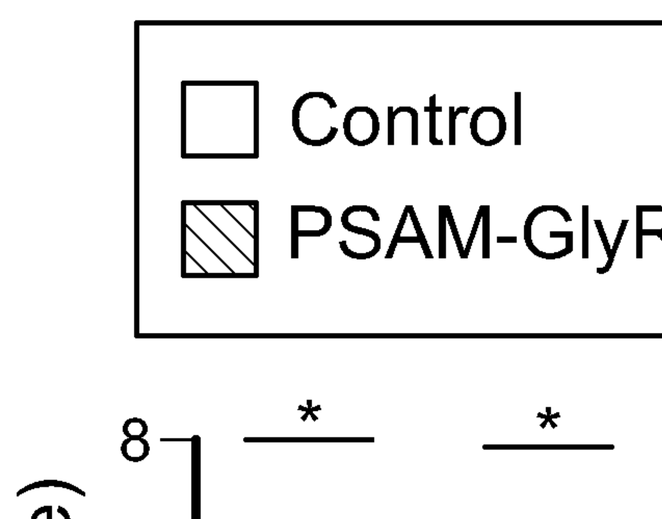


FIG. 14J

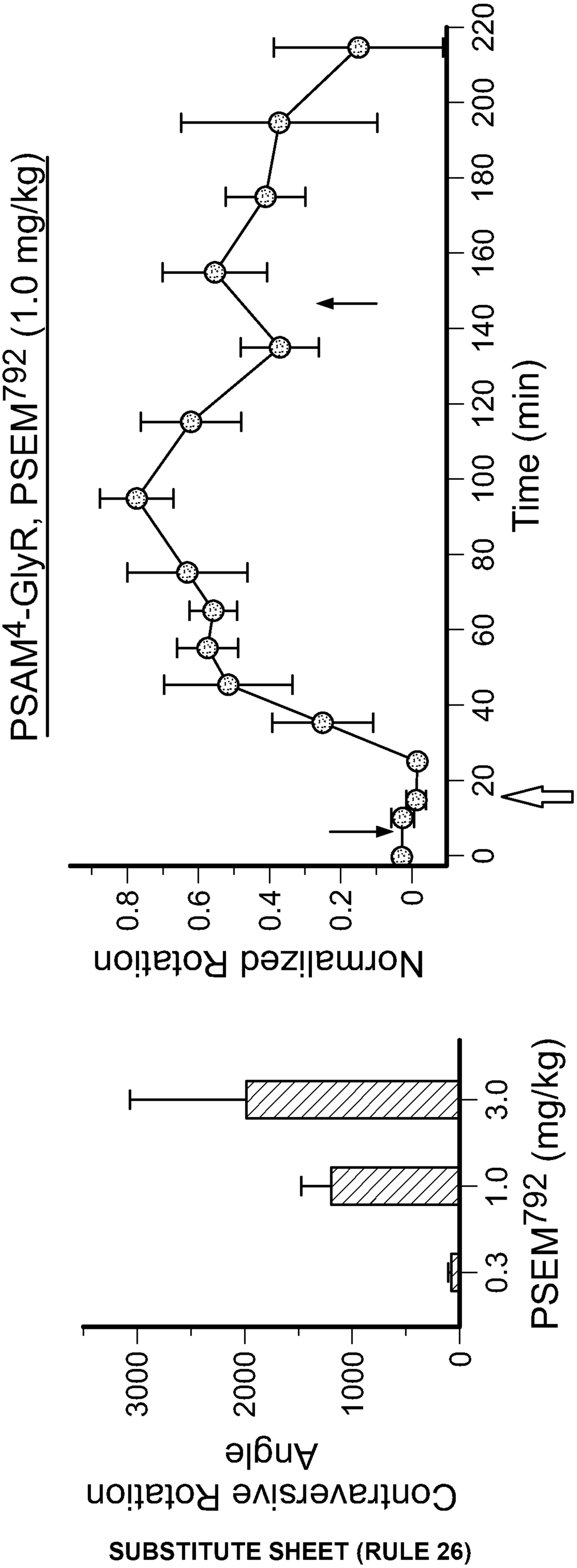


FIG. 15B

FIG. 15A

SUBSTITUTE SHEET (RULE 26)

