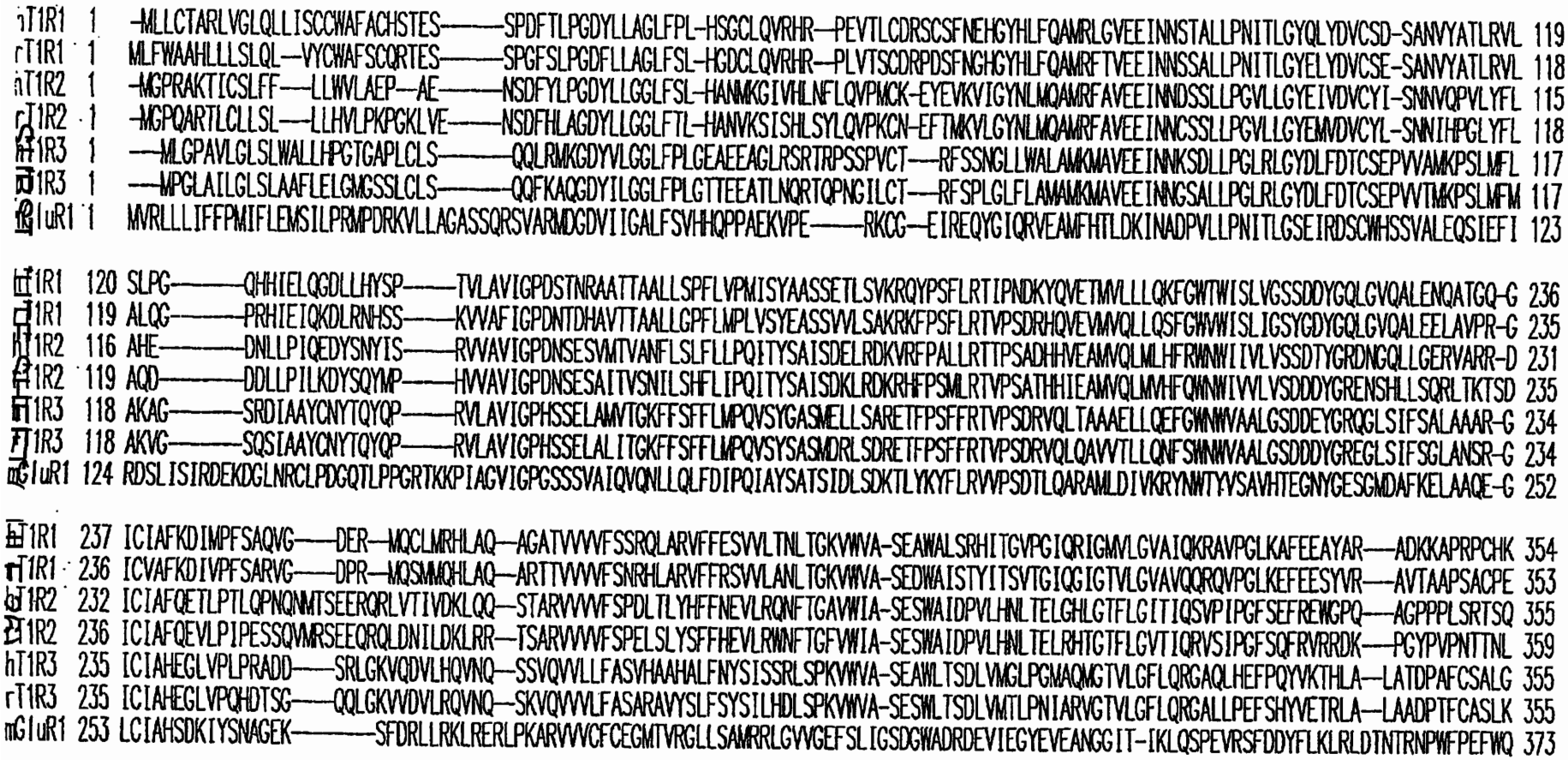


FIG. 1A



FIG.1B

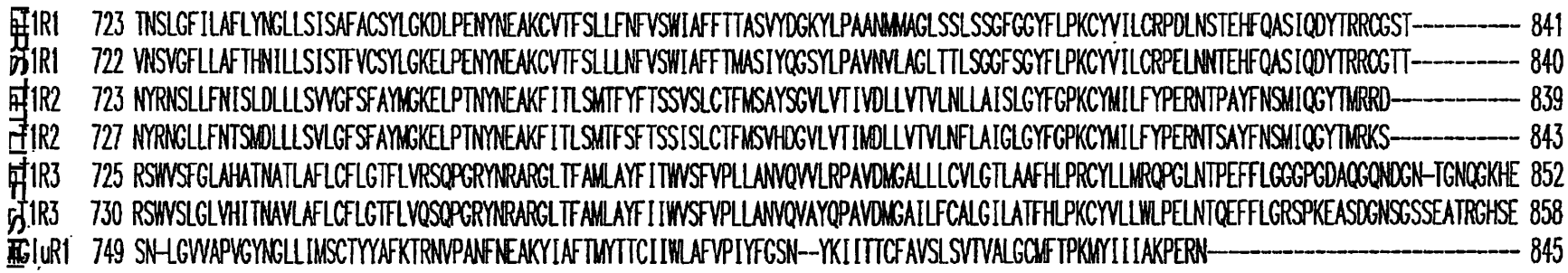

1R1 723 TNSLGFILAFLYNGLLSISAFACSYLGKDLPENYNEAKCVTFSLLFNFVSWIAFFTTASVYDGKYLPAANMMAGLSSLSSGFGGYFLPKCYVILCRPDLNSTEHFQASIQDYTRRCGST---------- 841
1R1 722 VNSVGFLLAFTHNILLSISTFVCSYLGKELPENYNEAKCVTFSLLLNFVSWIAFFTMASIYQGSYLPAVNVLAGLTTLSGGFSGYFLPKCYVILCRPELNNTEHFQASIQDYTRRCGTT---------- 840
1R2 723 NYRNSLLFNISLDLLLSVVGFSFAYMGKELPTNYNEAKFITLSMTFYFTSSVSLCTFMSAYSGVLVTIVDLL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

