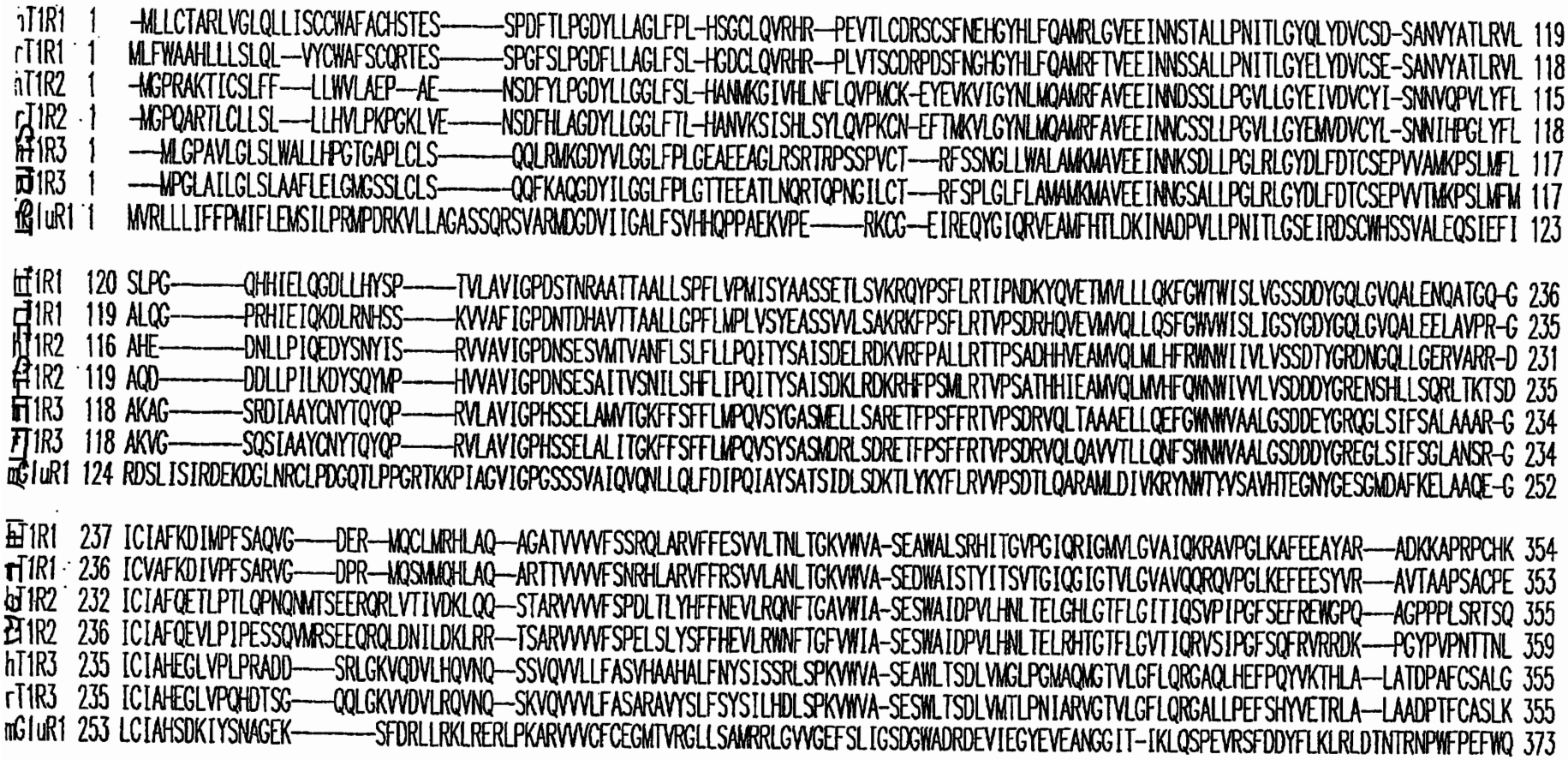


FIG. 1A



FIG.1B

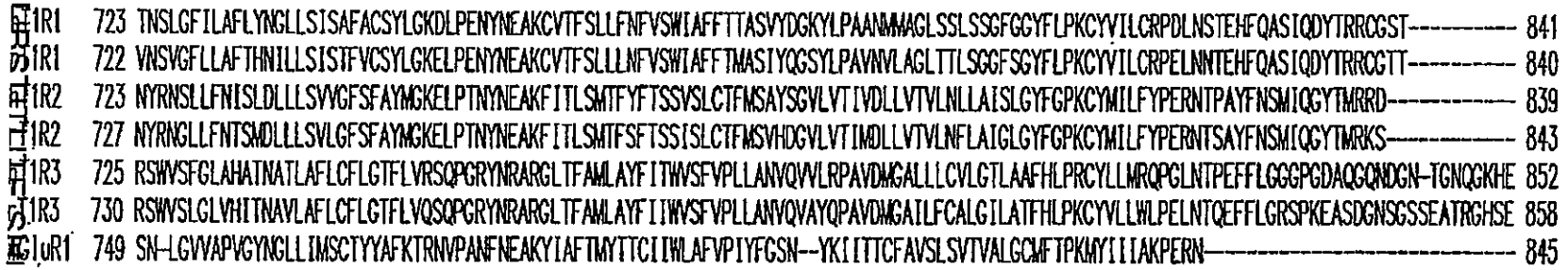

1R1 723 TNSLGFILAFLYNGLLSISAFACSYLGKDLPENYNEAKCVTFSLLFNFVSWIAFFTTASVYDGKYLPAANMMAGLSSLSSGFGGYFLPKCYVILCRPDLNSTEHFQASIQDYTRRCGST---------- 841
1R1 722 VNSVGFLLAFTHNILLSISTFVCSYLGKELPENYNEAKCVTFSLLLNFVSWIAFFTMASIYQGSYLPAVNVLAGLTTLSGGFSGYFLPKCYVILCRPELNNTEHFQASIQDYTRRCGTT---------- 840
1R2 723 NYRNSLLFNISLDLLLSVVGFSFAYMGKELPTNYNEAKFITLSMTFYFTSSVSLCTFMSAYSGVLVTIVDLLVTVLNLLAISLGYFGPKCYMILFYPERNTPAYFNSMIQGYTMRRD---------- 839
1R2 727 NYRNGLLFNTSMDLLLSVLGFSFAYMGKELPTNYNEAKFITLSMTFSFTSSISLCTFMSVHDGVLVTIMDLLVTVLNFLAIGLGYFGPKCYMILFYPERNTSAYFNSMIQGYTMRKS---------- 843
1R3 725 RSWVSFGLAHATNATLAFLCFLGTFLVRSQPGRYNRARGLTFAMLAYFITWVSFVPLLANVQVVLRPAVDMGALLLCVLGTLAAFHLPRCYLLMRQPGLNTPEFFLGGGPGDAQGQNDGN-TGNQGKHE 852
1R3 730 RSWVSLGLVHITNAVLAFLCFLGTFLVQSQPGRYNRARGLTFAMLAYFIIWVSFVPLLANVQVAYQPAVDMGAILFCALGILATFHLPKCYVLLWLPELNTQEFFLGRSPKEASDGNSGSSEATRGHSE 858
uR1 749 SN-LGVVAPVGYNGLLIMSCTYYAFKTRNVPANFNEAKYIAFTMYTTCIIWLAFVPIYFGSN--YKIITTCFAVSLSVTVALGCMFTPKMYIIIAKPERN---------- 845

FIG. 1C



hT1R2 AND hT1R3 ARE EXPRESSED IN HUMAN TONGUE EPITHELIUM. cDNA-SPECIFIC AMPLIFICATION PRODUCTS CAN BE AMPLIFIED FROM cDNA PREPARED FROM RESECTED HUMAN CIRCUMVALLATE PAPILLAE.

FIG.2

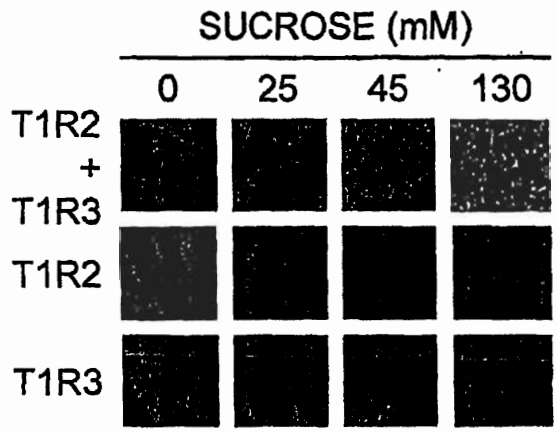

SUCROSE (mM)
0
25
45
130
T1R2
+
T1R3
T1R2
T1R3

FIG.3A

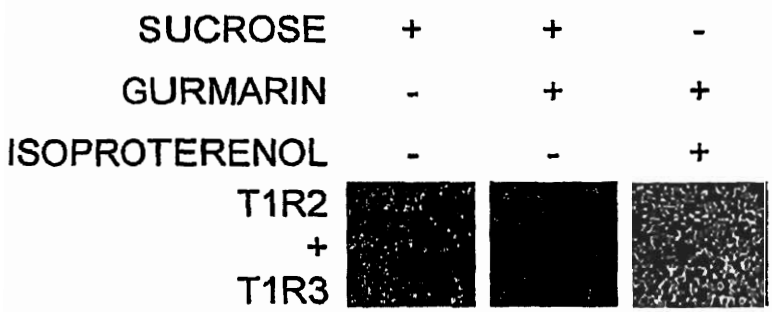

SUCROSE + + -
GURMARIN - + +
ISOPROTERENOL - - +
T1R2
+
T1R3

FIG.3B

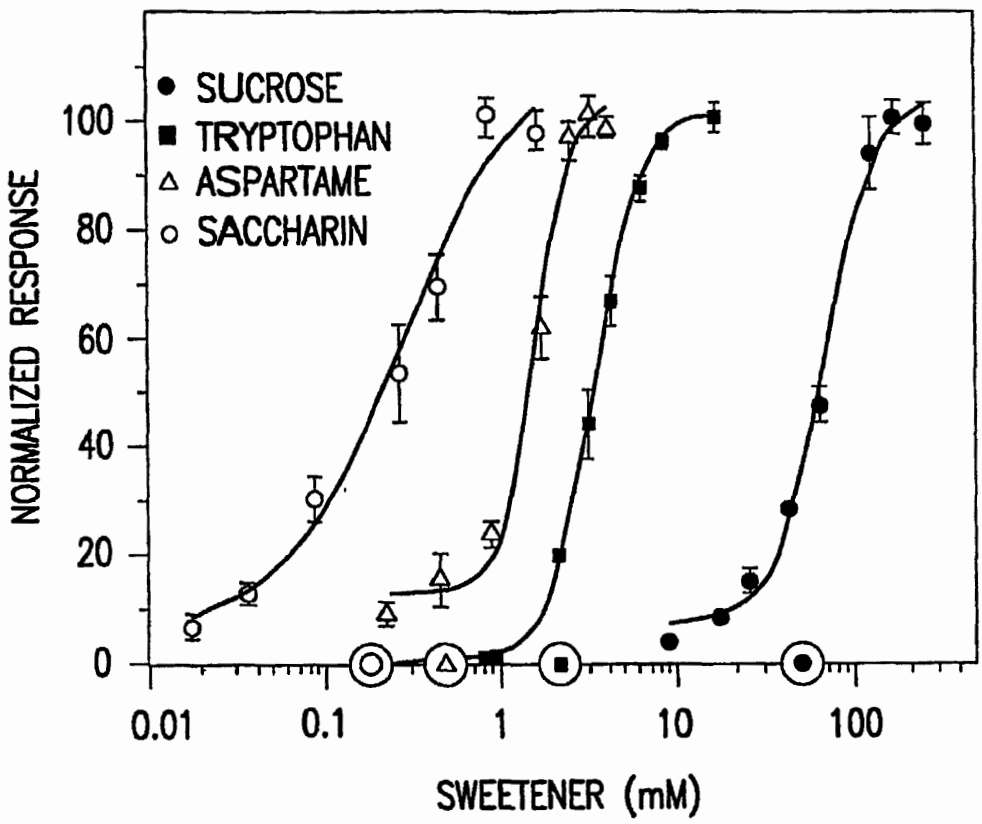

SUCROSE
TRYPTOPHAN
ASPARTAME
SACCHARIN
NORMALIZED RESPONSE
0
20
40
60
80
100
0.01
0.1
1
10
100
SWEETENER (mM)