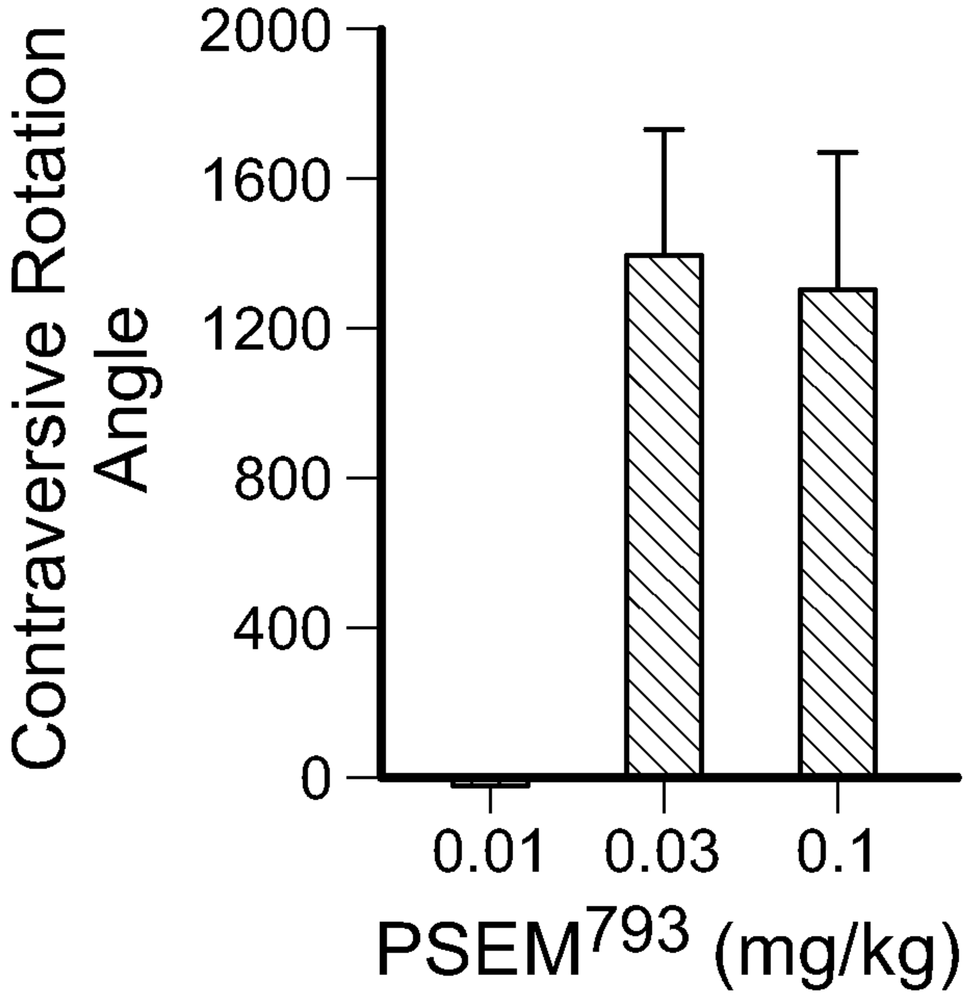


FIG. 15C

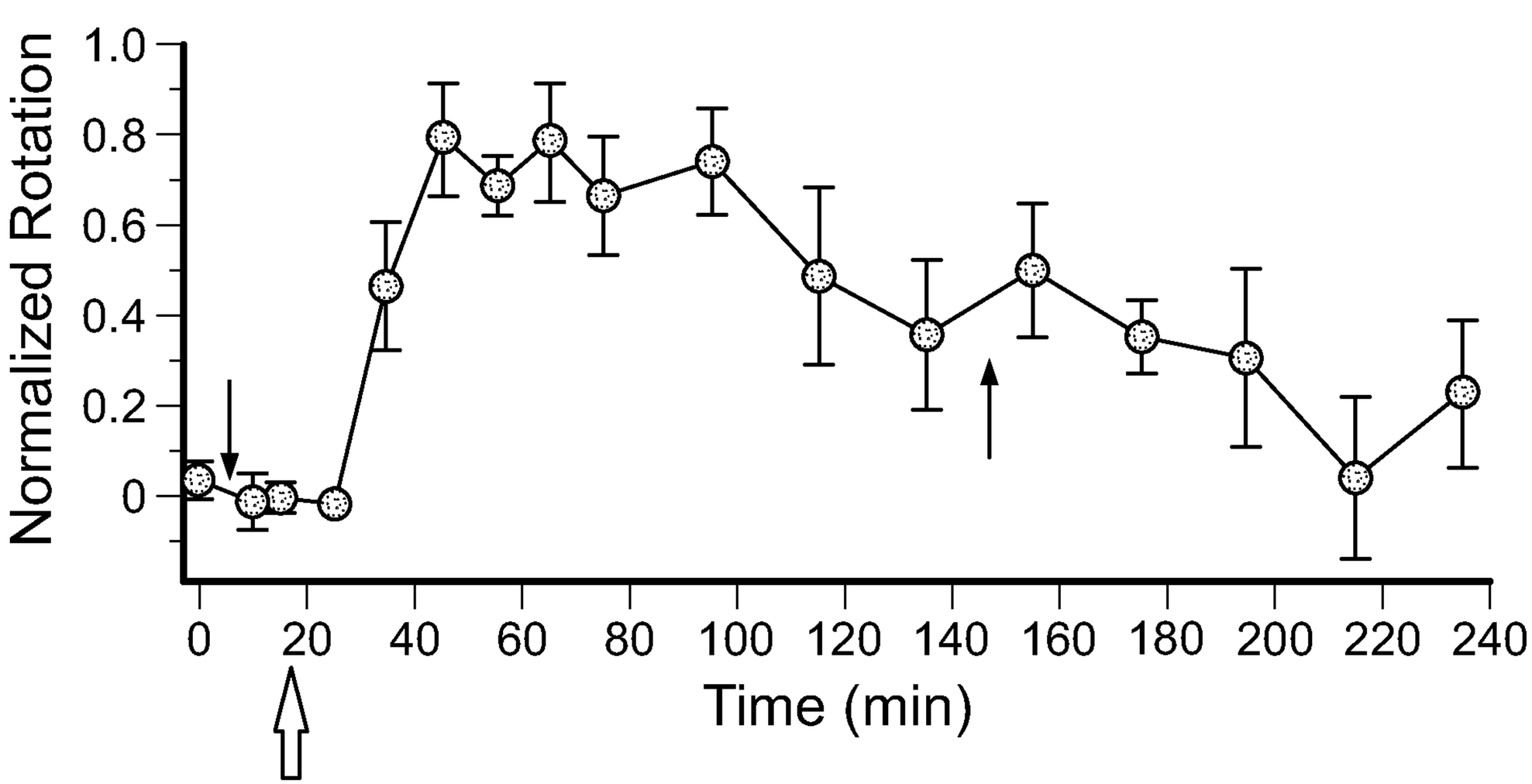


FIG. 15D