FIG.3C



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

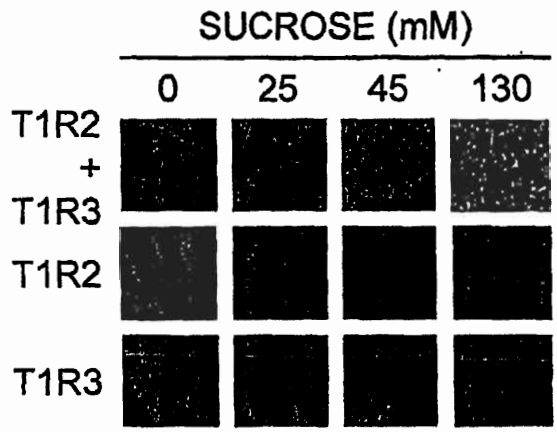

SUCROSE (mM)
0
25
45
130
T1R2
+
T1R3
T1R2
T1R3

FIG.3A

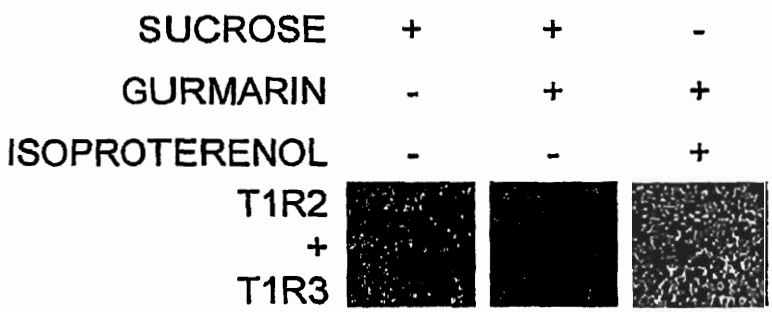

SUCROSE + + -
GURMARIN - + +
ISOPROTERENOL - - +
T1R2
+
T1R3

FIG.3B

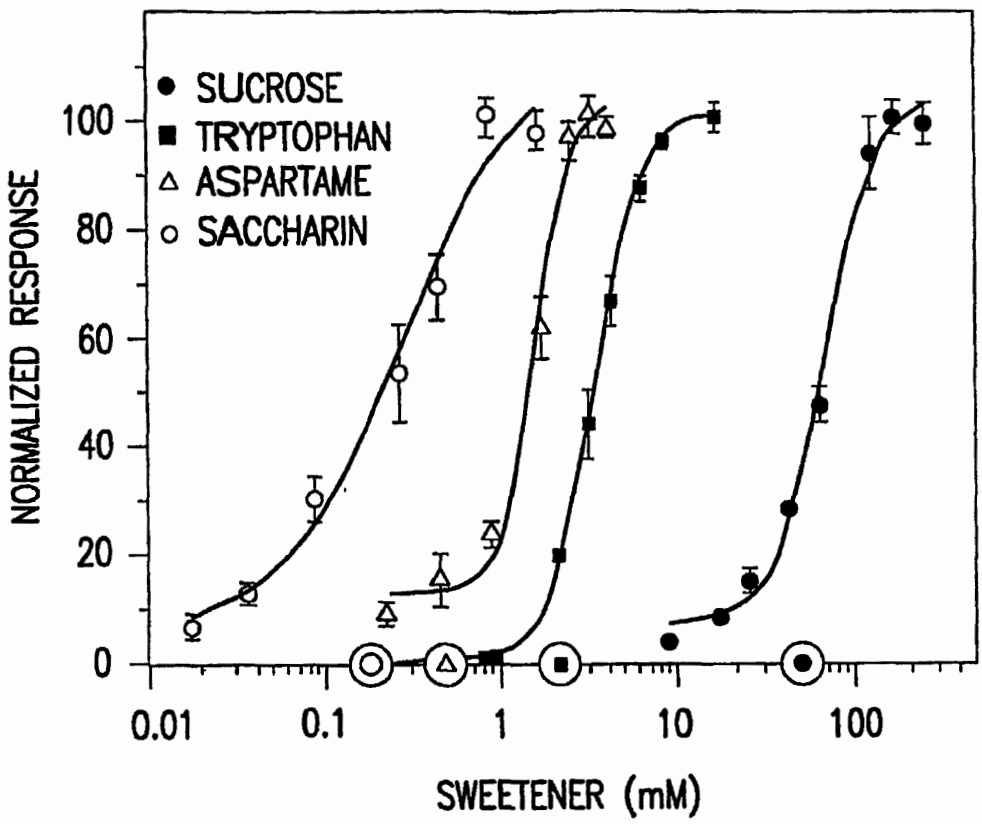

SUCROSE
TRYPTOPHAN
ASPARTAME
SACCHARIN
NORMALIZED RESPONSE
0
20
40
60
80
100
0.01
0.1
1
10
100
SWEETENER (mM)