FIG.3C

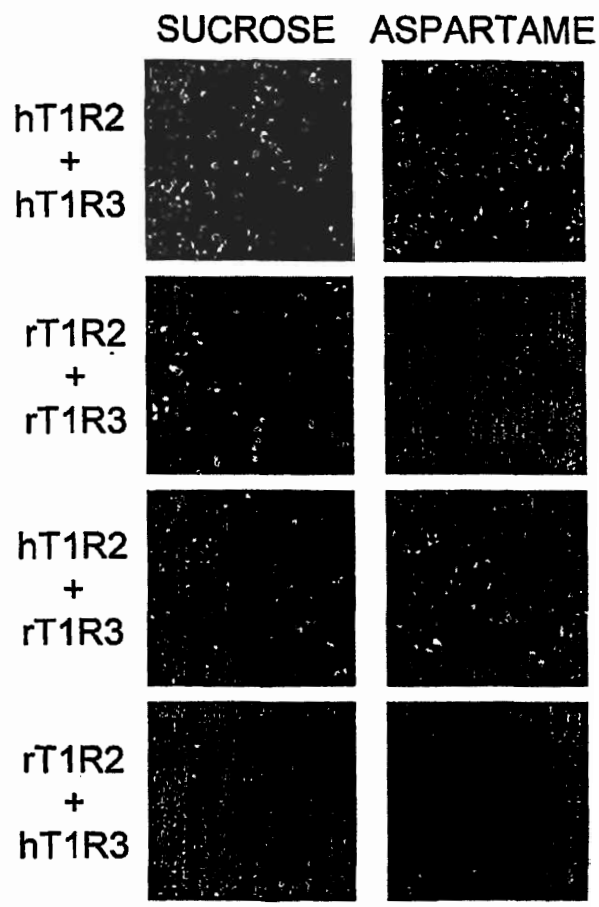

SUCROSE
ASPARTAME
hT1R2 + hT1R3
rT1R2 + rT1R3
hT1R2 + rT1R3
rT1R2 + hT1R3

FIG.4

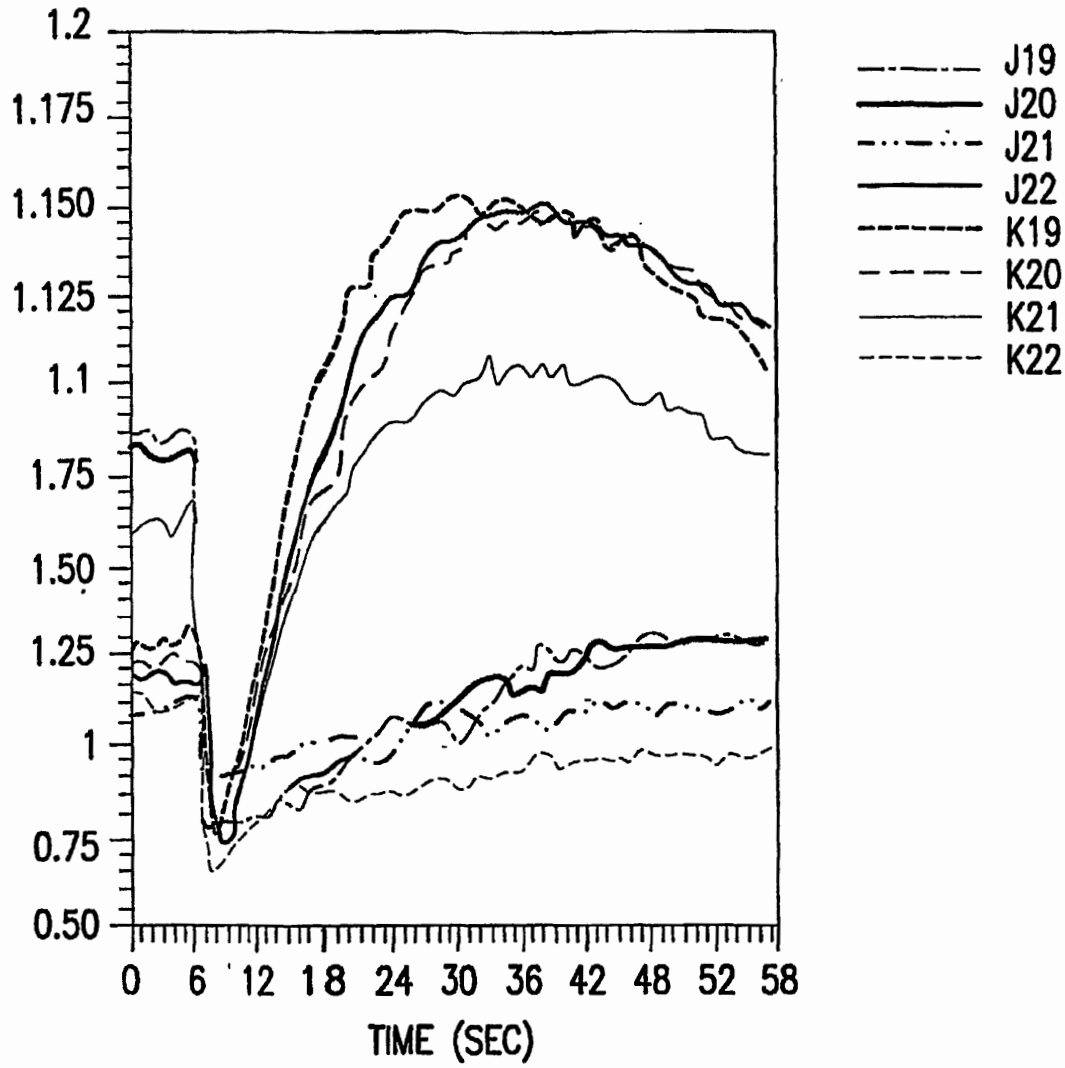

1.2
1.175
1.150
1.125
1.1
1.75
1.50
1.25
1
0.75
0.50
0
6
12
18
24
30
36
42
48
52
58
TIME (SEC)
J19
J20
J21
J22
K19
K20
K21
K22

FIG.5

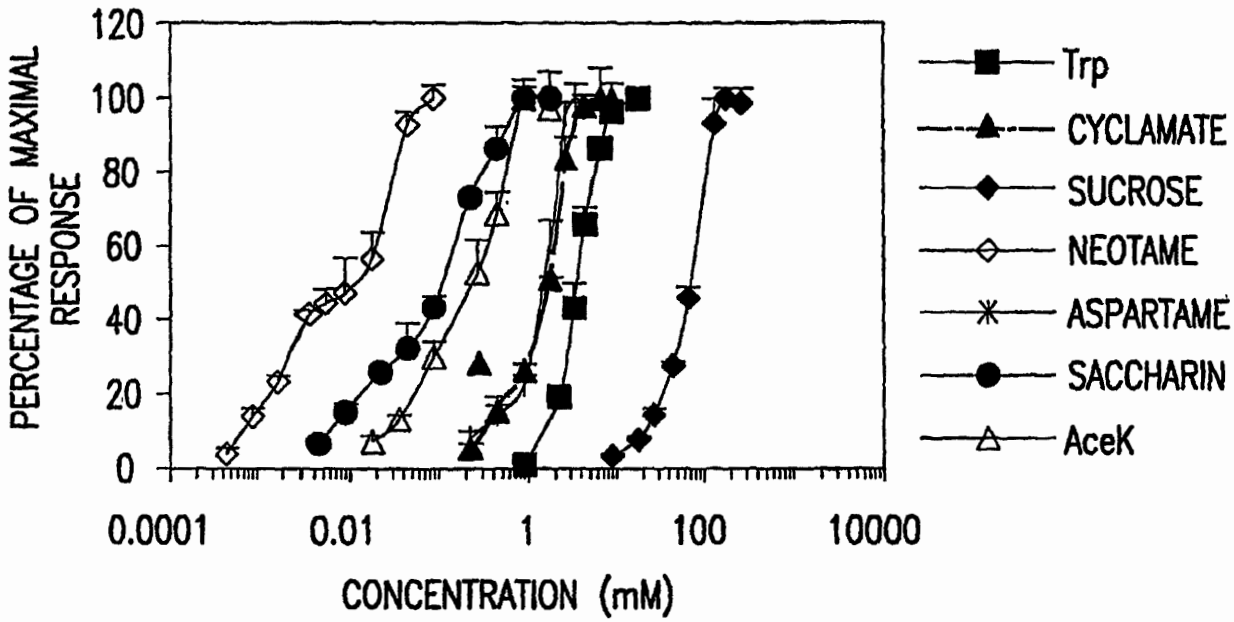

PERCENTAGE OF MAXIMAL RESPONSE
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
CONCENTRATION (mM)
Trp
CYCLAMATE
SUCROSE
NEOTAME
ASPARTAME
SACCHARIN
AceK

FIG.6

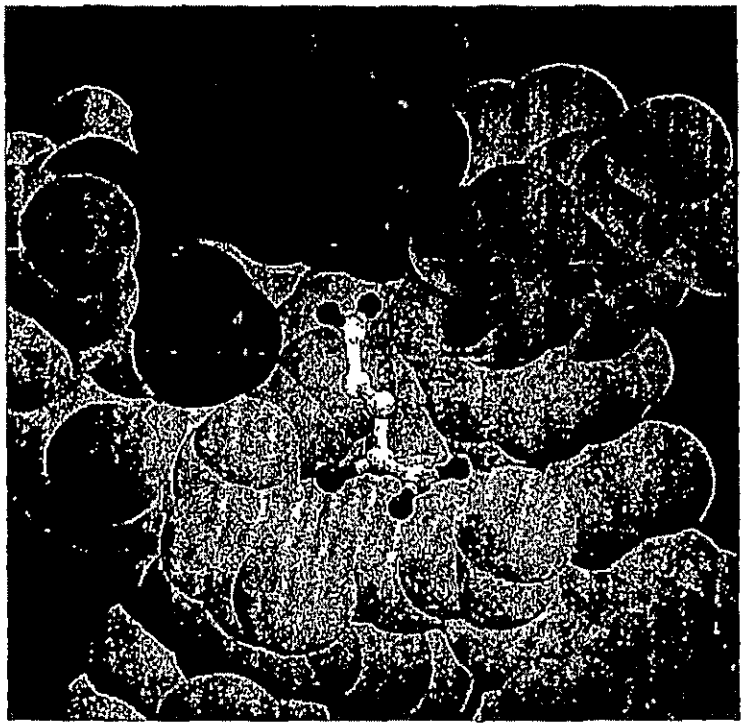


FIG.7

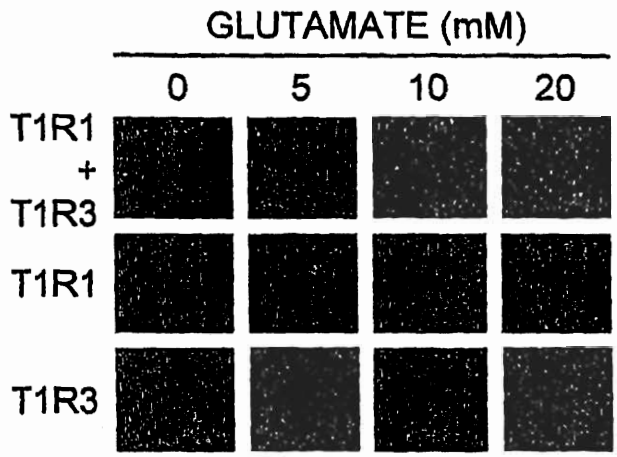

GLUTAMATE (mM)
0
5
10
20
T1R1
+
T1R3
T1R1
T1R3

FIG.8A

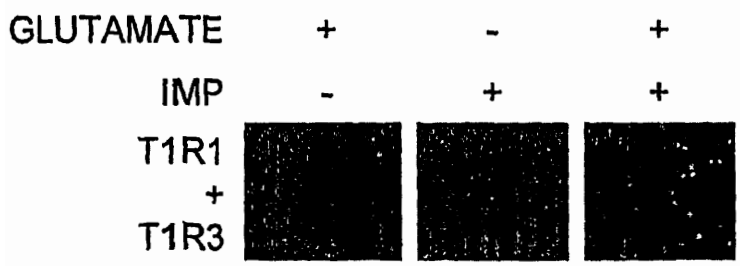

GLUTAMATE
+
-
+
IMP
-
+
+
T1R1
+
T1R3

FIG.8B

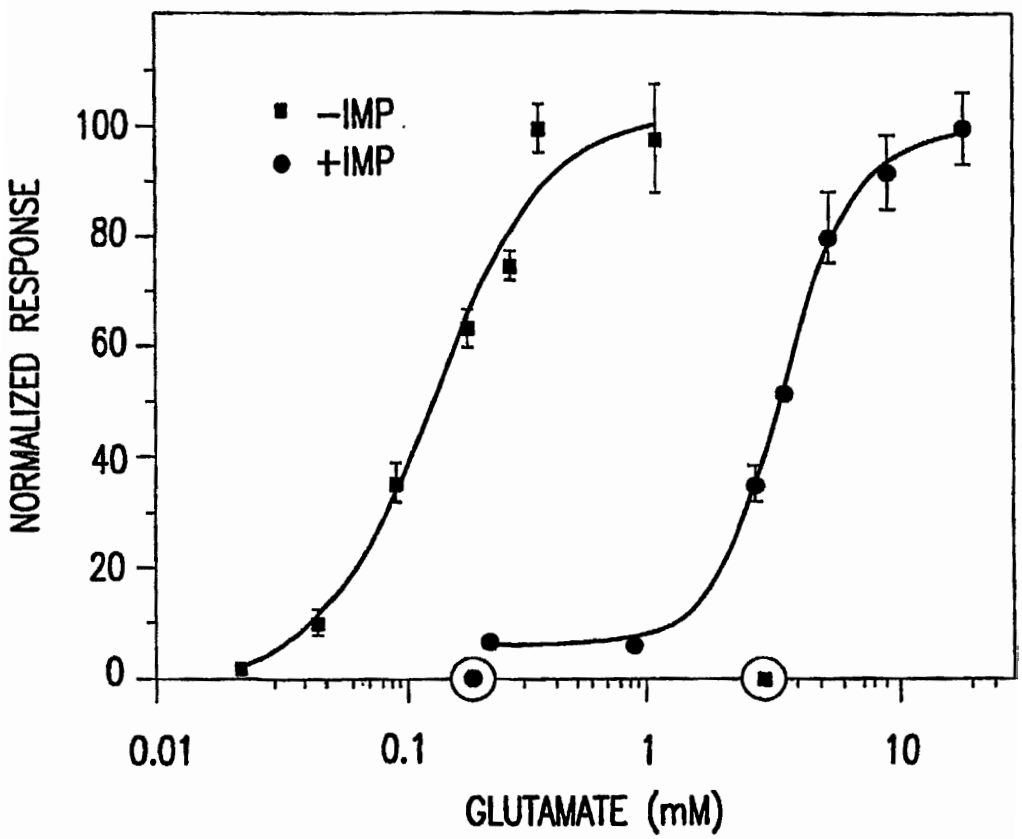

NORMALIZED RESPONSE
100
80
60
40
20
0
−IMP
+IMP
0.01
0.1
1
10
GLUTAMATE (mM)

FIG.8C

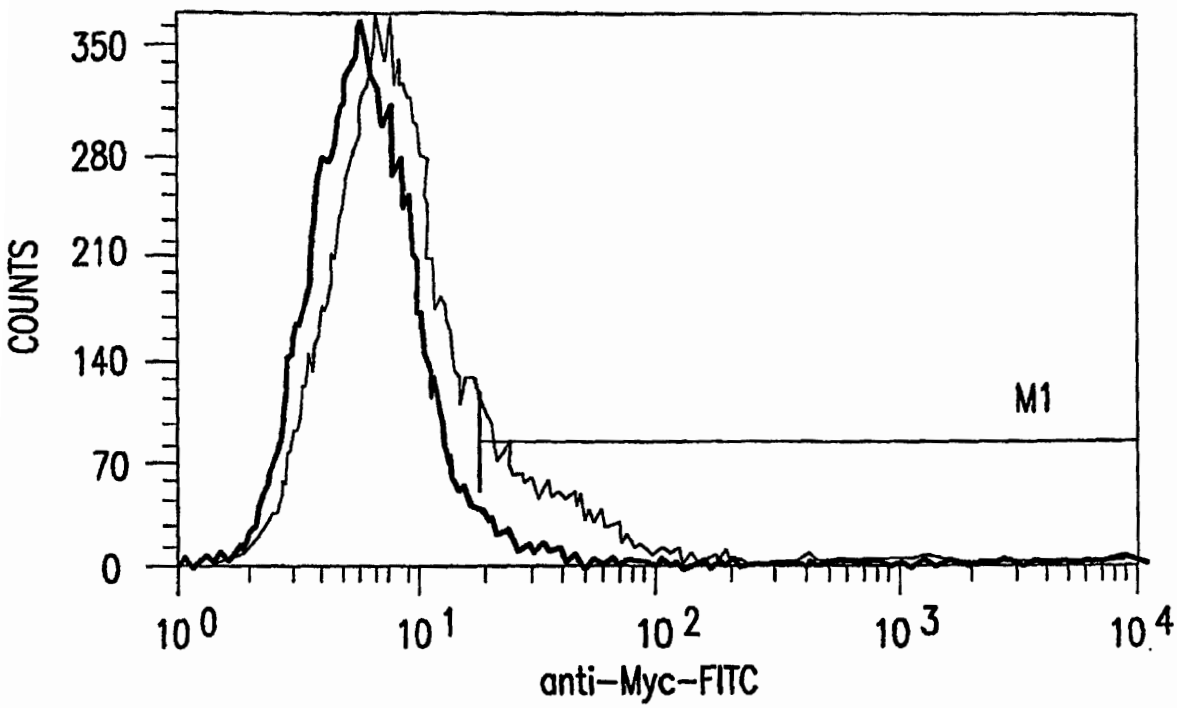


H2-IT-Myc H2-PDZIP-IT-Myc

PDZIP FACILITATE THE SURFACE EXPRESSION OF HUMAN T1R2.