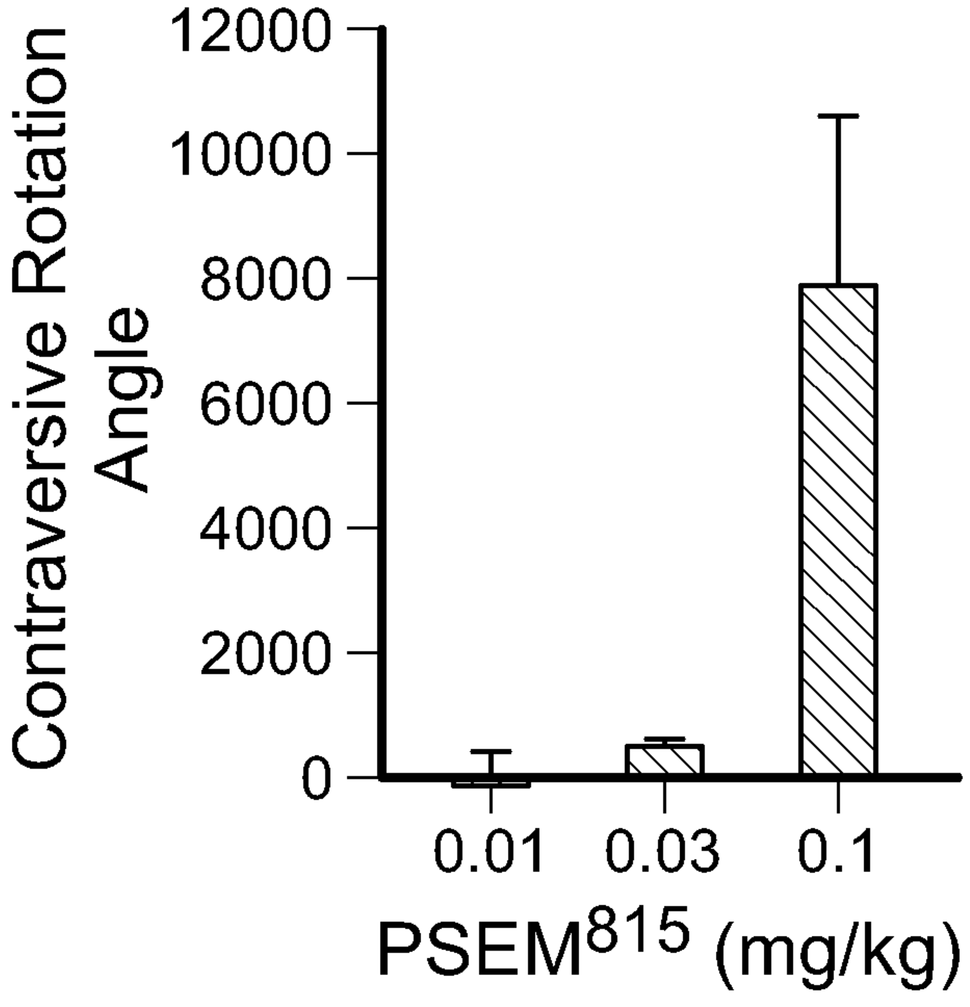


FIG. 15E

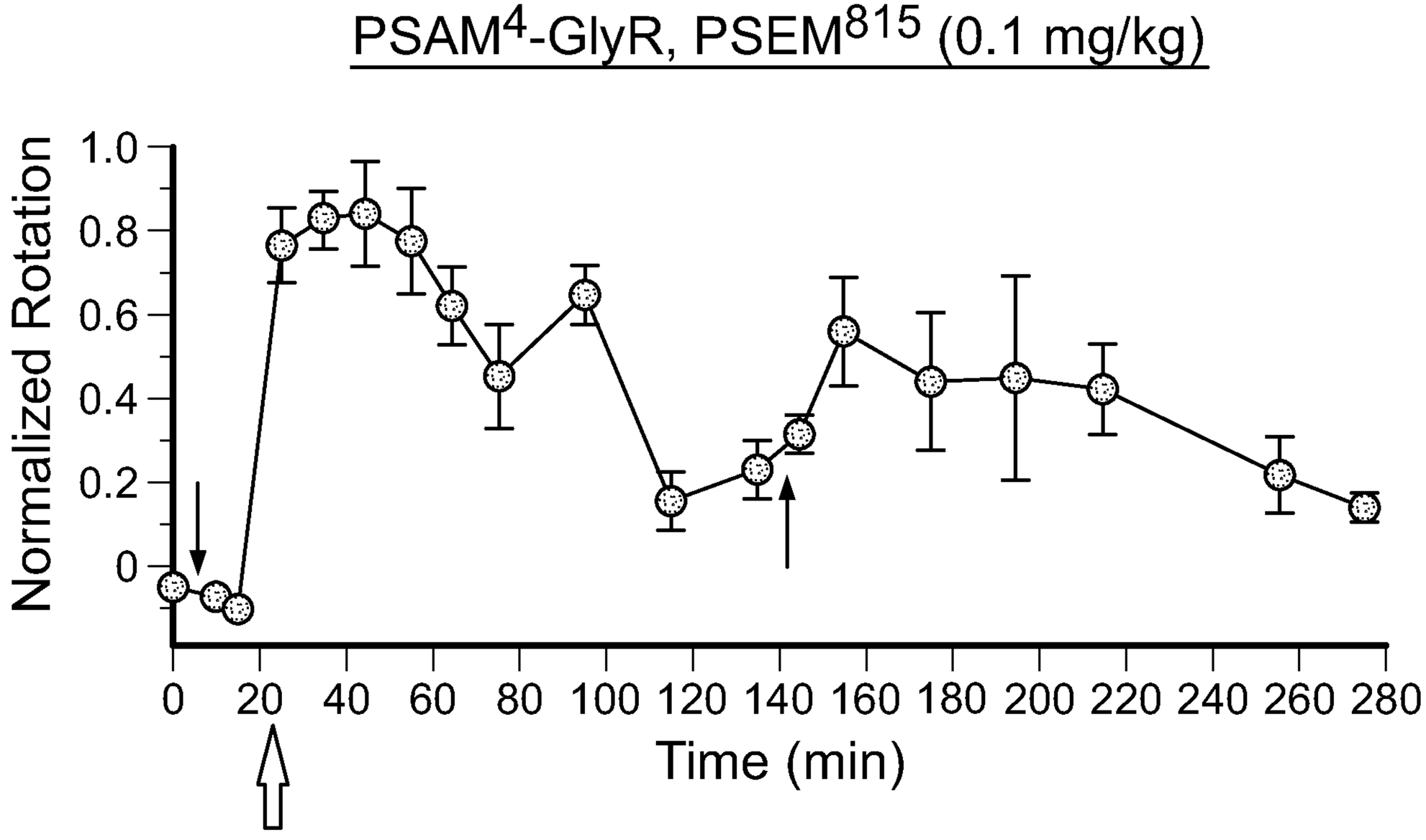


FIG. 15F

SUBSTITUTE SHEET (RULE 26)