FIG.3C

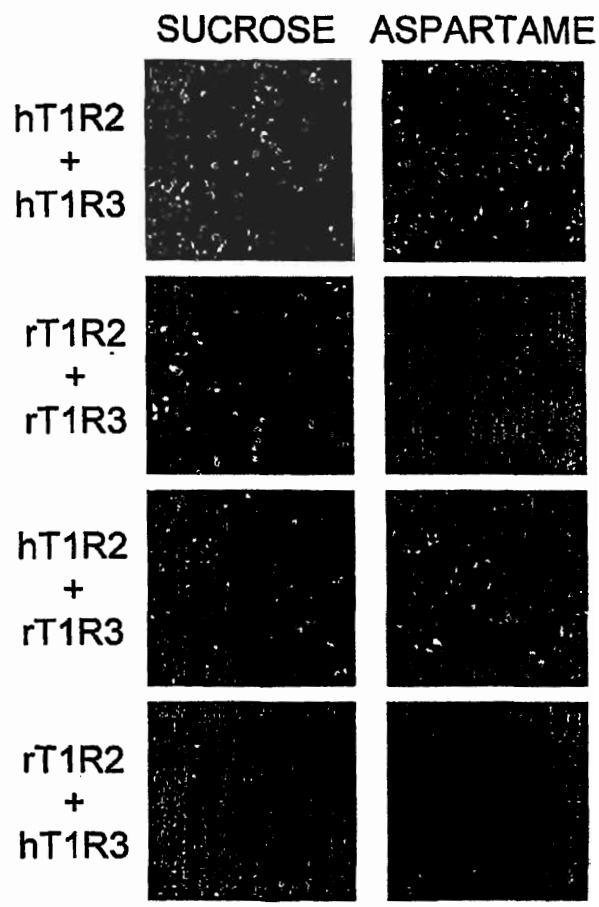

SUCROSE
ASPARTAME
hT1R2 + hT1R3
rT1R2 + rT1R3
hT1R2 + rT1R3
rT1R2 + hT1R3

FIG.4

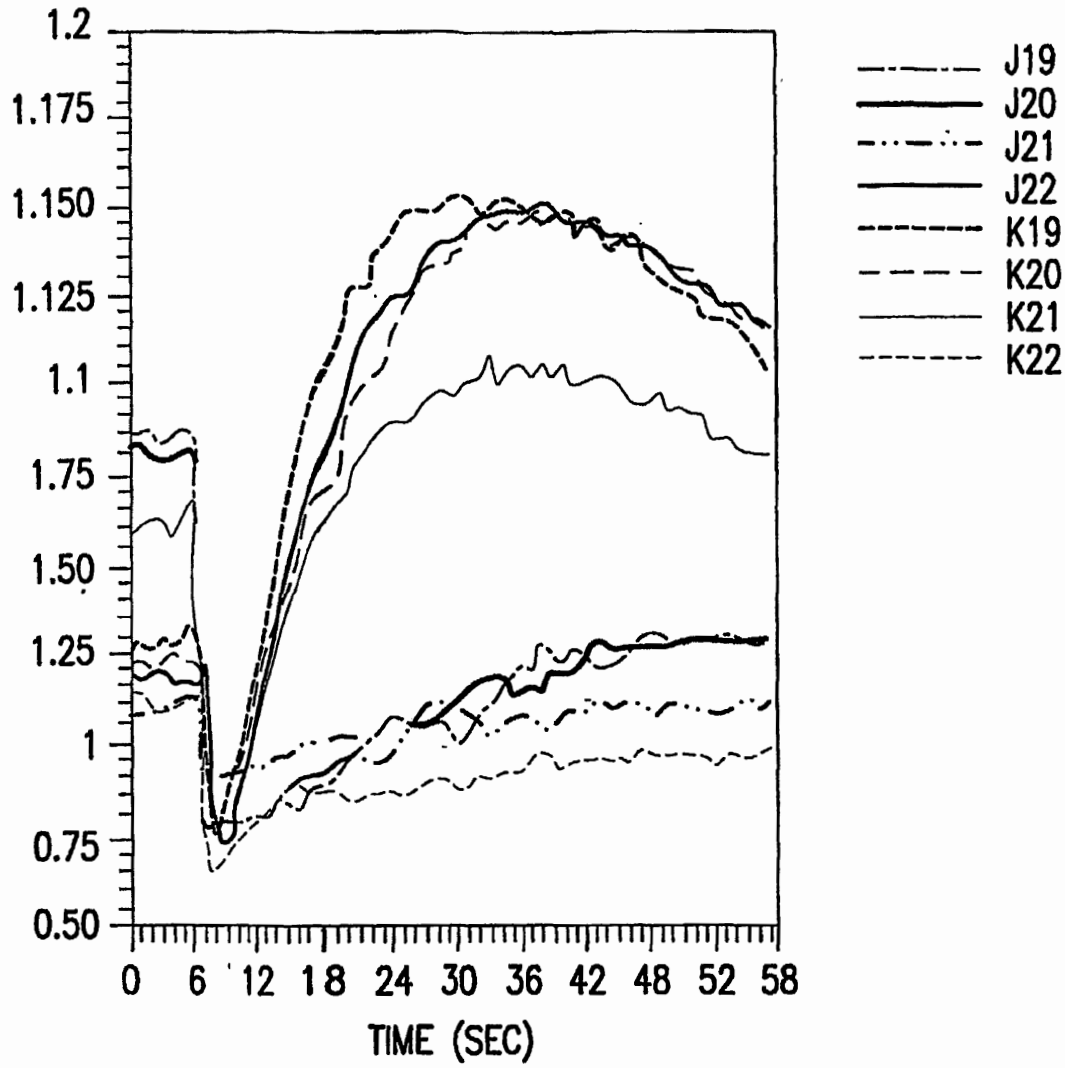

1.2
1.175
1.150
1.125
1.1
1.75
1.50
1.25
1
0.75
0.50
0
6
12
18
24
30
36
42
48
52
58
TIME (SEC)
J19
J20
J21
J22
K19
K20
K21
K22

FIG.5

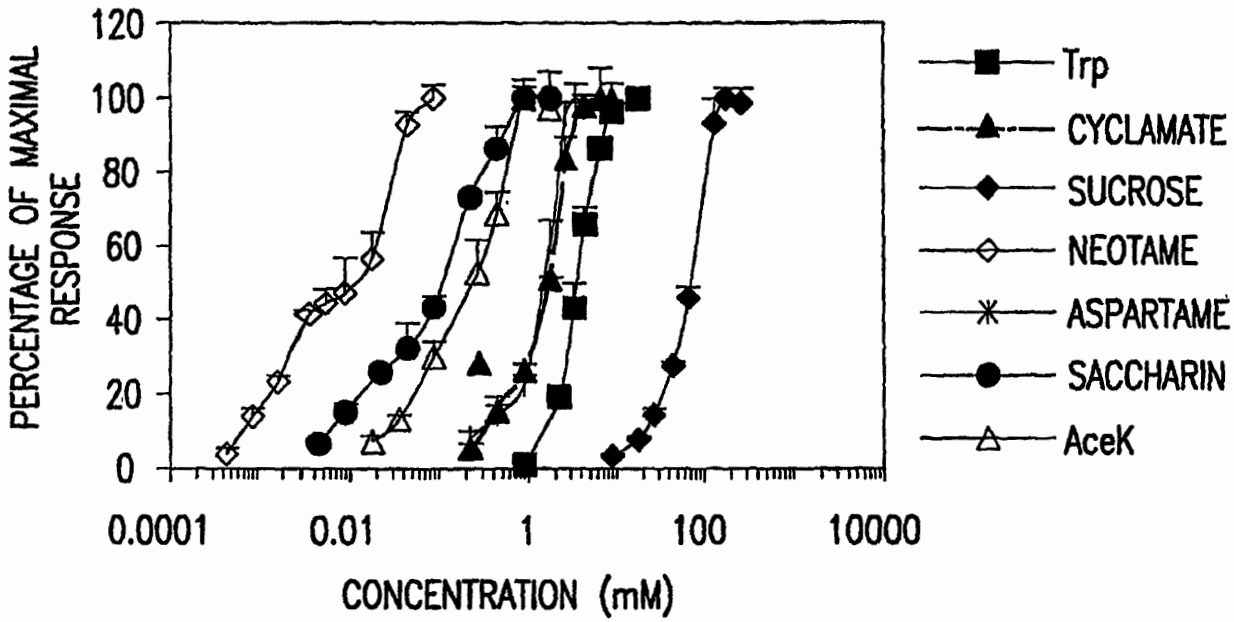

PERCENTAGE OF MAXIMAL RESPONSE
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
CONCENTRATION (mM)
Trp
CYCLAMATE
SUCROSE
NEOTAME
ASPARTAME
SACCHARIN
AceK