IMMUNOFLUORESCENCE STAINING OF Myc-TAGGED hT1R2 INDICATES THAT PDZIP SIGNIFICANTLY INCREASES THE AMOUNT OF HUMAN T1R2 PROTEIN ON THE PLASMA MEMBRANE.

FIG.9A



FACS ANALYSIS DATA DEMONSTRATING THE SAME RESULT.
—— Myc-TAGGED HUMAN T1R2: DARK LINE.
—— Myc-TAGGED HUMAN T1R2 WITH PDZIP: LIGHT LINE.

FIG.9B

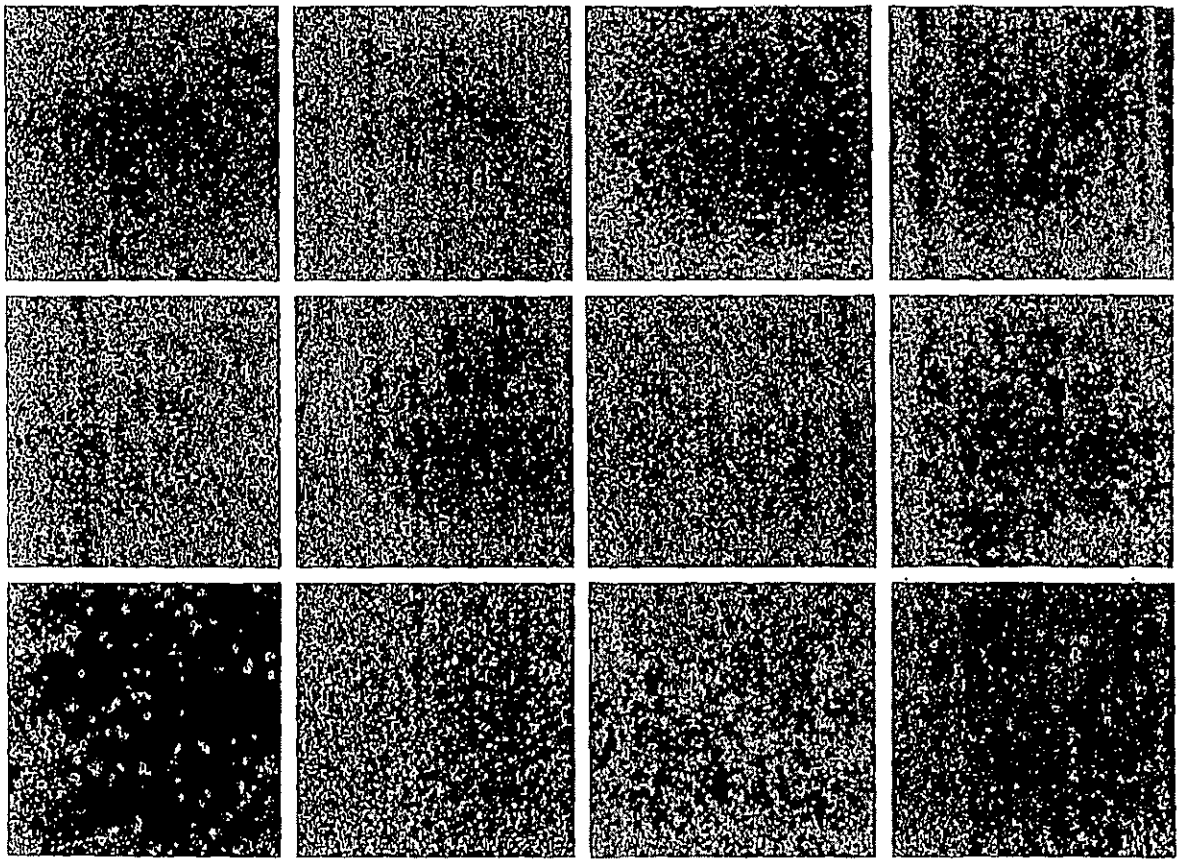


FIG.10

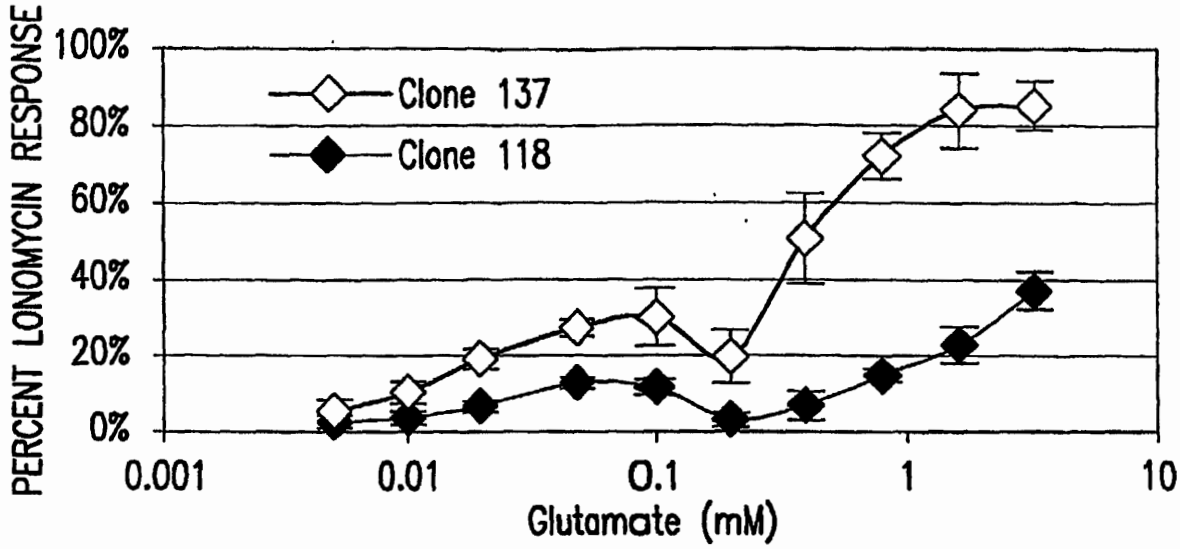

PERCENT LONOMYCIN RESPONSE
100%
80%
60%
40%
20%
0%
Clone 137
Clone 118
0.001
0.01
0.1
1
10
Glutamate (mM)

FIG. 11

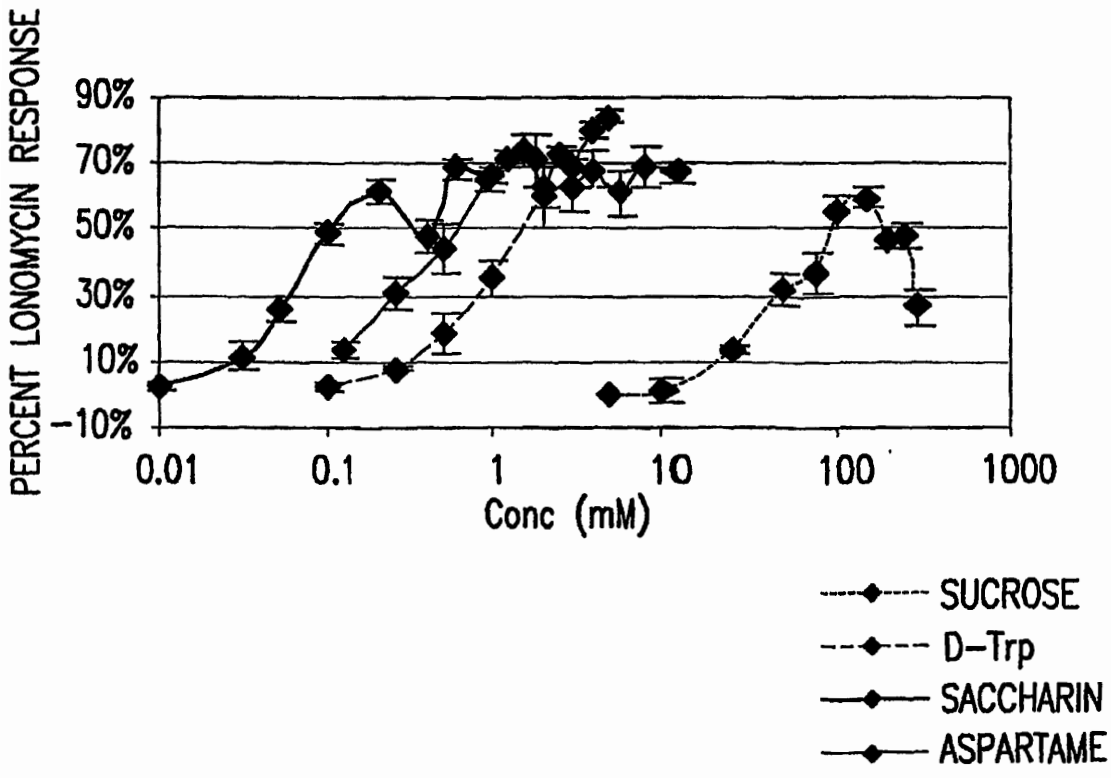

PERCENT LONOMYCIN RESPONSE
90%
70%
50%
30%
10%
-10%
0.01
0.1
1
10
100
1000
Conc (mM)
SUCROSE
D-Trp
SACCHARIN
ASPARTAME

FIG 12

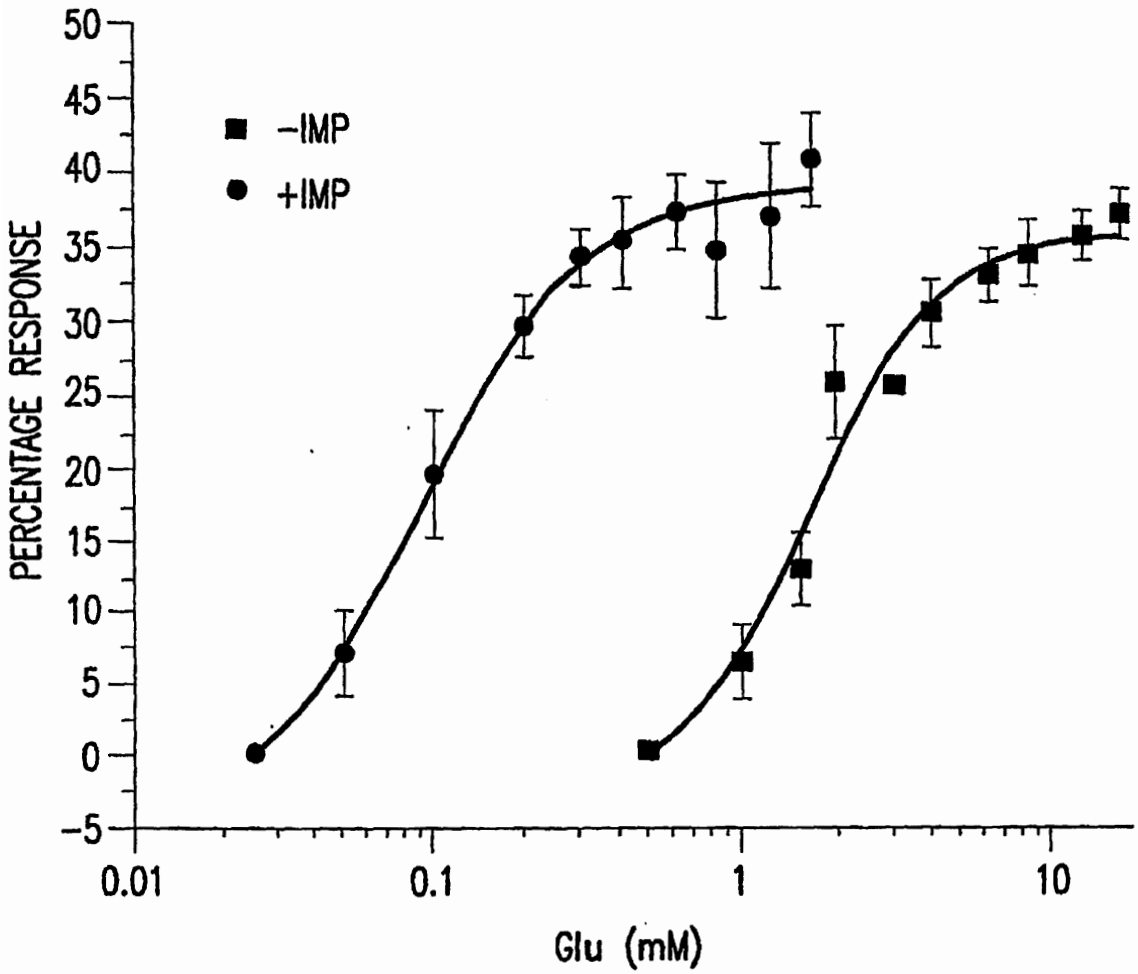

50
45
40
35
30
25
20
15
10
5
0
−5
PERCENTAGE RESPONSE
−IMP
+IMP
0.01
0.1
1
10
Glu (mM)