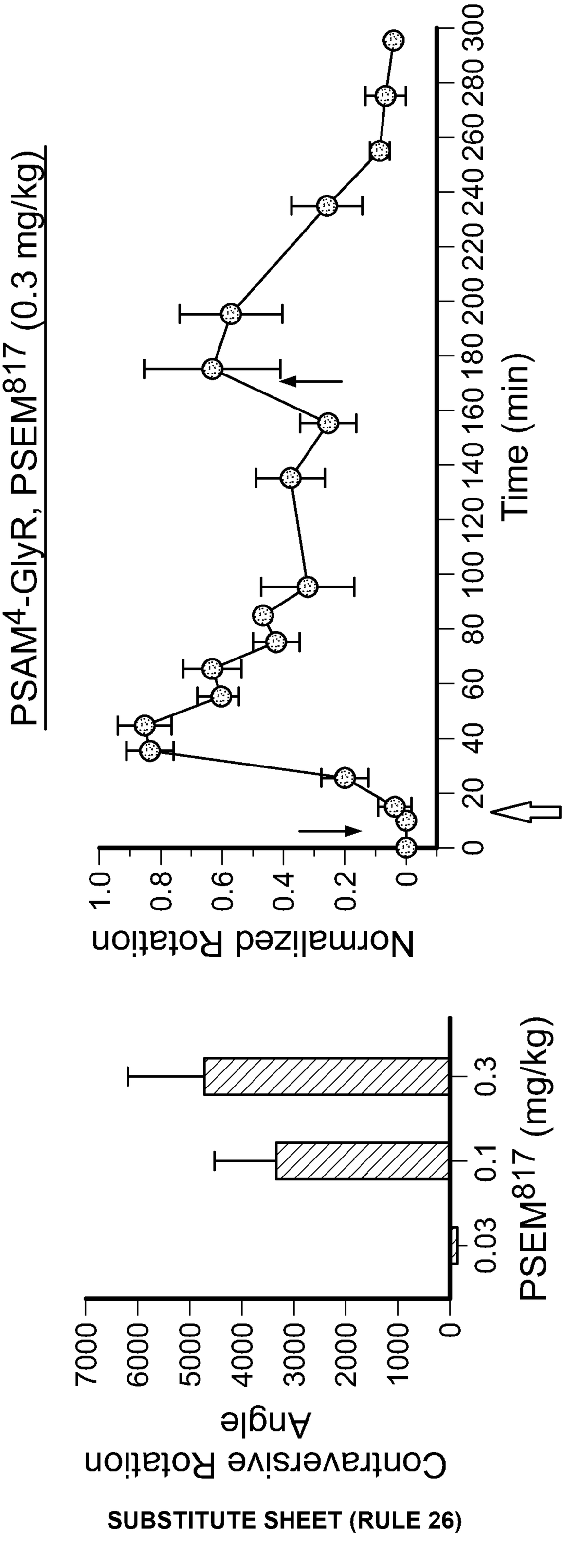

PSAM4-GlyR, PSEM817 (0.3 mg/kg)
Normalized Rotation
1.0
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
Time (min)
Contraversive Rotation
Angle
7000
6000
5000
4000
3000
2000
1000
0
0.03
0.1
0.3
PSEM817 (mg/kg)

FIG. 15H

```
MRCSPGGVWLALAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQP   50

LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTV  100

REPDGQIWKPDILLYNSADERFDATFHTNVGVNSSGHCLYLPPGIFKSSC  150

YIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVG  200

IPGKRSERFYECCKEPFPDVTFTVTMRRRMGYYLIQMYIPSLLIVILSWI  250

SFWINMDAAPARVGLGITTVLTMTTQSSGSRSSLPKVSYVKAIDIWMAVC  300

LLFVFSALLEYAAVNFVSRQHKELLRFRRKRRHHKEDEAGEGRFNFSAYG  350

MGPACLQAKDGISVKGANNSNFCYENEVTTNPPPAPSKSPEEMRKLFIQR  400

AKKIDKISRIGFPMAFLIFNMFYWIIYKIVRREDVHNQ.              439
```

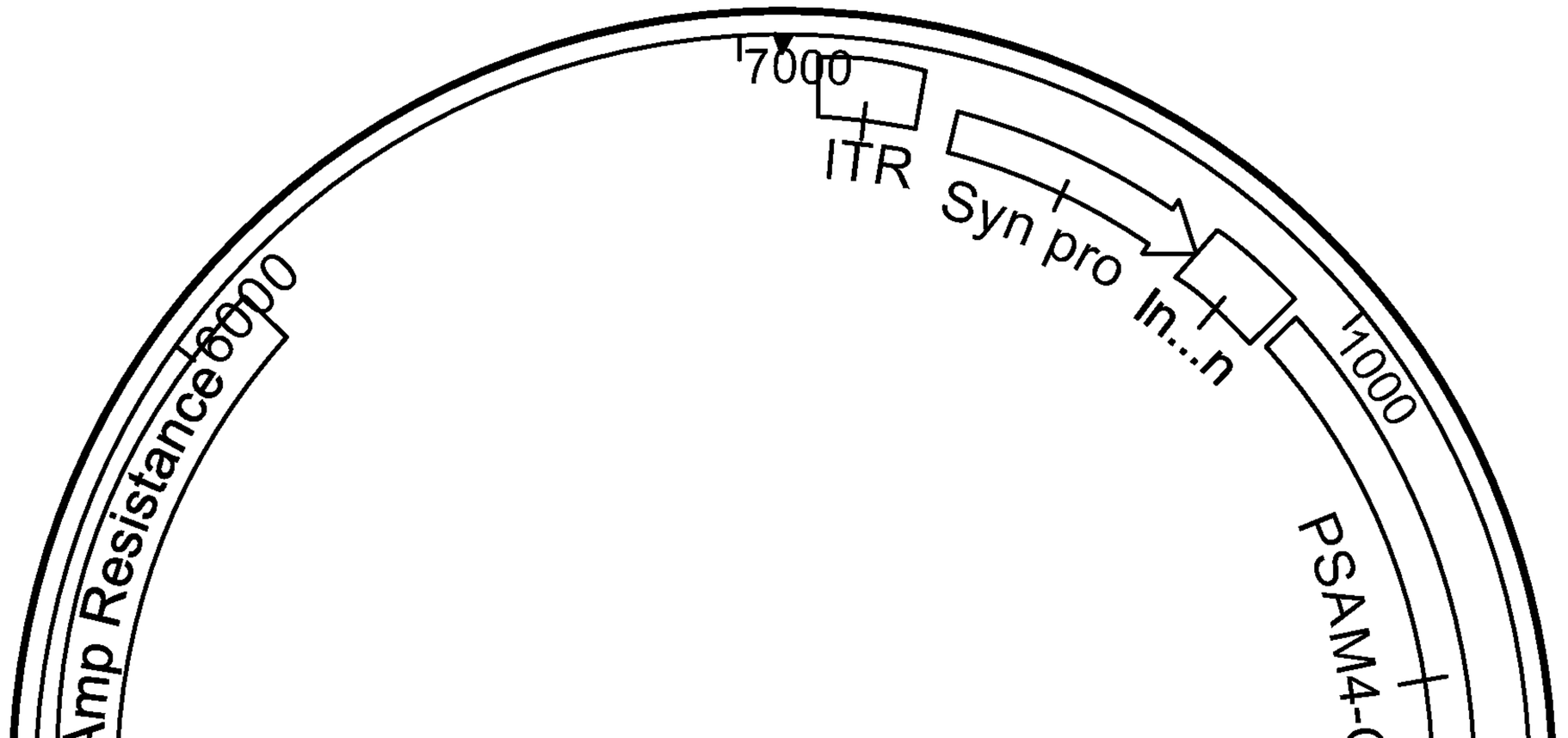
FIG. 16

```
MRRAPSLVLFFLVALCGRGNCGEFQRKLYKELVKNYNPLERPVANDSQPL   50

TVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTVR  100

FPDGQIWKPDILLYNSADERFDATFHTNVGVNSSGHCLYLPPGIFKSSCY  150

IDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVGI  200

PGKRSERFYECCKEPFPDVTFTVTMRRRMGYYLIQMYIPSLLIVILSWIS  250

FWINMDAAPARVGLGITTVLTMTTQSSGSRSSLPKVSYVKAIDIWMAVCL  300

LFVFSALLEYAAVNFVSRQHKELLRFRRKRRHHKEDEAGEGRFNFSAYGM  350

GPACLQAKDGISVKGANNSNFCYENEVTTNPPPAPSKSPEEMRKLFIQRA  400

KKIDKISRIGFPMAFLIFNMFYWIIYKIVRREDVHNQ.               438
```