FIG.6

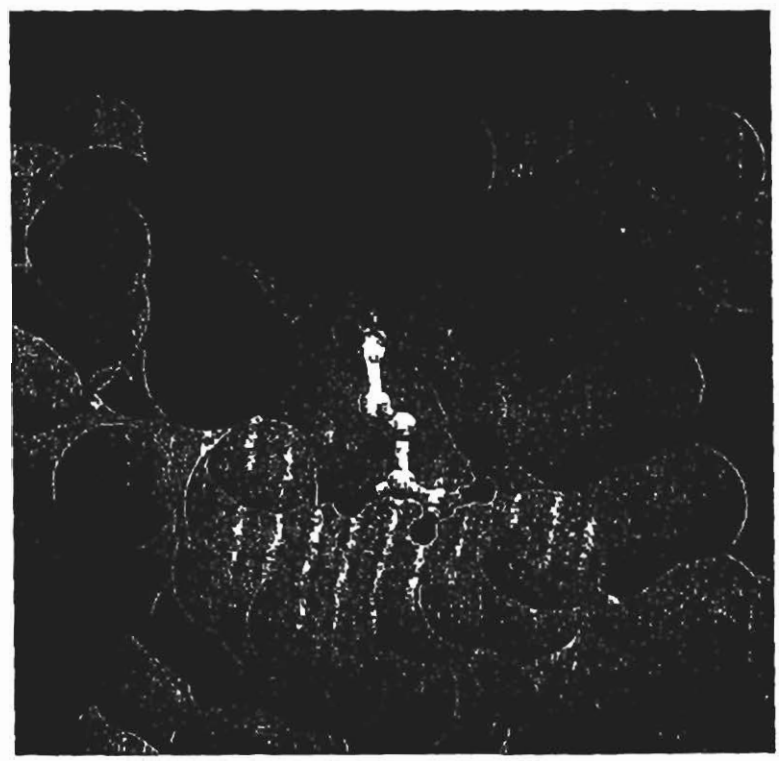


FIG.7

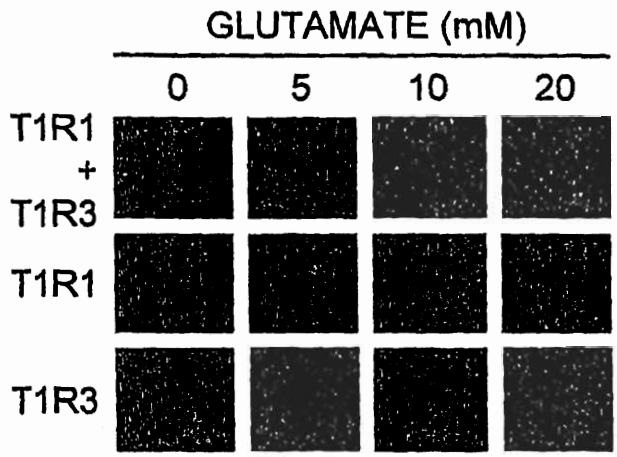

GLUTAMATE (mM)
0
5
10
20
T1R1
+
T1R3
T1R1
T1R3

FIG.8A

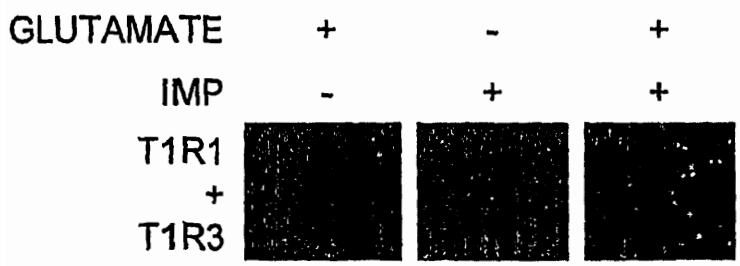

GLUTAMATE
+
-
+
IMP
-
+
+
T1R1
+
T1R3

FIG.8B

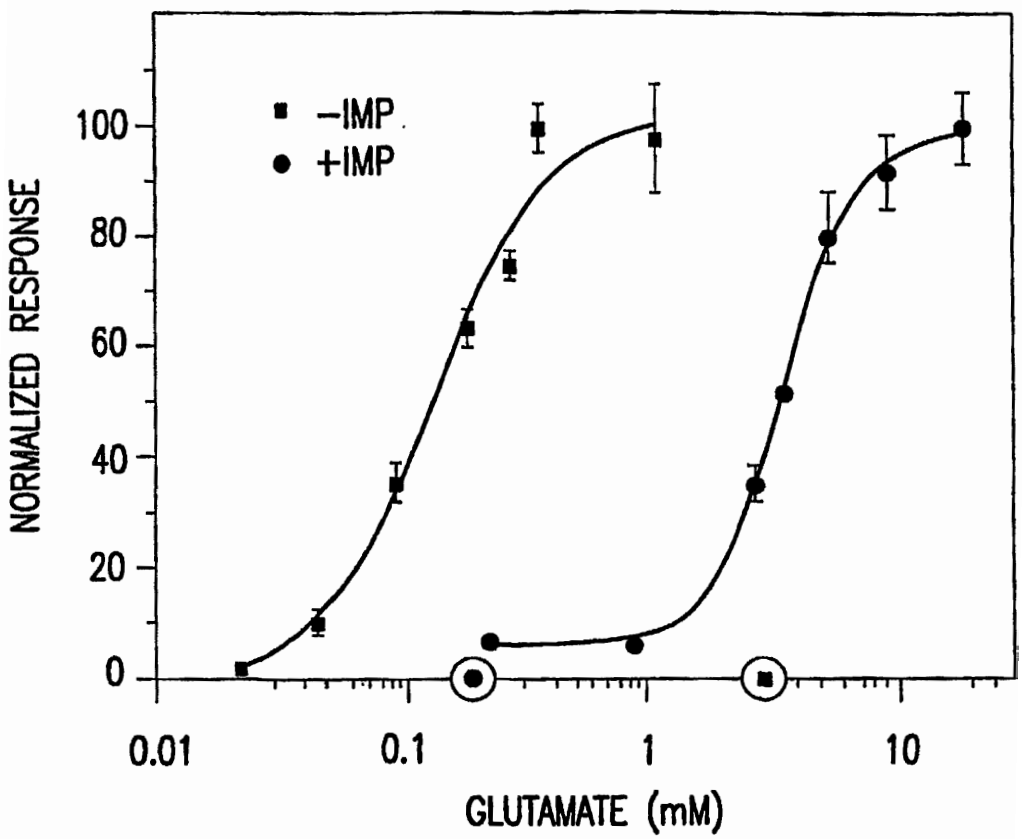

NORMALIZED RESPONSE
100
80
60
40
20
0
−IMP
+IMP
0.01
0.1
1
10
GLUTAMATE (mM)