FIG. 13

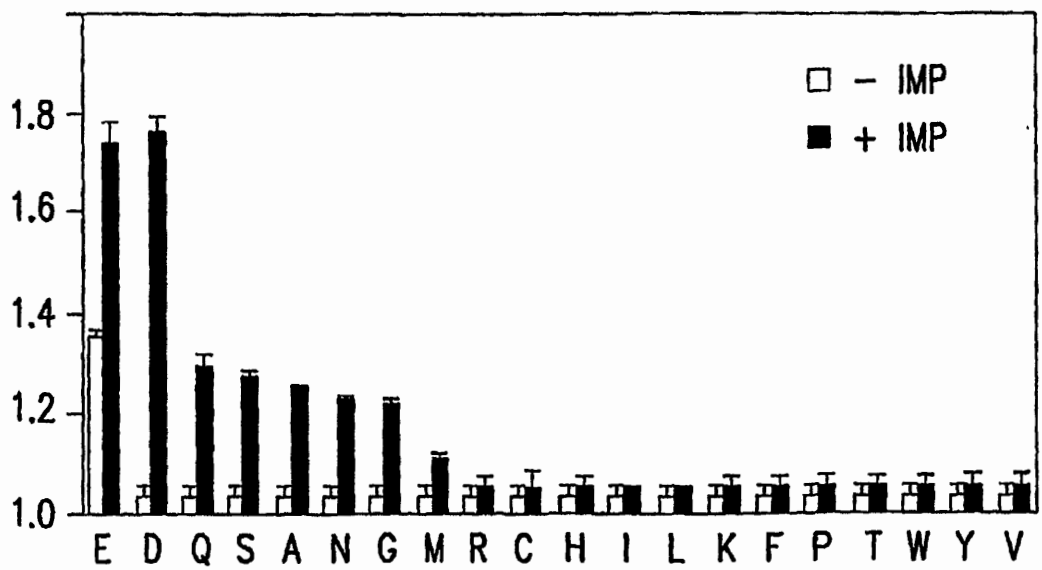

1.8
1.6
1.4
1.2
1.0
− IMP
+ IMP
E D Q S A N G M R C H I L K F P T W Y V

FIG. 14

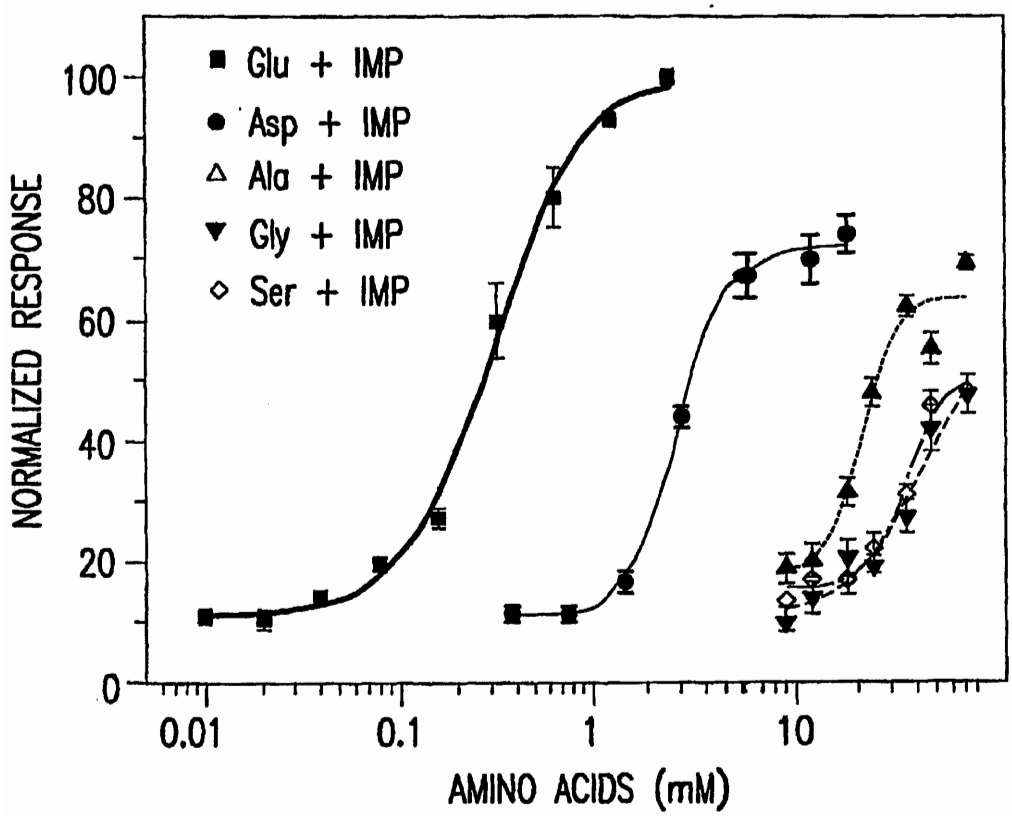

Glu + IMP
Asp + IMP
Ala + IMP
Gly + IMP
Ser + IMP
NORMALIZED RESPONSE
100
80
60
40
20
0
0.01
0.1
1
10
AMINO ACIDS (mM)

FIG.15

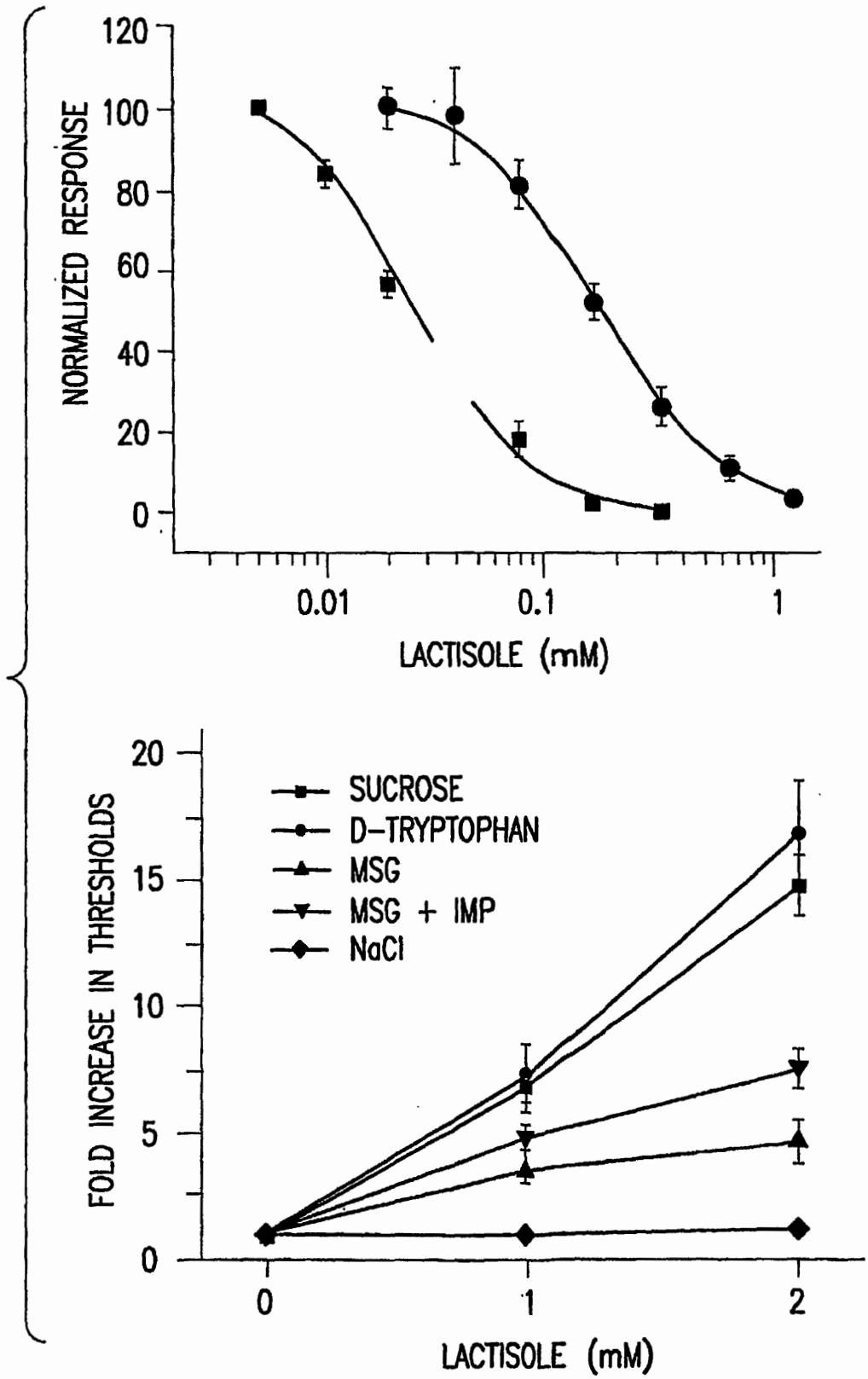

NORMALIZED RESPONSE
120
100
80
60
40
20
0
0.01
0.1
1
LACTISOLE (mM)
FOLD INCREASE IN THRESHOLDS
20
15
10
5
0
SUCROSE
D-TRYPTOPHAN
MSG
MSG + IMP
NaCl
0
1
2
LACTISOLE (mM)