FIG. 17

```
MRCSPGGVWLALAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQP   50

LTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTV  100

REPDGQIWKPDILLYNSADERFDATFHTNVGVNSSGHCLYLPPGIFKSSC  150

YIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQEADISGYIPNGEWDLVG  200

IPGKRSERFYECCKEPFPDVTFTVTMRRRMGYYLIQMYIPSLLIVILSWI  250

SFWINMDAAPARVGLGITTVLTMTTQSSGSRSSLPKVSYVKAIDIWMAVC  300

LLFVFSALLEYAAVNFVSRQHKELLRFRRKRRHHKEDEAGEGRFNFSAYG  350

MGPACLQAKDGISVKGANNSNQSQPILNTKEMAPQSKPPEELEMSSMPSP  400

VAPLPARTEGVIDMRSMSSIDSFISCATDFPEATRFTTNPPPAPSKSPEE  450

MRKLFIQRAKKIDKISRIGFPMAFLIFNMFYWIIYKIVRREDVHNQ.     497
```

FIG. 18



AAV-SYN::PSAM4-GlyR-IRES-EGFP-EPRE

FIG. 19A

AAV-Syn::PSAM4-GlyR-IRES-EGFP-WPRE

AGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGCGCGCTCGCTCGC
TCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGA
GCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAATGATTAACCCGCCATGCTA
CTTATCTACGTAGCCATGCTCTAGGAAGATCCGAGCTCCAGTGTGCTGGAATTCGCCCTTTTCAGTATTTA
AATTGACGACCGACCCCGACCCACTGGACAAGCACCCAACCCCCATTCCCCAAATTGCGCATCCCCTATCA
GAGAGGGGGAGGGGAAACAGGATGCGGCGAGGCGCGTGCGCACTGCCAGCTTCAGCACCGCGGACAGTGCC
TTCGCCCCCGCCTGGCGGCGCGCCACCGCCGCCTCAGCACTGAAGGCGCGCTGACGTCACTCGCCGGTC
CCCCGCAAACTCCCCTTCCCGGCCACCTTGGTCGCGTCCGCGCCGCCGCCGGCCCAGCCGGACCGCACCAC
GCGAGGCGCGAGATAGGGGGGCACGGGCGCGACCATCTGCGCTGCGGCGCCGGCGACTCAGCGCTGCCTCA
GTCTGCGGTGGGCAGCGGAGGAGTCGTGTCGTGCCTGAGAGCGCAGCTGTGCTCCTGGGCACCGCGCAGTC
CGCCCCCGCGGCTCCTGGCCAGACCACCCCTAGGACCCCCTGCCCCAAGTCGCAGCCGTTGGATCAGGTAA
GTATCAAGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCTTGTCGAGACAGAGAAGACTCTTG
CGTTTCTGATAGGCACCTATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAGGTGATGATATCAC
TAGTGCTAGCGCCACCATGCGCTGTTCTCCAGGCGGCGTGTGGCTCGCCCTGGCTGCTTCCCTTCTGCACG
TTAGCCTGCAGGGTGAGTTCCAGCGCAAACTGTATAAGGAGCTTGTTAAGAATTATAACCCCCTGGAGCGG
CCGGTCGCAAATGATTCCCAGCCACTGACAGTGTACTTCAGCCTCTCCTTGCTGCAGATCATGGACGTGGA
TGAAAAGAACCAGGTGCTGACCACTAATATTTGGTTGCAGATGTCCTGGACCGATCACTACTTGCAGTGGA
ATGTGAGCGAATACCCAGGTGTAAAGACTGTAAGATTCCCTGACGGCCAAATCTGGAAACCAGATATCCTG
CTGTACAACAGCGCAGACGAAAGGTTTGATGCAACATTTCACACCAACGTGGGAGTCAATTCTTCAGGCCA
CTGCCTGTACCTGCCCCCTGGAATCTTCAAGTCCTCATGCTATATCGACGTCCGCTGGTTTCCCTTCGACG
TCCAGCACTGCAAACTCAAATTCGGGAGCTGGAGCTACGGCGGATGGAGCCTGGATCTGCAAATGCAGGAG
GCTGACATCTCTGGTTACATCCCGAATGGGGAGTGGGACCTTGTGGGAATCCCCGGTAAAAGAAGCGAGCG
ATTTTATGAATGCTGCAAAGAGCCCTTCCCAGATGTCACCTTCACAGTGACCATGCGGAGACGCATGGGTT
ATTATCTGATCCAAATGTATATCCCAAGCTTGCTTATAGTGATTTTGTCATGGATCTCCTTCTGGATTAAT
ATGGACGCCGCTCCAGCTAGGGTCGGACTGGGCATCACCACAGTGCTGACAATGACTACTCAGAGCTCAGG
CAGCCGAGCCAGCTTGCCCAAGGTTTCTTACGTGAAGGCCATCGATATCTGGATGGCTGTCTGCCTTCTGT
TTGTCTTCAGCGCACTGCTGGAATACGCCGCTGTCAATTTTGTGTCTCGACAGCATAAAGAGCTGTTGCGG
TTCAGAAGAAAACGACGCCACCACAAAGAGGATGAGGCAGGAGAAGGACGCTTCAACTTTAGCGCCTATGG
TATGGGACCTGCTTGCCTCCAGGCTAAAGACGGAATTTCCGTGAAGGGAGCCAACAATAGCAACACAACCA
ACCCACCCCCTGCTCCATCTAAGAGCCCGGAGGAAATGCGCAAACTCTTTATTCAGAGAGCGAAAAAGATC
GACAAAATCTCCCGGATCGGATTCCCCATGGCTTTCCTGATTTTCAACATGTTTTATTGGATCATCTACAA
GATTGTGCGAAGGGAGGACGTACACAACCAGTAAGCGGCCGCAATTCCCCCCGCCCCCCCCCCCCCCCCT
CACCCTCCCCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGGAATAAGGCCGGTGTGCGTTTGTCTATATG
TTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTGTCTTCTTGACGAG
CATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTC

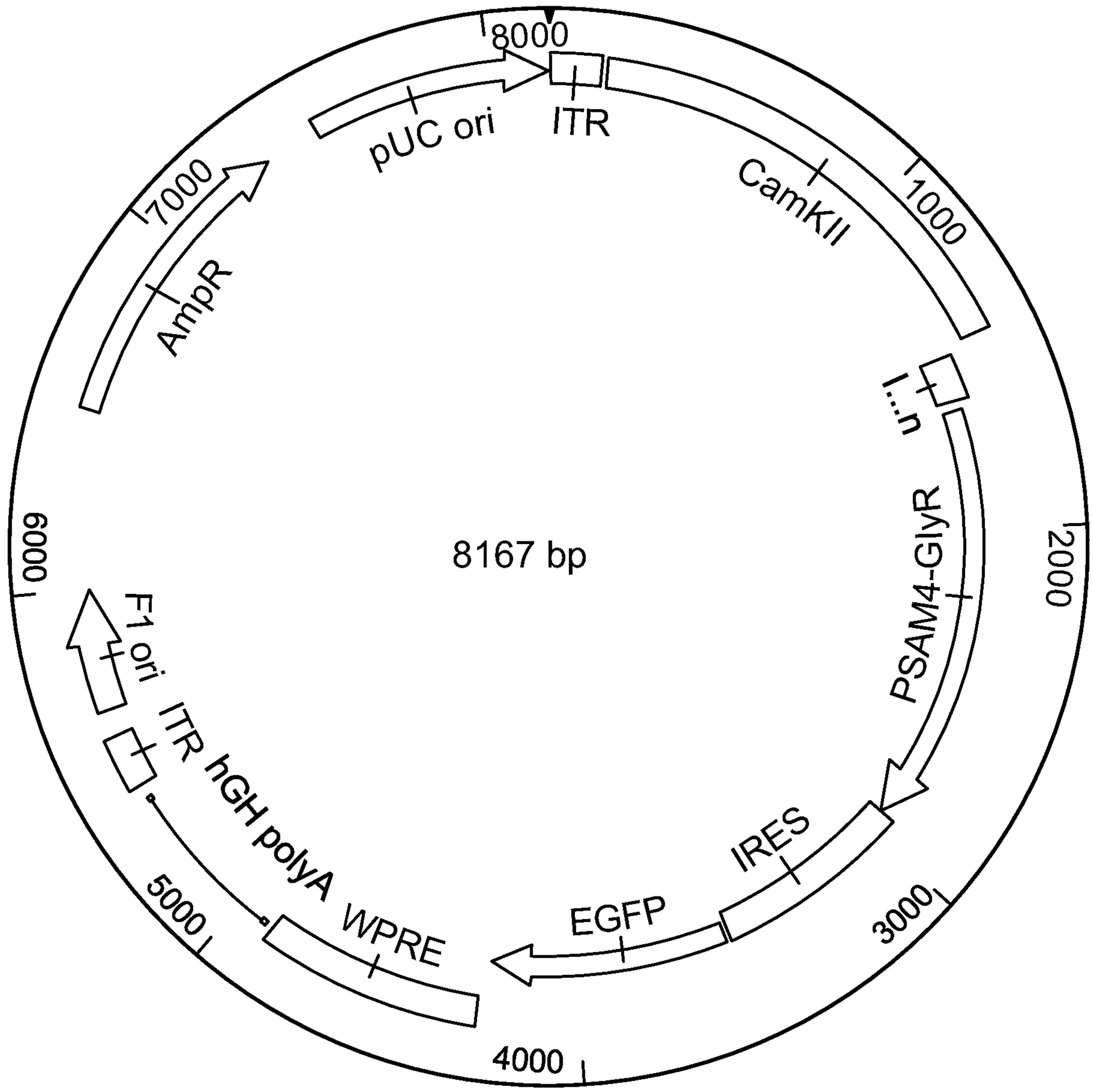
FIG. 19B

CTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGC
GACAGGTGCCTCTGCGGCCAAAAGCCACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCA
CGTTGTGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCTCTCCTAAGCGTATTCAACAAGGGGCTGAAGGA
TGCCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACATGTGTTTAGT
CGAGGTTAAAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCCTTTGAAAAACACGATGATAA
TATGGCCACAACCATGGGAGATCCGGTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGG
TCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTAC
GGCAAGCTGACCCTGAAGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCAC
CCTGACCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCG
CCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCCGCGCC
GAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGG
CAACATCCTGGGGCACAAGCTGGAGTACAACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGA
AGAACGGCATCAAGGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCAC
TACCAGCAGAACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTC
CAAGCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGGA
TCACTCTCGGCATGGACGAGCTGTACAAGTAAACCGGTAATCAACCTCTGGATTACAAAATTTGTGAAAGA
TTGACTGGTATTCTTAACTATGTTGCTCCTTTTACGCTATGTGGATACGCTGCTTTAATGCCTTTGTATCA
TGCTATTGCTTCCCGTATGGCTTTCATTTTCTCCTCCTTGTATAAATCCTGGTTGCTGTCTCTTTATGAGG
AGTTGTGGCCCGTTGTCAGGCAACGTGGCGTGGTGTGCACTGTGTTTGCTGACGCAACCCCCACTGGTTGG
GGCATTGCCACCACCTGTCAGCTCCTTTCCGGGACTTTCGCTTTCCCCCTCCCTATTGCCACGGCGGAACT
CATCGCCGCCTGCCTTGCCCGCTGCTGGACAGGGGCTCGGCTGTTGGGCACTGACAATTCCGTGGTGTTGT
CGGGGAAATCATCGTCCTTTCCTTGGCTGCTCGCCTGTGTTGCCACCTGGATTCTGCGCGGGACGTCCTTC
TGCTACGTCCCTTCGGCCCTCAATCCAGCGGACCTTCCTTCCCGCGGCCTGCTGCCGGCTCTGCGGCCTCT
TCCGCGTCTTCGCCTTCGCCCTCAGACGAGTCGGATCTCCCTTTGGGCCGCCTCCCCGCCGCTTCGAGCAG
ACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGT
GAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTG
CATTCATTTTATGTTTCAGGTTCAGGGGGAGATGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAAT
GTGGTAAAATCGATAAGGATCTTCCTAGAGCATGGCTACGTAGATAAGTAGCATGGCGGGTTAATCATTAA
CTACAAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGC
GACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCTGGCGT
AATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGGACGCGCC
CTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCC
TAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTA
AATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGG

FIG. 19B (Cont.)

TGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCT
TTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAA
GGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTTTAA
CAAAATATTAACGCTTACAATTTAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATT
TTTCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAA
AAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCT
GTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTA
CATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGA
GCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCGC
CGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCAT
GACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAA
CGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGT
TGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAAC
AACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGG
AGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCT
GGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGT
AGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCT
CACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACTTCAT
TTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTT
TTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCG
TAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCA
ACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTA
GTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGG
CTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAG
CGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATA
CCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCG
GCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTC
GGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAA
CGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGT
TATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACG
ACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAG

FIG. 19B (Cont.)



AAV-Camkll::PSAM4-GlyR-IRES-EGFP-WPRE

FIG. 20A

AAV-CamkII::PSAM4-GlyR-IRES-EGFP-WPRE

CCTGCAGGCAGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTT
GGTCGCCCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTG
CGGCCGCACGCGTTTAACATTATGGCCTTAGGTCACTTCATCTCCATGGGGTTCTTCTTCTGATTTTCTAG
AAAATGAGATGGGGGTGCAGAGAGCTTCCTCAGTGACCTGCCCAGGGTCACATCAGAAATGTCAGAGCTAG
AACTTGAACTCAGATTACTAATCTTAAATTCCATGCCTTGGGGGCATGCAAGTACGATATACAGAAGGAGT
GAACTCATTAGGGCAGATGACCAATGAGTTTAGGAAAGAAGAGTCCAGGGCAGGGTACATCTACACCACCC
GCCCAGCCCTGGGTGAGTCCAGCCACGTTCACCTCATTATAGTTGCCTCTCTCCAGTCCTACCTTGACGGG
AAGCACAAGCAGAAACTGGGACAGGAGCCCCAGGAGACCAAATCTTCATGGTCCCTCTGGGAGGATGGGTG
GGGAGAGCTGTGGCAGAGGCCTCAGGAGGGGCCCTGCTGCTCAGTGGTGACAGATAGGGGTGAGAAAGCAG
ACAGAGTCATTCCGTCAGCATTCTGGGTCTGTTTGGTACTTCTTCTCACGCTAAGGTGGCGGTGTGATATG
CACAATGGCTAAAAAGCAGGGAGAGCTGGAAAGAAACAAGGACAGAGACAGAGGCCAAGTCAACCAGACCA
ATTCCCAGAGGAAGCAAAGAAACCATTACAGAGACTACAAGGGGGAAGGGAAGGAGAGATGAATTAGCTTC
CCCTGTAAACCTTAGAACCCAGCTGTTGCCAGGGCAACGGGGCAATACCTGTCTCTTCAGAGGAGATGAAG
TTGCCAGGGTAACTACATCCTGTCTTTCTCAAGGACCATCCCAGAATGTGGCACCCACTAGCCGTTACCAT
AGCAACTGCCTCTTTGCCCCACTTAATCCCATCCCGTCTGTTAAAAGGGCCCTATAGTTGGAGGTGGGGGA
GGTAGGAAGAGCGATGATCACTTGTGGACTAAGTTTGTTCGCATCCCCTTCTCCAACCCCCTCAGTACATC
ACCCTGGGGGAACAGGGTCCACTTGCTCCTGGGCCCACACAGTCCTGCAGTATTGTGTATATAAGGCCAGG
GCAAAGAGGAGCAGGTTTTAAAGTGAAAGGCAGGCAGGTGTTGGGGAGGCAGTTACCGGGGCAACGGGAAC
AGGGCGTTTCGGAGGTGGTTGCCATGGGGACCTGGATGCTGACGAAGGCTCGCGAGGCTGTGAGCAGCCAC
AGTGCCCTGCTCAGAAGCCCCAAGCTCGTCAGTCAAGCCGGTTCTCCGTTTGCACTCAGGAGCACGGGCAG
GCGAGTGGCCCCTAGTTCTGGGGGCAGCTCTAGAGCGGTACCGGATCCAGGTAAGTATCAAGGTTACAAGA
CAGGTTTAAGGAGACCAATAGAAACTGGGCTTGTCGAGACAGAGAAGACTCTTGCGTTTCTGATAGGCACC
TATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAGGTGATGAATTCGCTAGCGCCACCATGCGCT
GTTCTCCAGGCGGCGTGTGGCTCGCCCTGGCTGCTTCCCTTCTGCACGTTAGCCTGCAGGGTGAGTTCCAG
CGCAAACTGTATAAGGAGCTTGTTAAGAATTATAACCCCCTGGAGCGGCCGGTCGCAAATGATTCCCAGCC
ACTGACAGTGTACTTCAGCCTCTCCTTGCTGCAGATCATGGACGTGGATGAAAAGAACCAGGTGCTGACCA
CTAATATTTGGTTGCAGATGTCCTGGACCGATCACTACTTGCAGTGGAATGTGAGCGAATACCCAGGTGTA
AAGACTGTAAGATTCCCTGACGGCCAAATCTGGAAACCAGATATCCTGCTGTACAACAGCGCAGACGAAAG
GTTTGATGCAACATTTCACACCAACGTGGGAGTCAATTCTTCAGGCCACTGCCTGTACCTGCCCCCTGGAA
TCTTCAAGTCCTCATGCTATATCGACGTCCGCTGGTTTCCCTTCGACGTCCAGCACTGCAAACTCAAATTC
GGGAGCTGGAGCTACGGCGGATGGAGCCTGGATCTGCAAATGCAGGAGGCTGACATCTCTGGTTACATCCC
GAATGGGGAGTGGGACCTTGTGGGAATCCCCGGTAAAAGAAGCGAGCGATTTTATGAATGCTGCAAAGAGC
CCTTCCCAGATGTCACCTTCACAGTGACCATGCGGAGACGCATGGGTTATTATCTGATCCAAATGTATATC
CCAAGCTTGCTTATAGTGATTTTGTCATGGATCTCCTTCTGGATTAATATGGACGCCGCTCCAGCTAGGGT
CGGACTGGGCATCACCACAGTGCTGACAATGACTACTCAGAGCTCAGGCAGCCGAGCCAGCTTGCCCAAGG
TTTCTTACGTGAAGGCCATCGATATCTGGATGGCTGTCTGCCTTCTGTTTGTCTTCAGCGCACTGCTGGAA
TACGCCGCTGTCAATTTTGTGTCTCGACAGCATAAAGAGCTGTTGCGGTTCAGAAGAAAACGACGCCACCA
CAAAGAGGATGAGGCAGGAGAAGGACGCTTCAACTTTAGCGCCTATGGTATGGGACCTGCTTGCCTCCAGG
CTAAAGACGGAATTTCCGTGAAGGGAGCCAACAATAGCAACACAACCAACCCACCCCCTGCTCCATCTAAG
AGCCCGGAGGAAATGCGCAAACTCTTTATTCAGAGAGCGAAAAAGATCGACAAAATCTCCCGGATCGGATT
CCCCATGGCTTTCCTGATTTTCAACATGTTTTATTGGATCATCTACAAGATTGTGCGAAGGGAGGACGTAC
ACAACCAGTAAGCGGCCGCAATTCCCCCCGCCCCCCCCCCCCCCCCCCTCACCCTCCCCCCCCCCCTAACGTT
ACTGGCCGAAGCCGCTTGGAATAAGGCCGGTGTGCGTTTGTCTATATGTTATTTTCCACCATATTGCCGTC
TTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTC

FIG. 20B

TCGCCAAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAA
ACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAA
GCCACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGTTGGATAGTTGTGG
AAAGAGTCAAATGGCTCTCCTAAGCGTATTCAACAAGGGGCTGAAGGATGCCCAGAAGGTACCCCATTGTA
TGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAACGTCTAGGC
CCCCCGAACCACGGGGACGTGGTTTTCCTTTGAAAAACACGATGATAATATGGCCACAACCATGGGAGATC
CGGTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAAC
GGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCAT
CTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAGTGCT
TCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCAG
GAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACAC
CCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGG
AGTACAACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTC
AAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCCATCGG
CGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCAAGCTGAGCAAAGACCCCAACG
AGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTG
TACAAGTAAACCGGTGTCGACAAGCTTATCGATAATCAACCTCTGGATTACAAAATTTGTGAAAGATTGAC
TGGTATTCTTAACTATGTTGCTCCTTTTACGCTATGTGGATACGCTGCTTTAATGCCTTTGTATCATGCTA
TTGCTTCCCGTATGGCTTTCATTTTCTCCTCCTTGTATAAATCCTGGTTGCTGTCTCTTTATGAGGAGTTG
TGGCCCGTTGTCAGGCAACGTGGCGTGGTGTGCACTGTGTTTGCTGACGCAACCCCCACTGGTTGGGGCAT
TGCCACCACCTGTCAGCTCCTTTCCGGAACTTTCGCTTTCCCCCTCCCTATTGCCACGGCGGAACTCATCG
CCGCCTGCCTTGCCCGCTGCTGGACAGGGGCTCGGCTGTTGGGCACTGACAATTCCGTGGTGTTGTCGGGG
AAATCATCGTCCTTTCCTTGGCTGCTCGCCTGTGTTGCCACCTGGATTCTGCGCGGGACGTCCTTCTGCTA
CGTCCCTTCGGCCCTCAATCCAGCGGACCTTCCTTCCCGCGGCCTGCTGCCGGCTCTGCGGCCTCTTCCGC
GTCTTCGCCTTCGCCCTCAGACGAGTCGGATCTCCCTTTGGGCCGCCTCCCCGCATCGATACCGAGCGCTG
CTCGAGAGATCTACGGGTGGCATCCCTGTGACCCCTCCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACT
CCAGTGCCCACCAGCCTTGTCCTAATAAAATTAAGTTGCATCATTTTGTCTGACTAGGTGTCCTTCTATAA
TATTATGGGGTGGAGGGGGGTGGTATGGAGCAAGGGGCAAGTTGGGAAGACAACCTGTAGGGCCTGCGGGG
TCTATTGGGAACCAAGCTGGAGTGCAGTGGCACAATCTTGGCTCACTGCAATCTCCGCCTCCTGGGTTCAA
GCGATTCTCCTGCCTCAGCCTCCCGAGTTGTTGGGATTCCAGGCATGCATGACCAGGCTCAGCTAATTTTT
GTTTTTTTGGTAGAGACGGGGTTTCACCATATTGGCCAGGCTGGTCTCCAACTCCTAATCTCAGGTGATCT
ACCCACCTTGGCCTCCCAAATTGCTGGGATTACAGGCGTGAACCACTGCTCCCTTCCCTGTCCTTCTGATT
TTGTAGGTAACCACGTGCGGACCGAGCGGCCGCAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTG
CGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTC
AGTGAGCGAGCGAGCGCGCAGCTGCCTGCAGGGGCGCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCG
GTATTTCACACCGCATACGTCAAAGCAACCATAGTACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTG
TGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCT
TCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATT
TAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTTGGGTGATGGTTCACGTAGTGGGCCATCGCCCT
GATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGA
ACAACACTCAACCCTATCTCGGGCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTT
AAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTTTAACAAAATATTAACGTTTACAATTTTATGGT
GCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACCCGCTGAC

FIG. 20B(Cont.)

GCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGCTGCAT
GTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTTAT
AGGTTAATGTCATGATAATAATGGTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACC
CCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCT
TCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGG
CATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGT
GCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACG
TTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAG
AGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCAT
CTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAA
CTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAA
CTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCT
GTAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATT
AATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTA
TTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAG
CCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGC
TGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTG
ATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATC
CCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCC
TTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGG
ATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTT
CTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAAT
CCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTAC
CGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTAC
ACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAG
GTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATC
TTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGG
AGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACAT
GT

FIG. 20B(Cont.)