FIG.8C

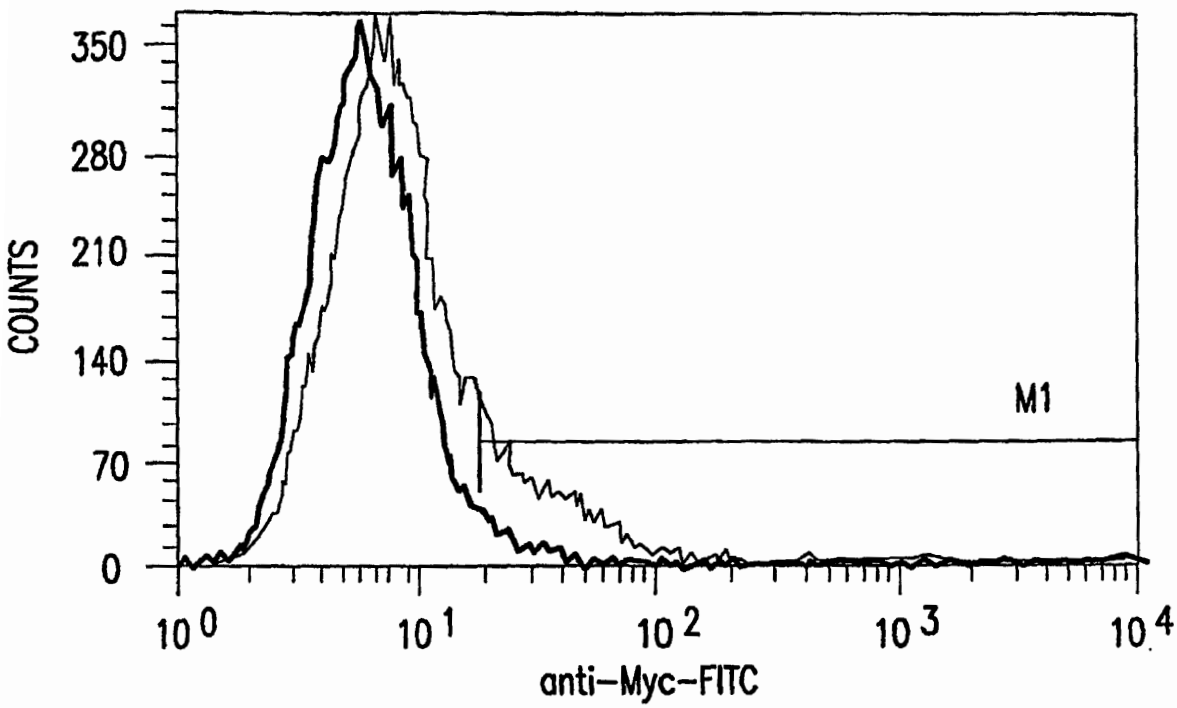


H2-IT-Myc H2-PDZIP-IT-Myc

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

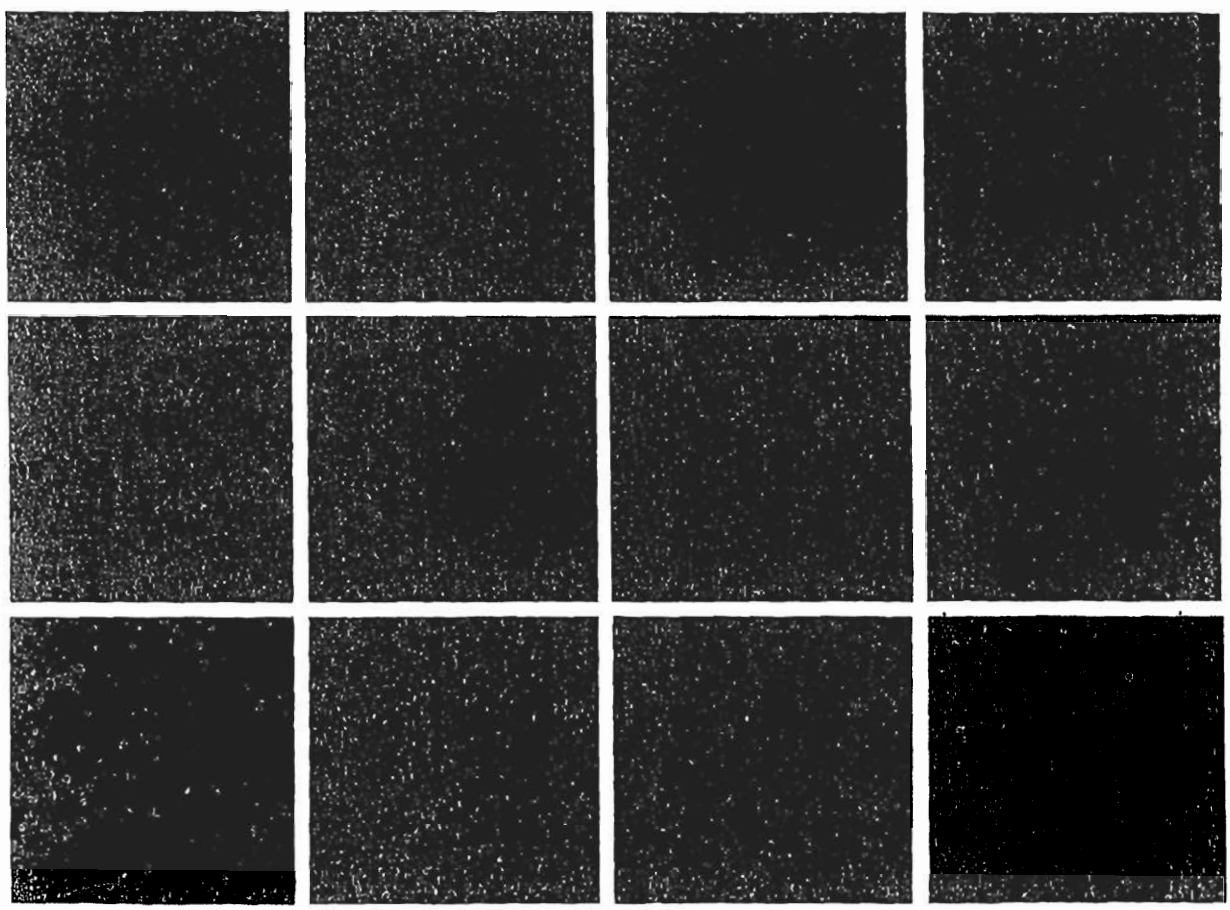


FIG.10

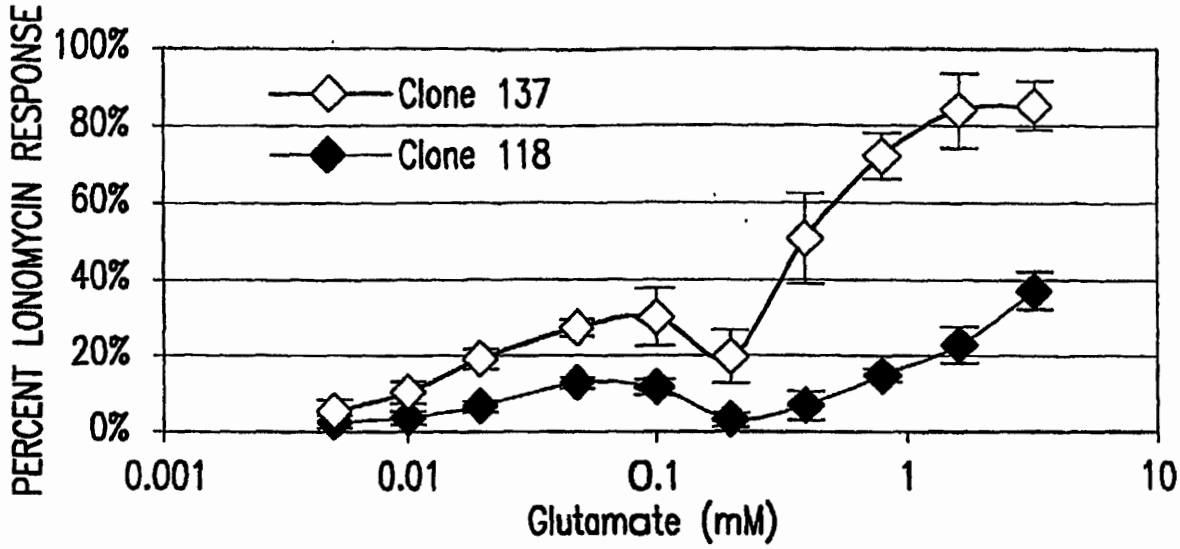

PERCENT LONOMYCIN RESPONSE
100%
80%
60%
40%
20%
0%
Clone 137
Clone 118
0.001
0.01
0.1
1
10
Glutamate (mM)