FIG.16

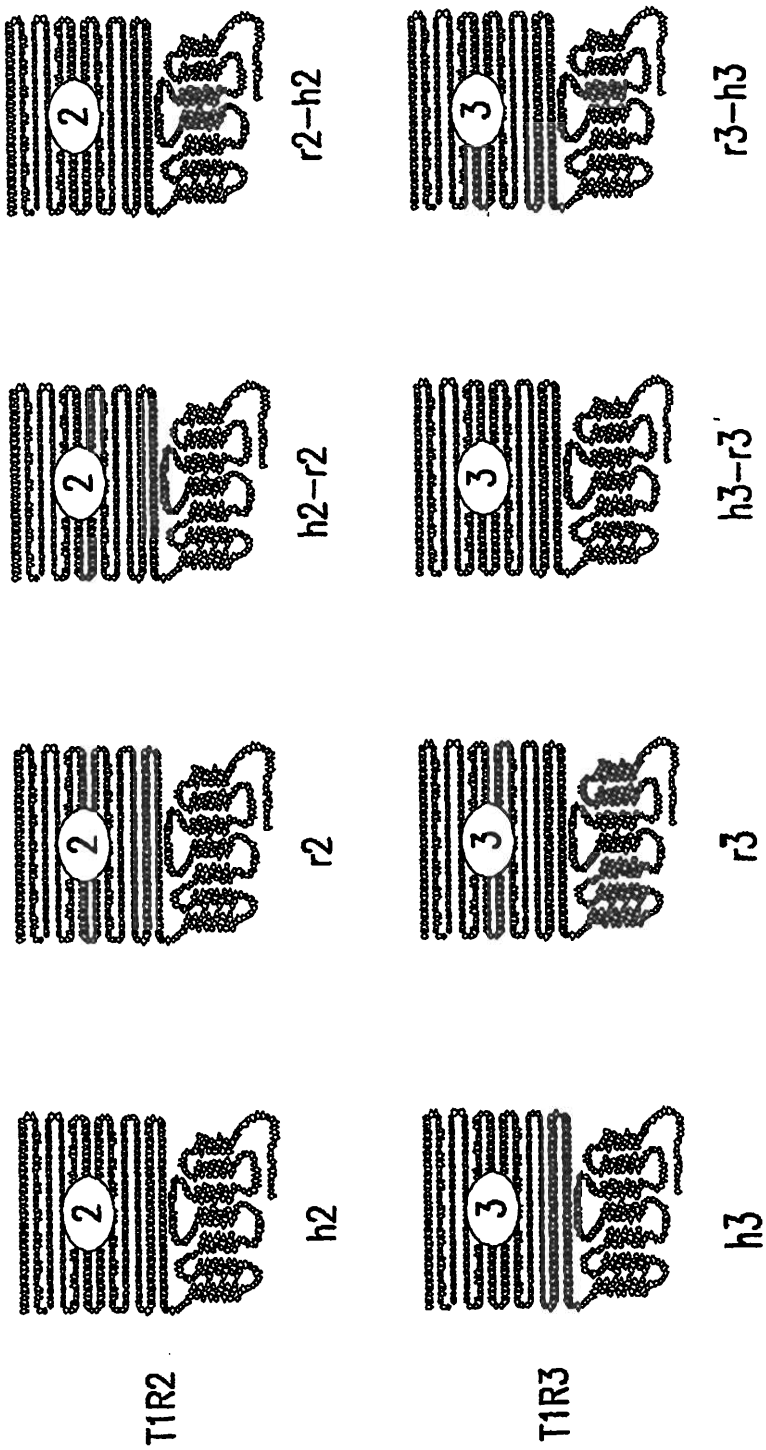


FIG. 17

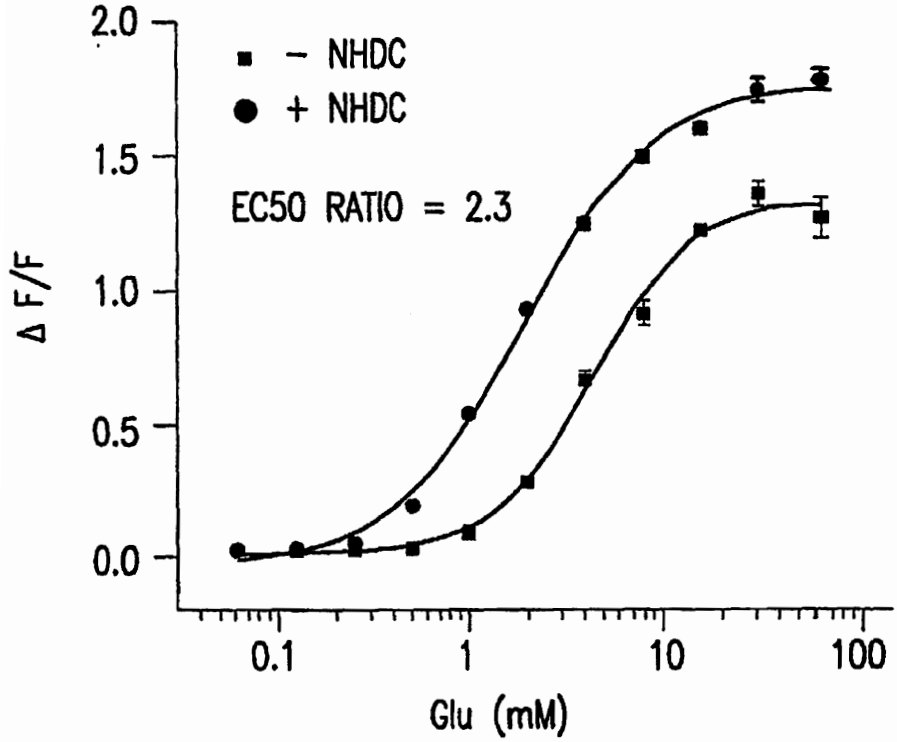


FIG.18A

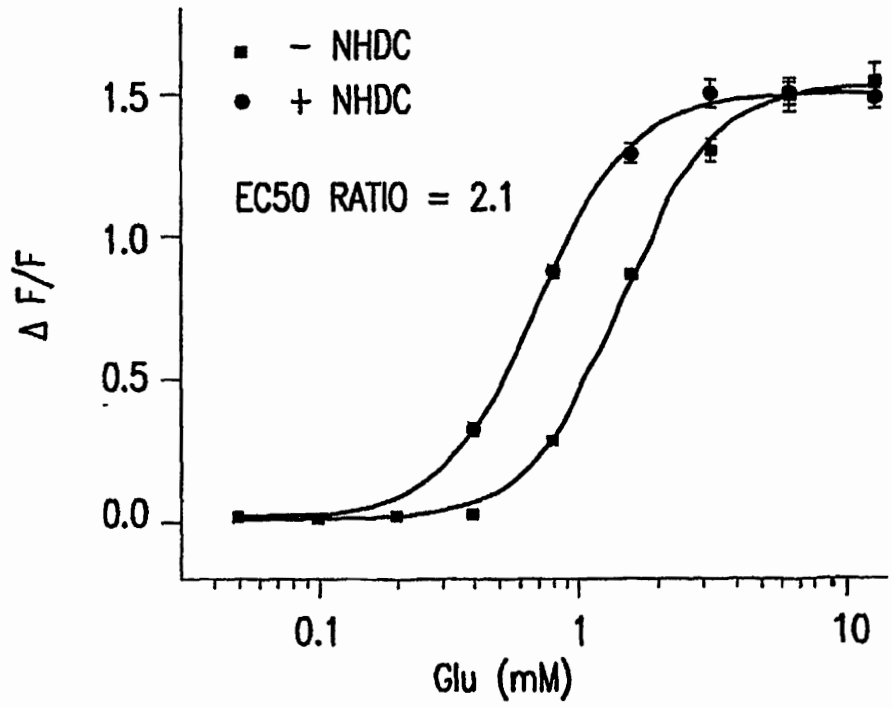


FIG.18B

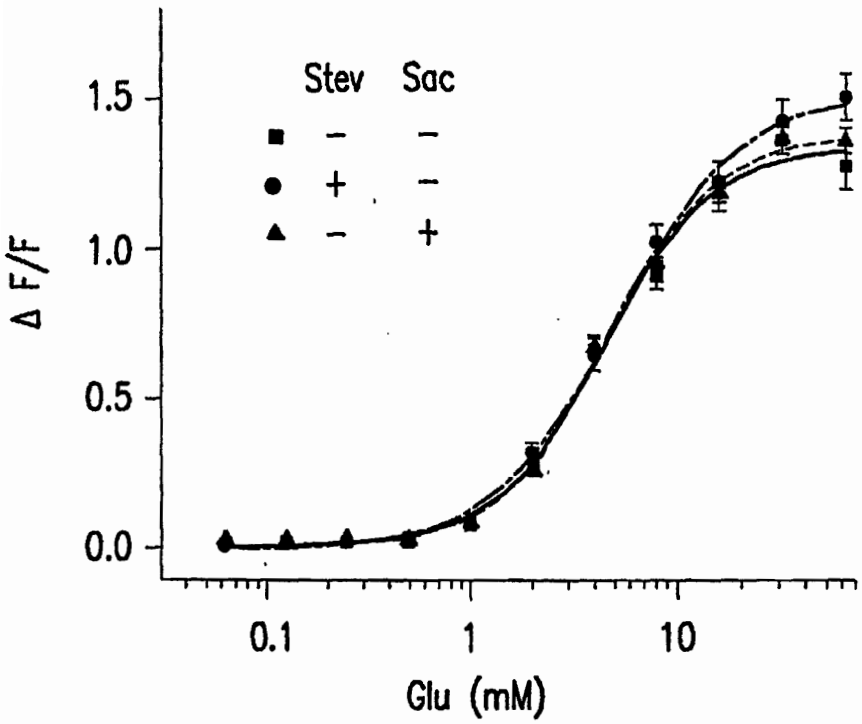


FIG.19A

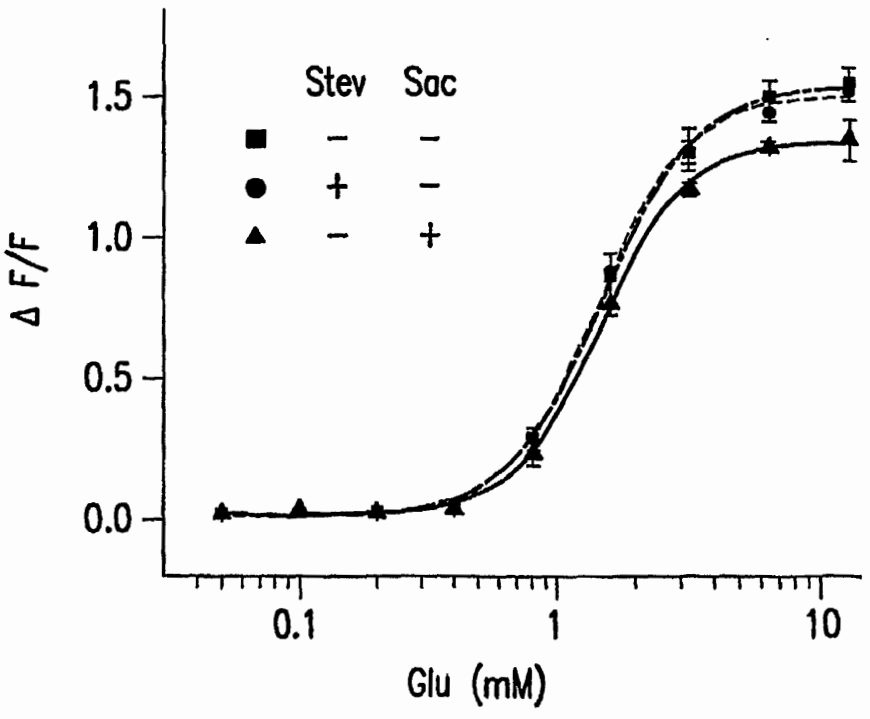


FIG.19B

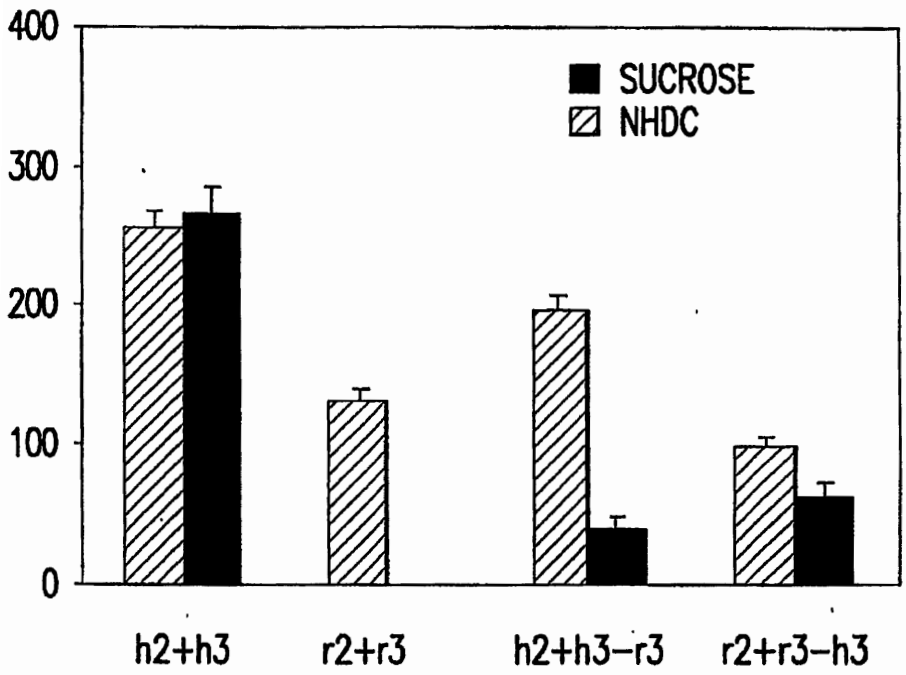


FIG.20

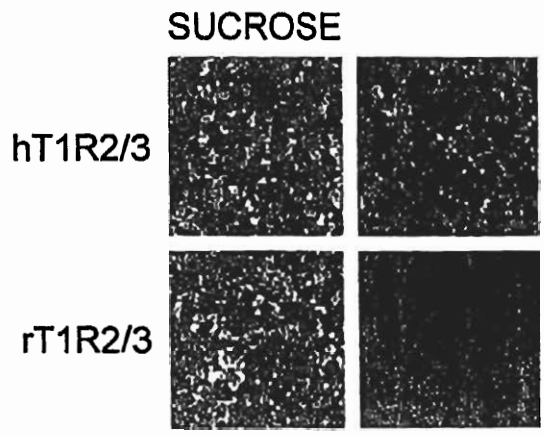


FIG.21A

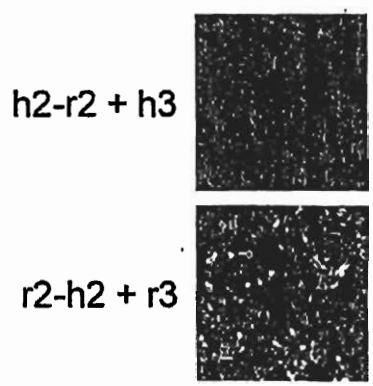


FIG.21B

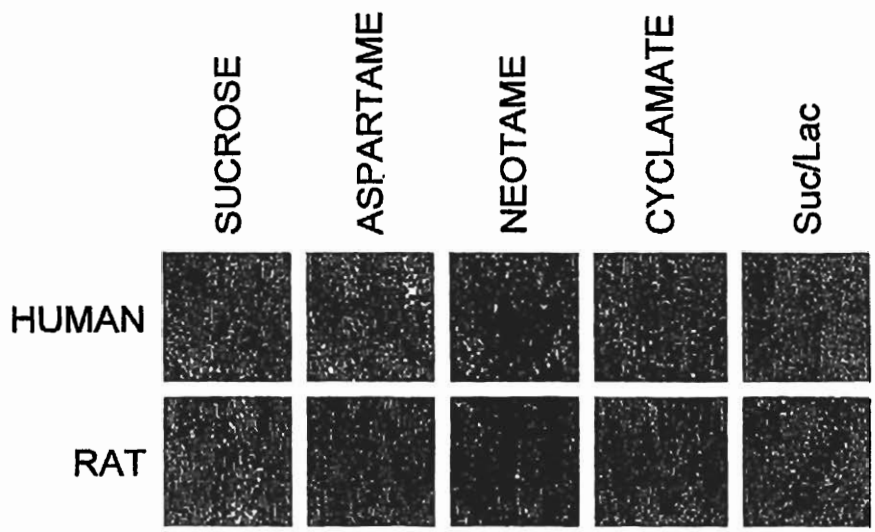


FIG.22A

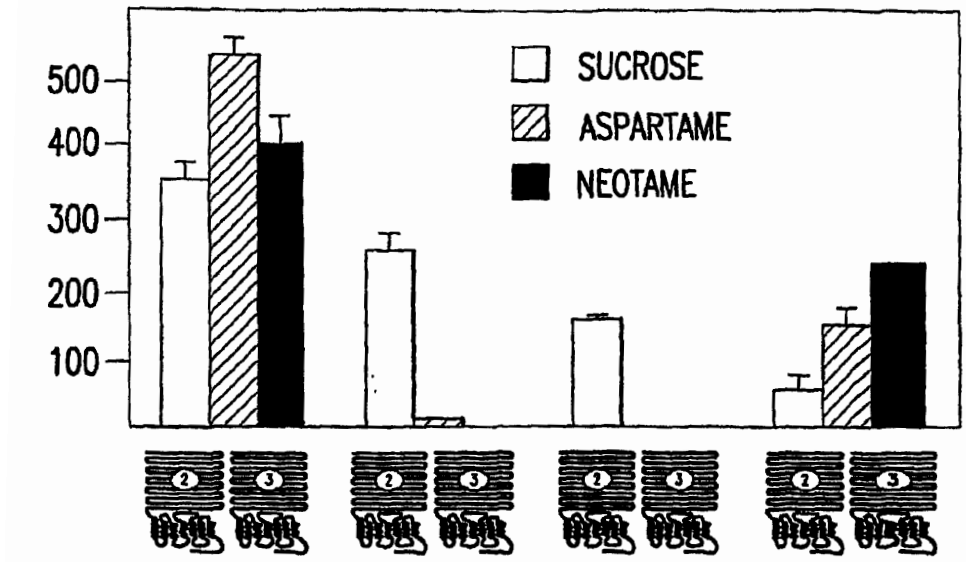


FIG.22B

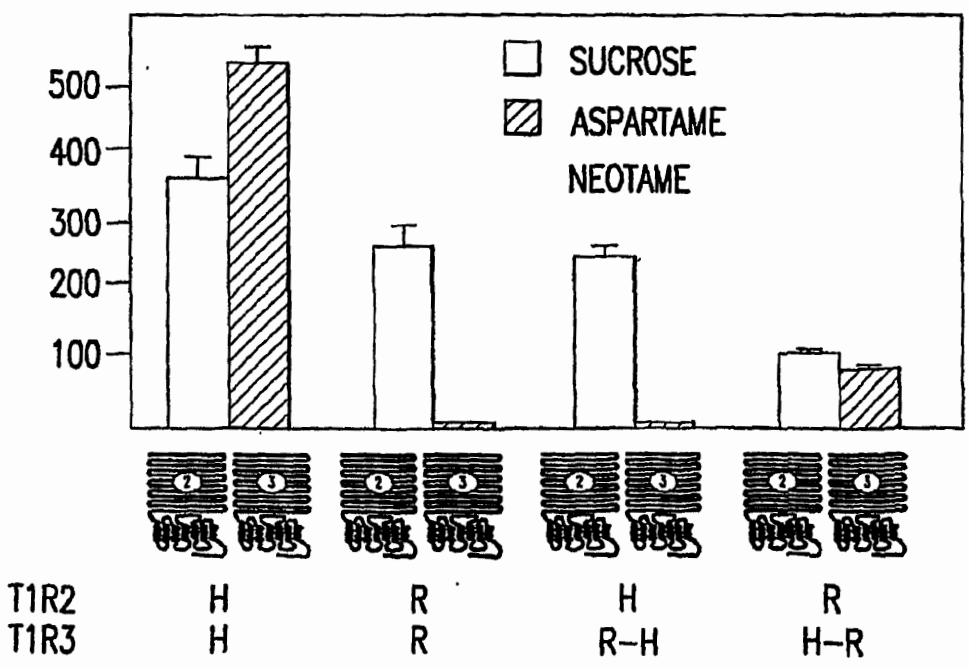


FIG.22C

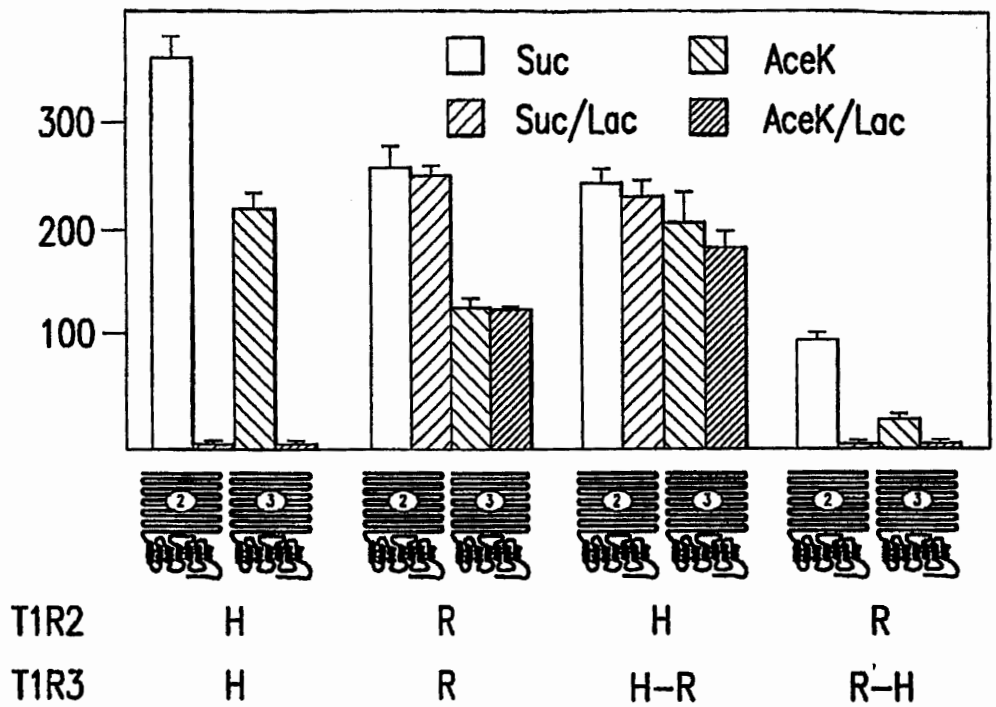


FIG.22D

```
rT1R2     1 -MGPQARTLCLLSLLLHVLPKPG--------KLVENSDFHLAGDYLLGGLFTLHANVKSI
mT1R2     1 -MGPQARTLHLLFLLLHALPKPV--------MLVGNSDFHLAGDYLLGGLFTLHANVKSV
hT1R2     1 -MGPRAKTICSLFFLLWVIAEP----------AENSDFYLPGDYLLGGLFSLHANMKGI
rmGluR1   1 MVRLLLIFFPMIFLEMSILPRMPDRKVLLAGASSQRSVARMDGDVIIGALFSVHHQPP--

rT1R2    52 SHLSYLQVPKCNEFTMKVLGYNLMQAMRFAVEEINNCSSLLPGVLLGYEMVDVCYLSNNI
mT1R2    52 SHLSYLQVPKCNEYNMKVLGYNLMQAMRFAVEEINNCSSLLPGVLLGYEMVDVCYLSNNI
ht1r2    49 VHLNFLQVPMCKEYEVKVIGYNLMQAMRFAVEEINNDSSLLPGVLLGYEIVDVCYISNNV
rmGluR1  59 --AEKVPERKCGEIREQYG-IQRVEAMFHTLDKINADPVLLPNITLGSEIRDSCWHSSVA

rT1R2   112 HPGLYFLAQD---------DDLLPILKDYSQYMP-----HVVAVIGPDNSESAITVSNIL
mTR1R2  112 QPGLYFLSQI---------DDFLPILKDYSQYRP-----QVVAVIGPDNSESAITVSNIL
hT1R2   109 QPVLYFLAHE---------DNLLPIQEDYSNYIS-----RVVAVIGPDNSESVMTVANFL
rmGluR1 116 LEQSIEFIRDSLISIRDEKDGLNRCLPDGQTLPPGRTKKPIAGVIGPGSSSVAIQVQNLL

rTIR2   158 SHFLIPQITYSAISDKLRDKRHFPSMLRTVPSATHHIEAMVQLMVHFQWNWIVVLVSDDD
mT1R2   158 SYFLVPQVTYSAITDKLRDKRRFPAMLRTVPSATHHIEAMVQLMVHFQWNWIVVLVSDDD
hT1R2   155 SLFLLPQITYSAISDELRDKVRFPALLRTTPSADHHVEAMVQLMLHFRWNWIIVLVSSDT
rmGluR1 176 QLFDIPQIAYSATSIDLSDKTLYKYFLRVVPSDTLQARAMLDIVKRYNWTYVSAVHTEGN

rT1R2   218 YGRENSHLLSQRLTKTSDICIAFQEVLPIPESSQVMRSEEQRQLDNILDKLRRTSARVVV
mT1R2   218 YGRENSHLLSQRLTNTGDICIAFQEVLPVPEPNQAVRPEEQDQLDNILDKLRRTSARVVV
hT1R2   215 YGRDNGQLLGERVARR-DICIAFQETLPTLQPNQNMTSEERQRLVTIVDKLQQSTARVVV
rmGluR1 236 YG-ESGMDAFKELAAQEGLCIAHSDKIYS---NAGEKSFDRLLR--KLR-ERLPKARVVV

rT1R2   278 VFSPELSLYSFFHEVLRWNFTG-FVWIASESWAIDPVLHNLTELRHTG---TFLGVTIQR
mT1R2   278 IFSPELSLHNFFREVLRWNFTG-FVWIASESWAIDPVLHNLTELRHTG---TFLGVTIQR
hT1R2   274 VFSPDLTLYHFFNEVLRQNFTG-AVWIASESWAIDPVLHNLTELGHLG---TFLGITIQS
rmGluR1 289 CFCEGMTVRGLLSAMRRLGVVGEFSLIGSDGWADRDEVIEGYEVEANGGITIKLQSPEVR

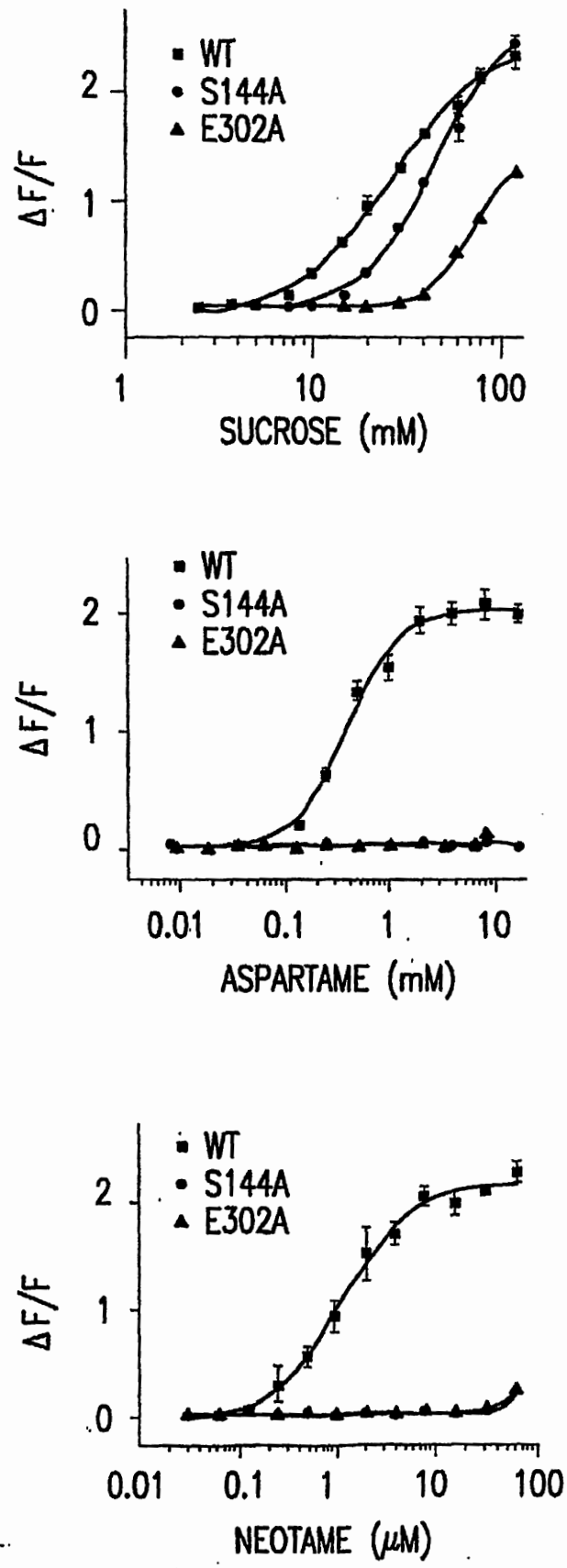
rT1R2   334 VSIPGFSQFRVRRDKPGYPVPNTTNLRTTCNQDCDACLNTTKSFNNILILSGER------
mT1R2   334 VSIPGFSQFRVRHDKPEYPMPNETSLRTTCNQDCDACMNITESFNNVLMLSGER------
hT1R2   330 VPIPGFSEFREWGPQAGPPPLSRTSQSYTCNQECDNCLNATLSFNTILRLSGER------
rmGluR1 349 SFDDYFLKLRLDTNTRNPWFPEFWQHRFQCRLPGHLLENPNFKKVCTGNESLEENYVQDS

rt1r2   388 ----VVYSVYSAVYAVAHALHRLLGCNRVRCTKQKVYPWQLLREIWHVN--FTLLGNRLF
mT1R2   388 ----VVYSVYSAVYAVAHTLHRLLHCNQVRCTKQIVYPWQLLREIWHVN--FTLLGNQLF
hT1R2   384 ----VVYSVYSAVYAVAHALHSLLGCDKSTCTKRVVYPWQLLEEIWKVN--FTLLDHQIF
rmGluR1 409 KMGFVINAIYAMAHGLQNMHHALCPGHVGLCDAMKPIDGRKLLDFLIKSSFVGVSGEEVW

rT1R2   442 FDQQGDMPMLLDIIQWQWDLSQNPFQSIASYSPTSKRLTYINNVSWYTPNNTVPVSMCSK
mT1R2   442 FDEQGDMPMLLDIIQWQWGLSQNPFQSIASYSPTETRLTYISNVSWYTPNNTVPISMCSK
hT1R2   438 FDPQGDVALHLEIVQWQWDRSQNPFQSVASYYPLQRQLKNIQDISWHTVNNTIPMSMCSK
rmGluR1 469 FDEKGDAPGRYDIMNLQYTEAN--RYDYVHVGTWHEGVLNIDDYKIQMNKSGMVRSVCSE
```

FIG.23A

FIG.23B


WT
S144A
E302A
ΔF/F
2
1
0
1
10
100
SUCROSE (mM)
WT
S144A
E302A
ΔF/F
2
1
0
0.01
0.1
1
10
ASPARTAME (mM)
WT
S144A
E302A
ΔF/F
2
1
0
0.01
0.1
1
10
100
NEOTAME (μM)

```
rT1R3 598 YWDSPLVQASGGSLFCFGLICLGLFCLSVLLFPGRPRSASCLAQQPMAHLPLTGCLSTLF
mT1R3 598 HWDSPLVQASGGSQFCFGLICLGLFCLSVLLFPGRPSSASCLAQQPMAHLPLTGCLSTLF
hT1R3 593 HRDSPLVQASGGPLACFGLVCLGLVCLSVLLFPGQPSPARCLAQQPLSHLPLTGCLSTLF

rT1R3 658 LQAAEIFVESELPLSWANWLCSYLRGPWAWLVVLLATLVEAALCAWYLMAFPPEVVTDWQ
mTIR3 658 LQAAETFVESELPLSWANWLCSYLRGLWAWLVVLLATFVEAALCAWYLIAFPPEVVTDWS
hT1R3 653 LQAAEIFVESELPLSWADRLSGCLRGPWAWLVVLLAMLVEVALCTWYLVAFPPEVVTDWH

rT1R3 718 VLPTEVLEHCRMRSWVSLGLVHITNAVLAFLCFLGTFLVQSQPGRYNRARGLTFAMLAYF
mTIR3 718 VLPTEVLEHCHVRSWVSLGLVHITNAMLAFLCFLGTFLVQSQPGRYNRARGLTFAMLAYF
  hT1R3 713 MLPTEALVHCRTRSWVSFGLAHATNATLAFLCFLGTFLVRSQPGRYNRARGLTFAMLAYF

rT1R3 778 IIWVSFVPLLANVQVAYQPAVQMGAILFCALGILATFHLPKCYVLLWLPELNTQEFFLGR
mTIR3 778 ITWVSFVPLLANVQVAYQPAVQMGAILVCALGILVTFHLPKCYVLLWLPKLNTQEFFLGR
hTIR3 773 ITWVSFVPLLANVQVVLRPAVQMGALLLCVLGILAAFHLPRCYLLMRQPGLNTPEFFLGG

rTIR3 838 SPKEASDGNSGSSEATRGHSE
mTIR3 838 NAKKAADENSGGGEAAQGHNE
hTIR3 833 GPGDAQGQNDGNTGNQGKHE-
```