FIG. 11

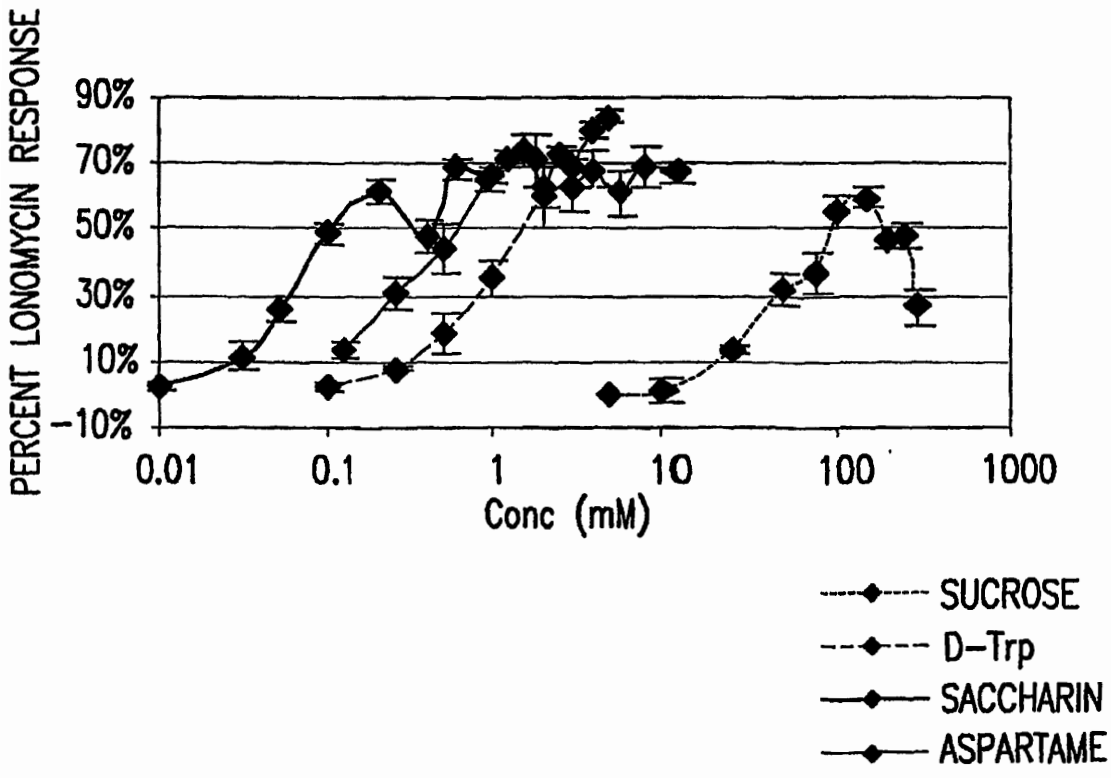

PERCENT LONOMYCIN RESPONSE
90%
70%
50%
30%
10%
-10%
0.01
0.1
1
10
100
1000
Conc (mM)
SUCROSE
D-Trp
SACCHARIN
ASPARTAME

FIG 12

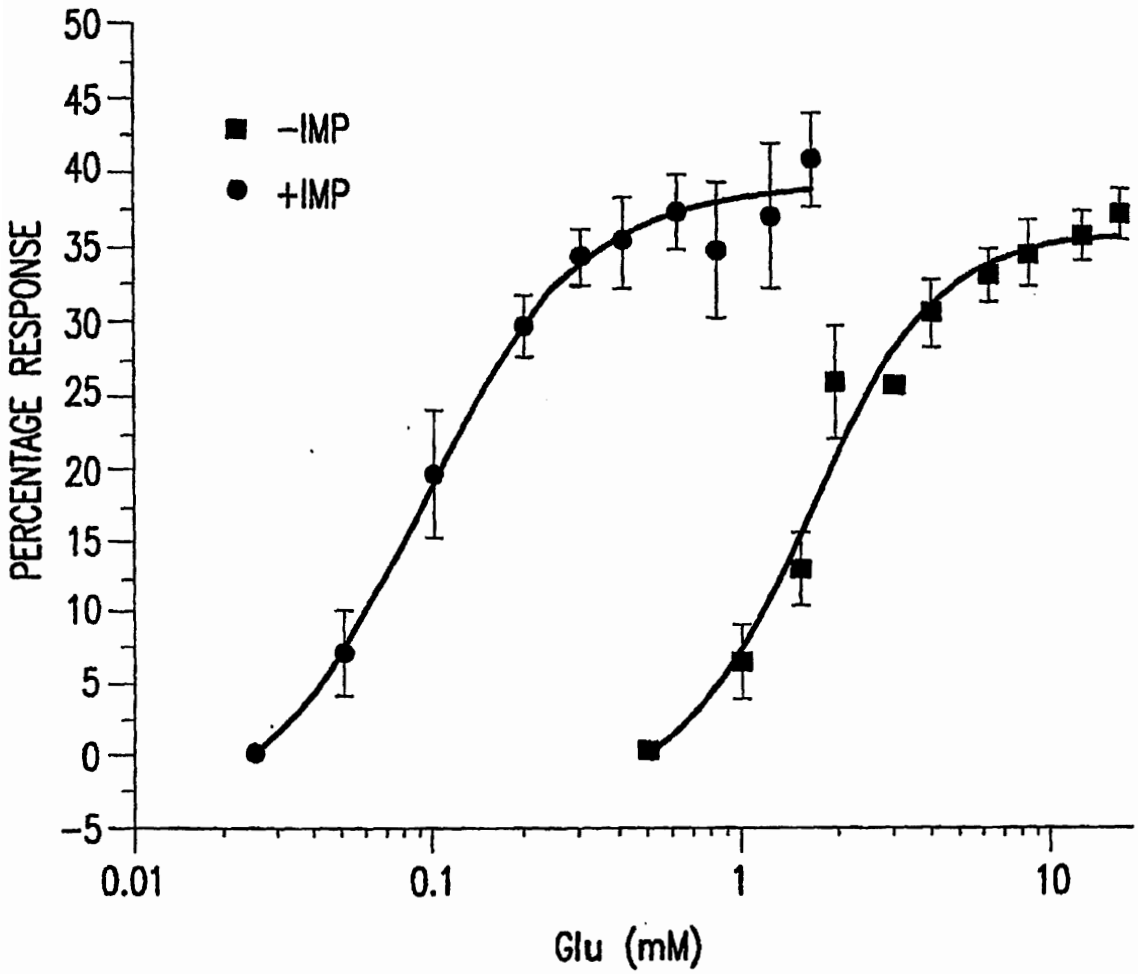

50
45
40
35
30
25
20
15
10
5
0
−5
PERCENTAGE RESPONSE
−IMP
+IMP
0.01
0.1
1
10
Glu (mM)