FIG.23C

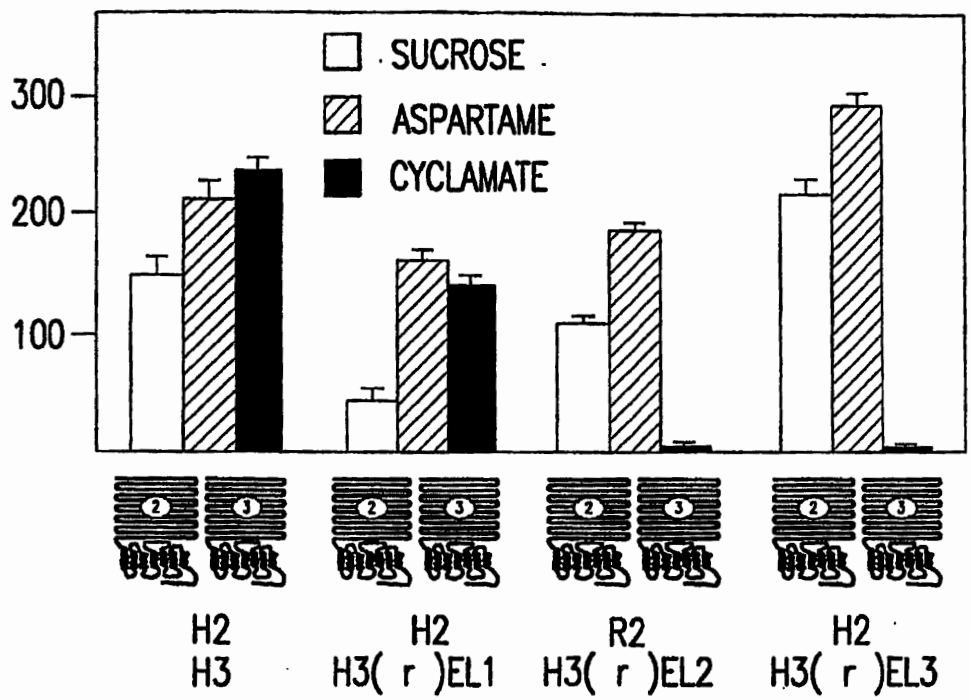

SUCROSE
ASPARTAME
CYCLAMATE
300
200
100
H2
H3
H2
H3(r)EL1
R2
H3(r)EL2
H2
H3(r)EL3

FIG.23D

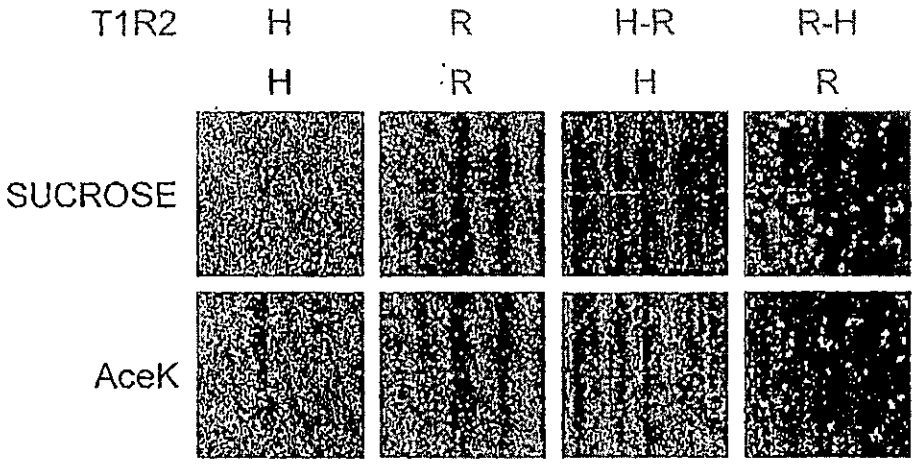


FIG.24A

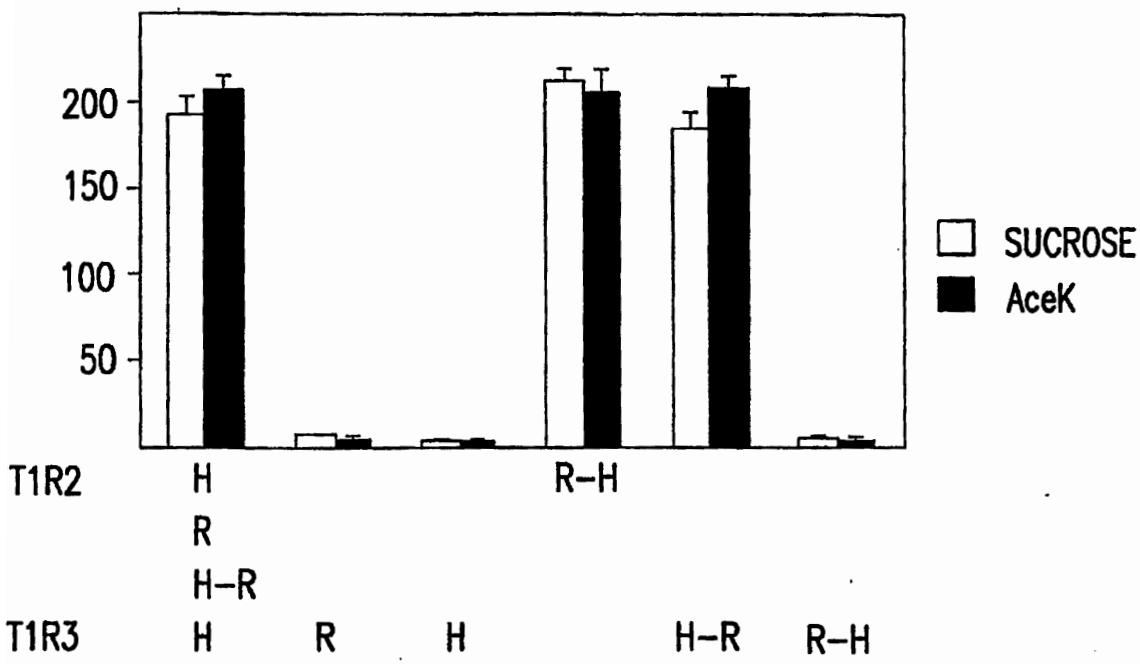


FIG.24B

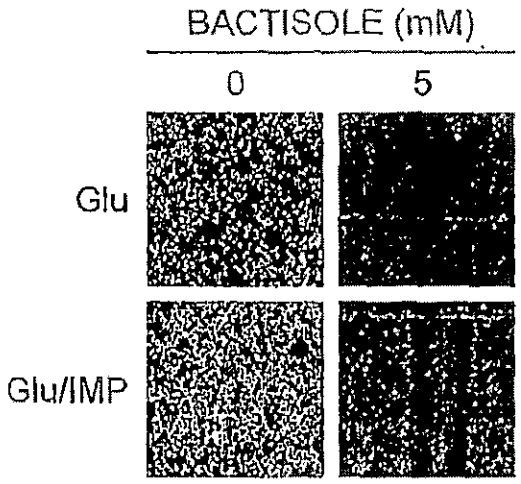


FIG.25A

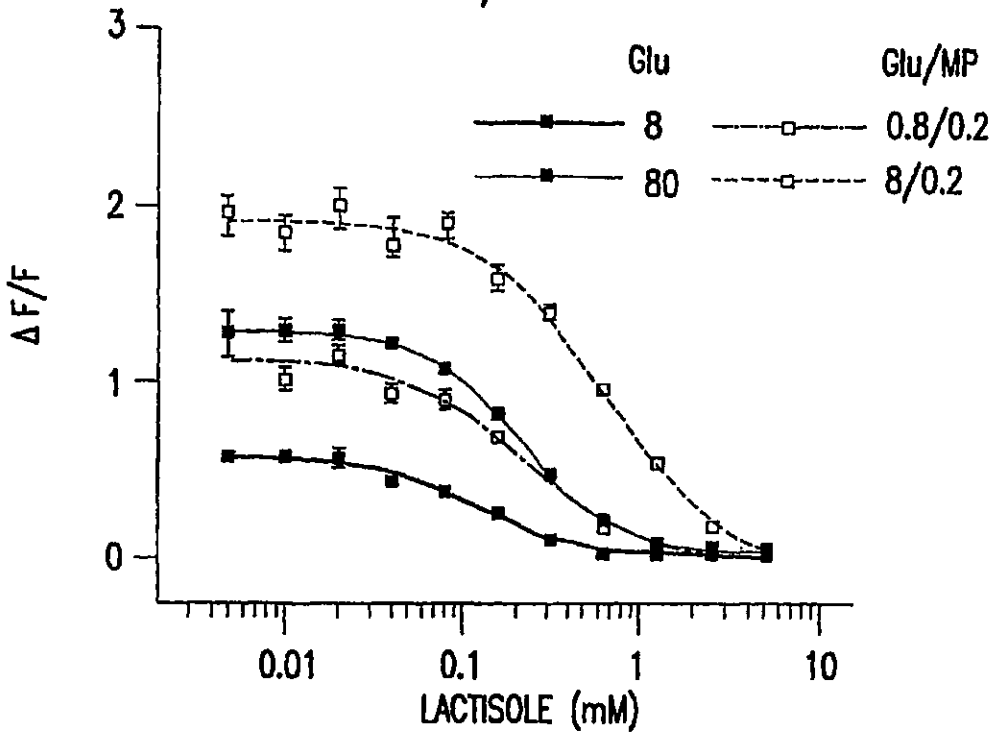


FIG.25B

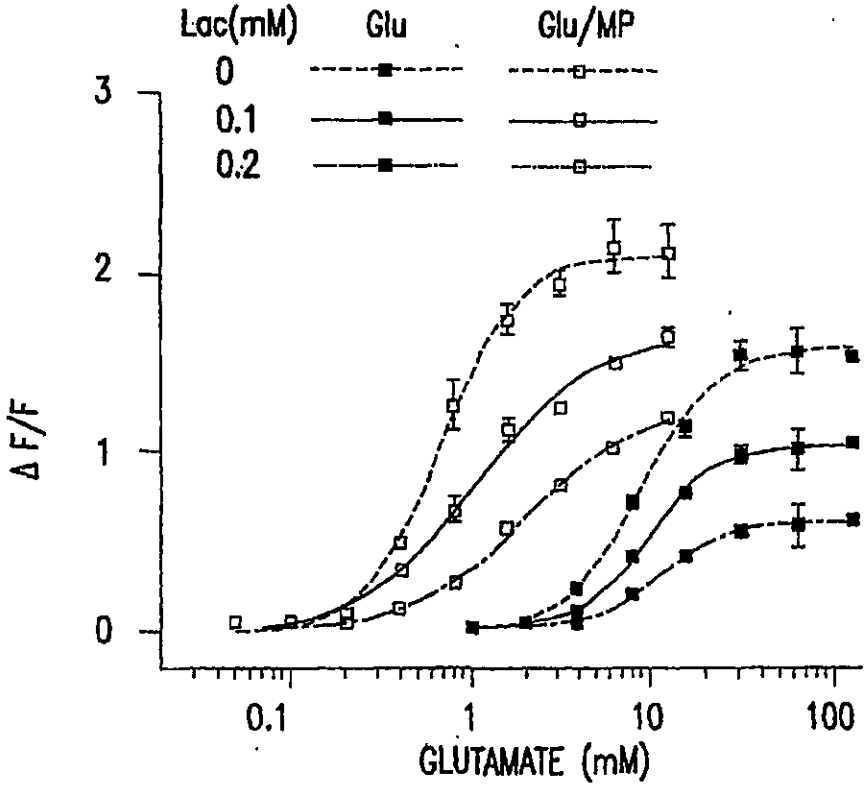


FIG. 25C