FIG. 13

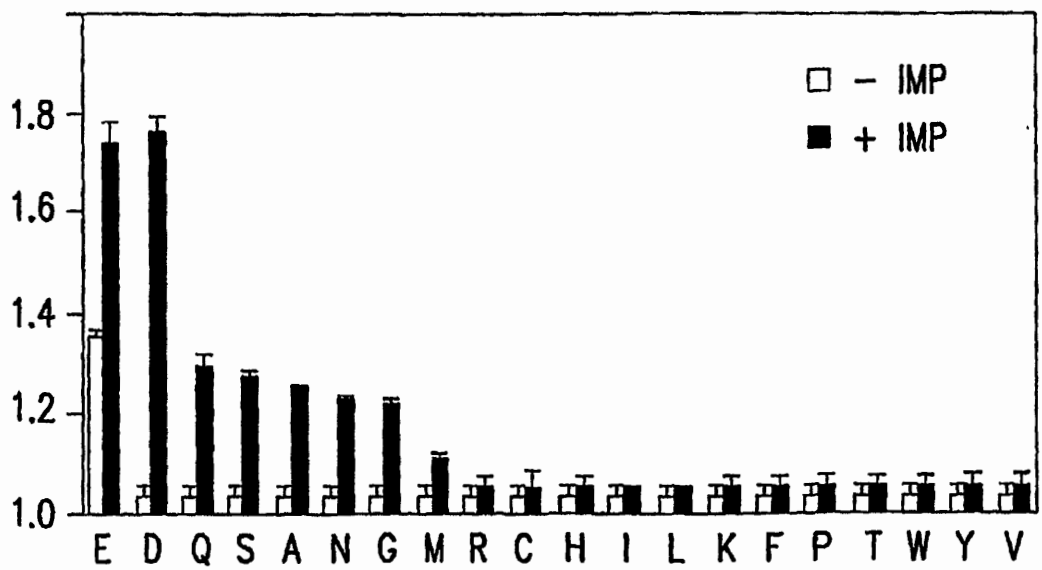

1.8
1.6
1.4
1.2
1.0
− IMP
+ IMP
E D Q S A N G M R C H I L K F P T W Y V

FIG. 14

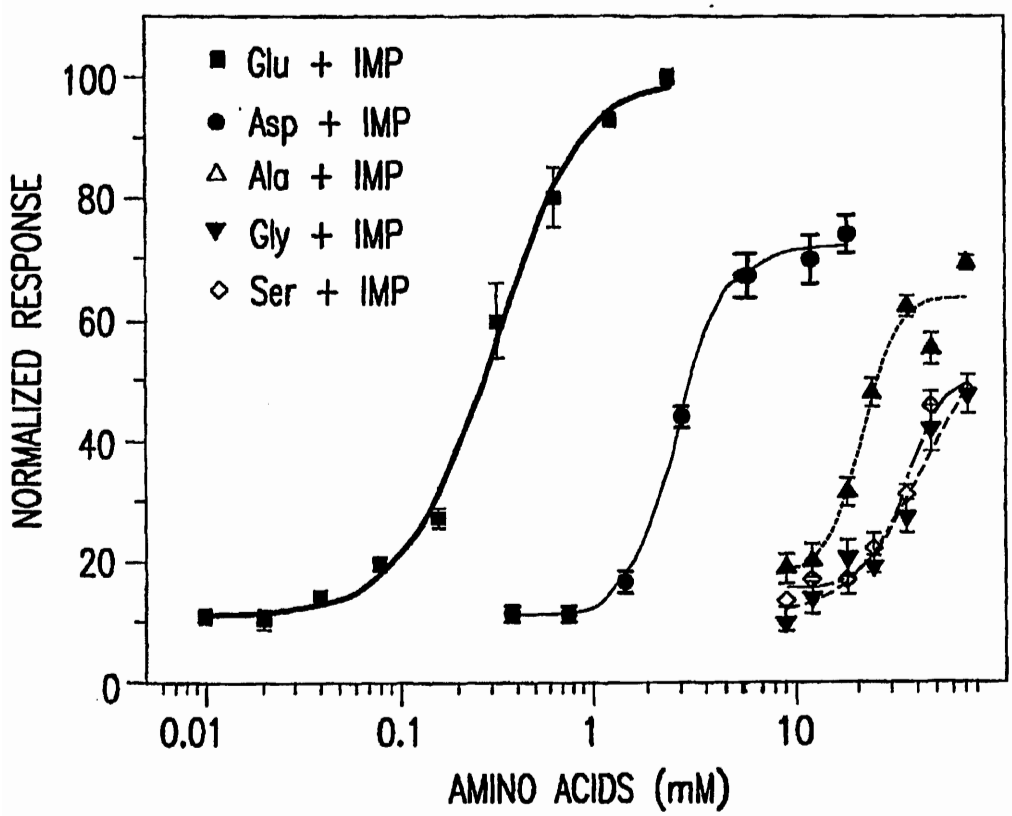

Glu + IMP
Asp + IMP
Ala + IMP
Gly + IMP
Ser + IMP
NORMALIZED RESPONSE
100
80
60
40
20
0
0.01
0.1
1
10
AMINO ACIDS (mM)