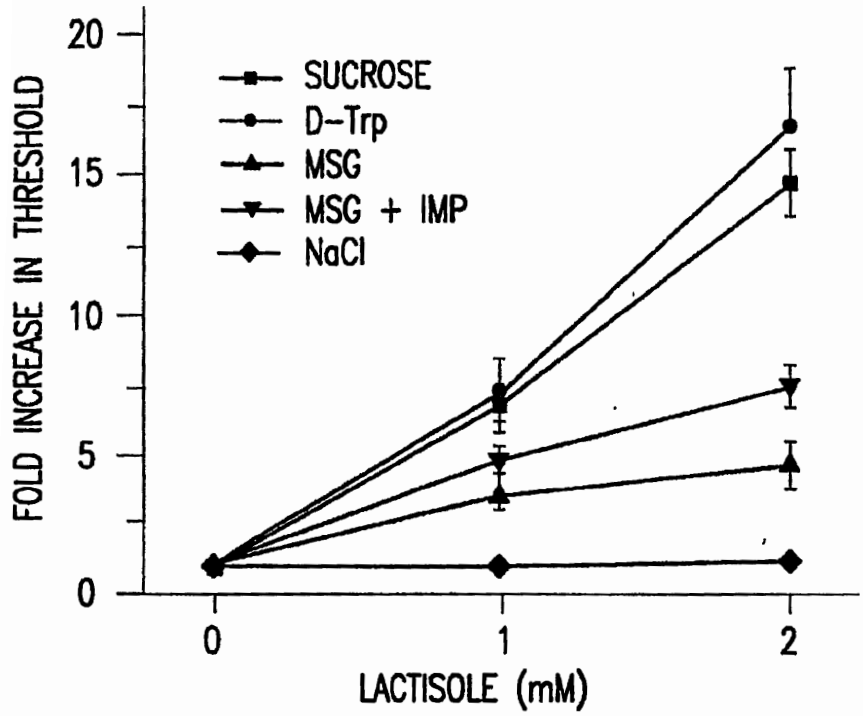


FIG.25D

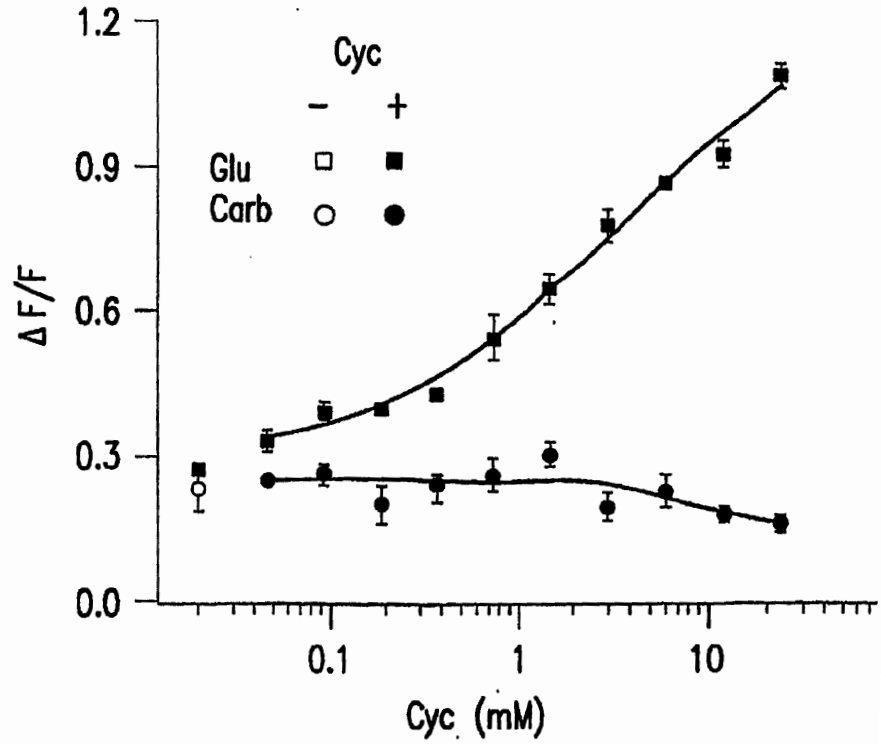


FIG.25E

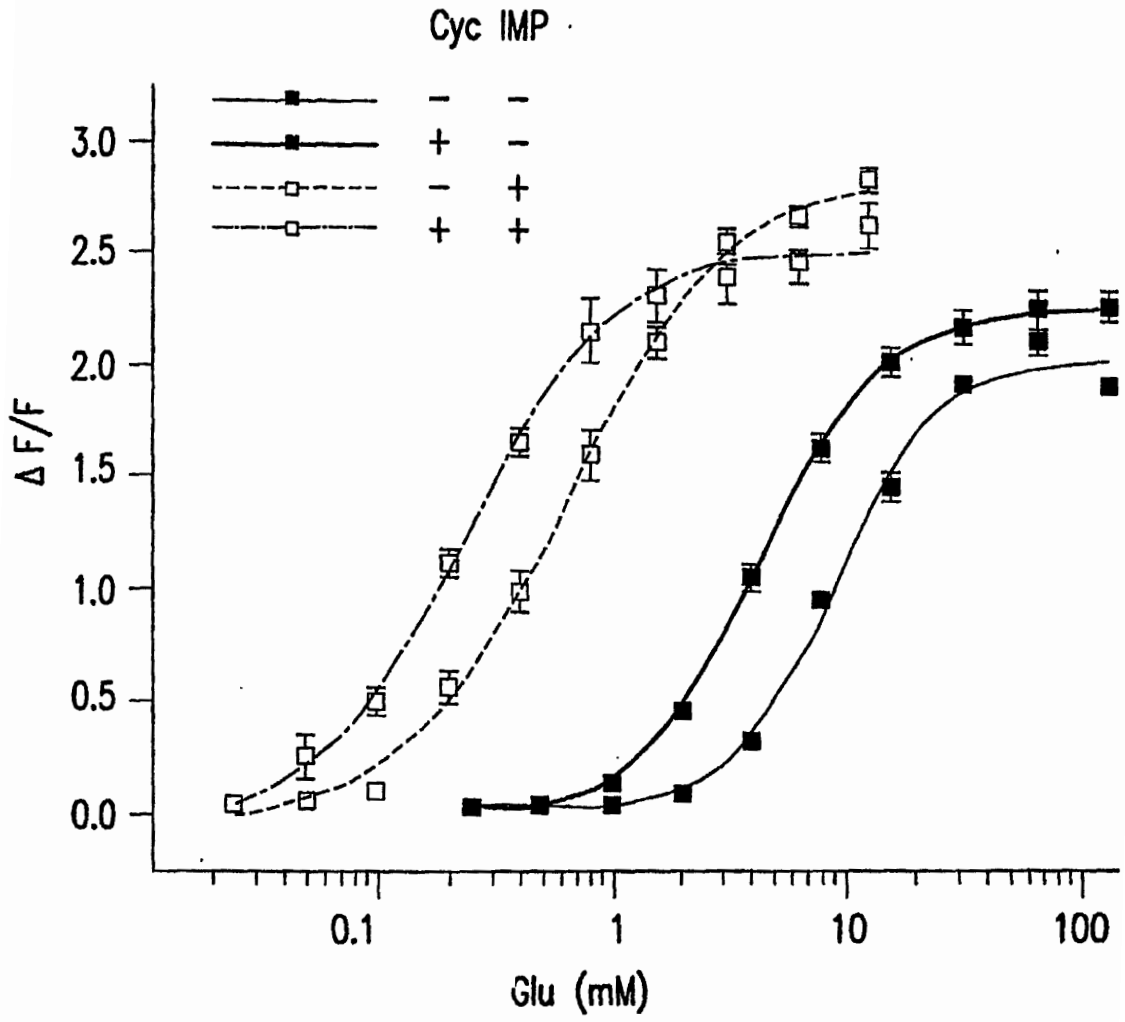


FIG.25F

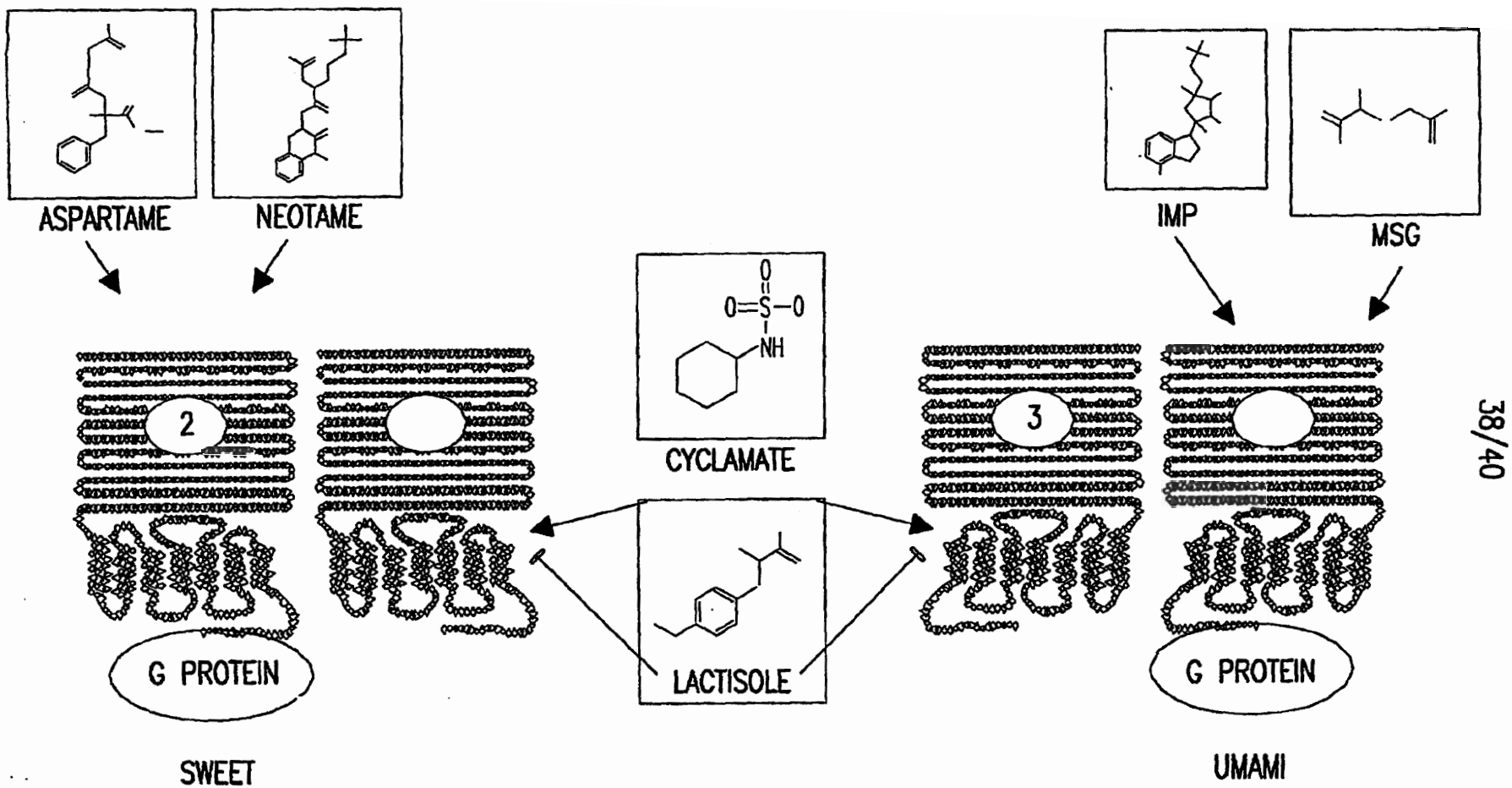

ASPARTAME
NEOTAME
IMP
MSG
CYCLAMATE
LACTISOLE
2
3
G PROTEIN
G PROTEIN
SWEET
UMAMI

FIG.26

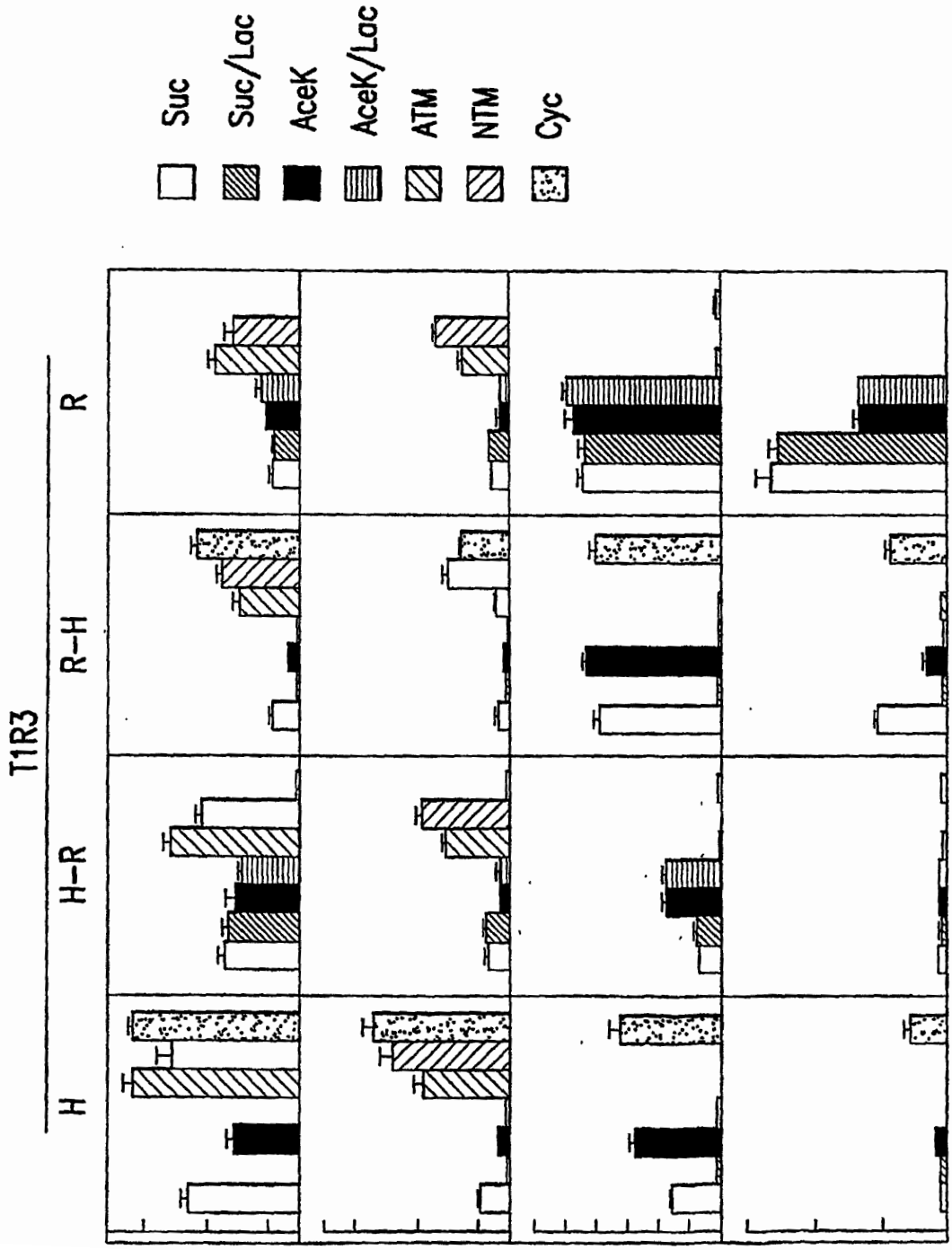


FIG.27A

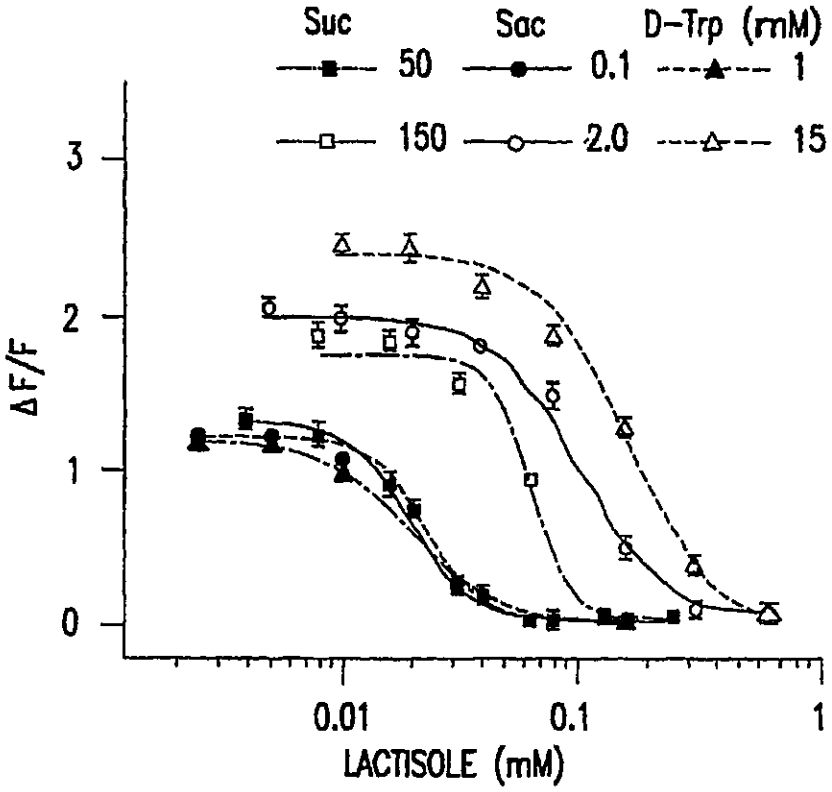


FIG.27B

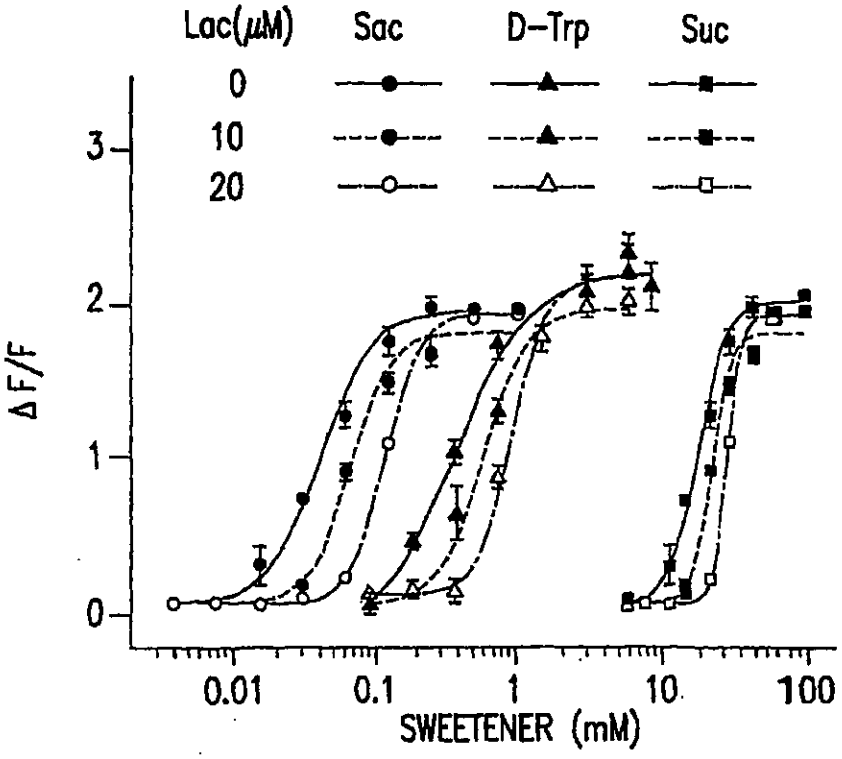


FIG. 27C