FIG.15

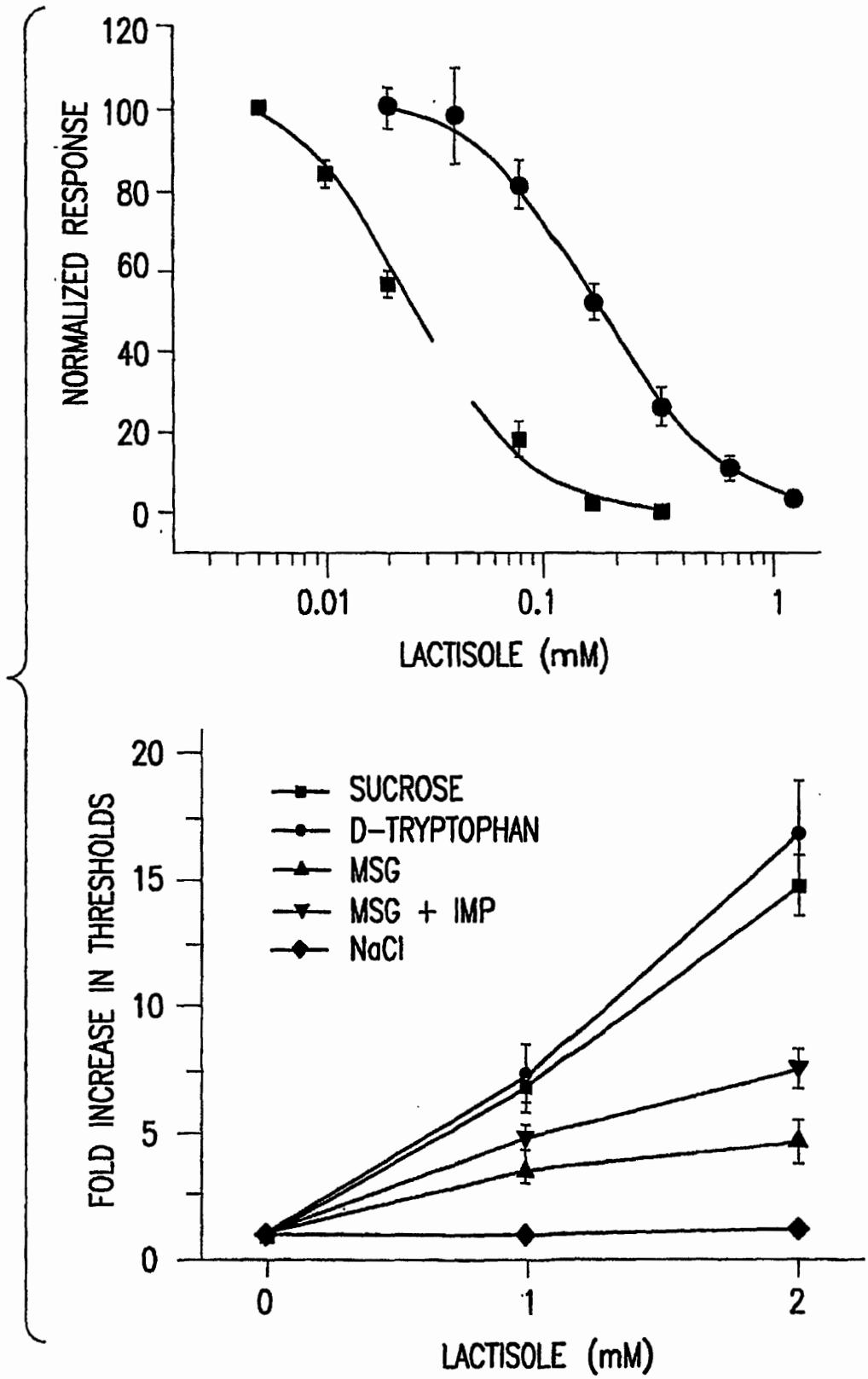

NORMALIZED RESPONSE
120
100
80
60
40
20
0
0.01
0.1
1
LACTISOLE (mM)
FOLD INCREASE IN THRESHOLDS
20
15
10
5
0
SUCROSE
D-TRYPTOPHAN
MSG
MSG + IMP
NaCl
0
1
2
LACTISOLE (mM)

FIG.16

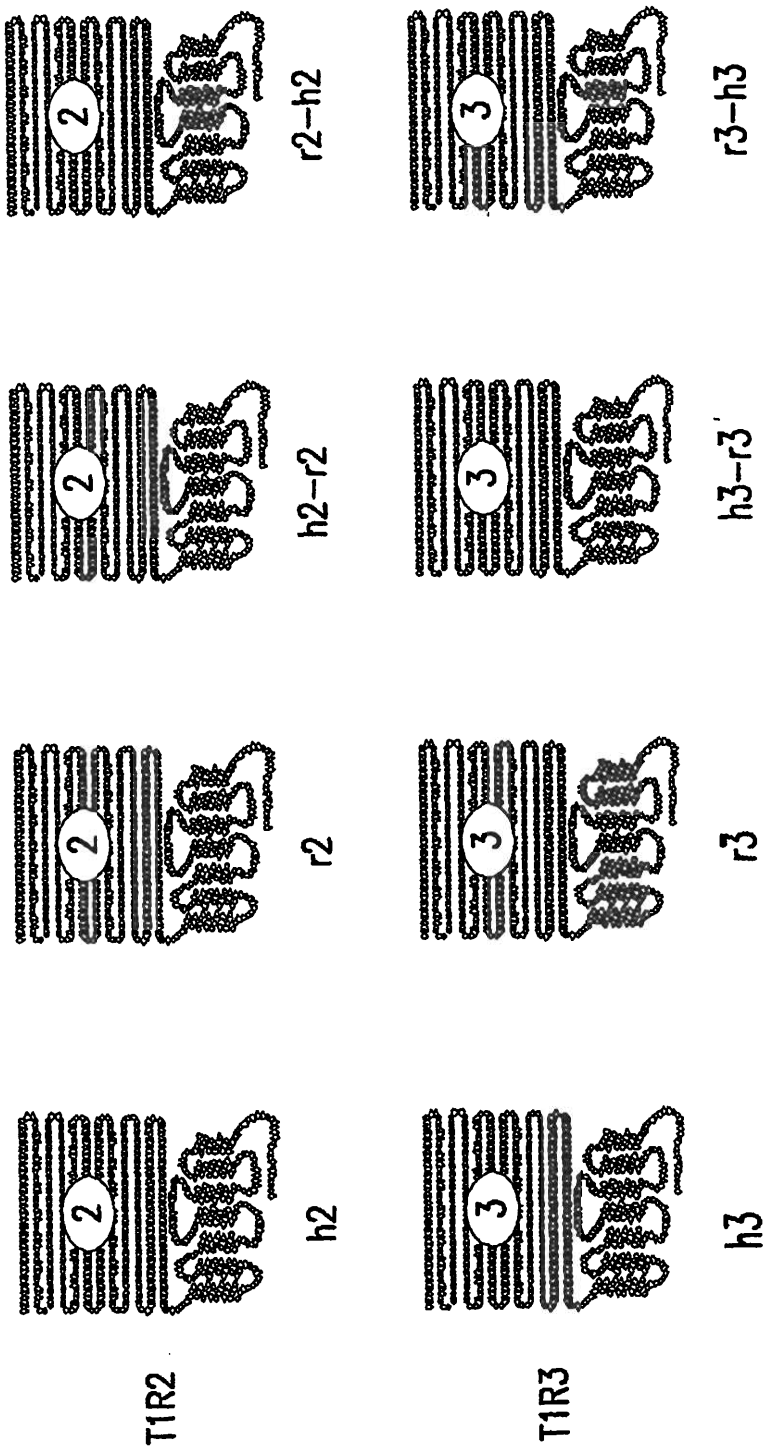


FIG. 17

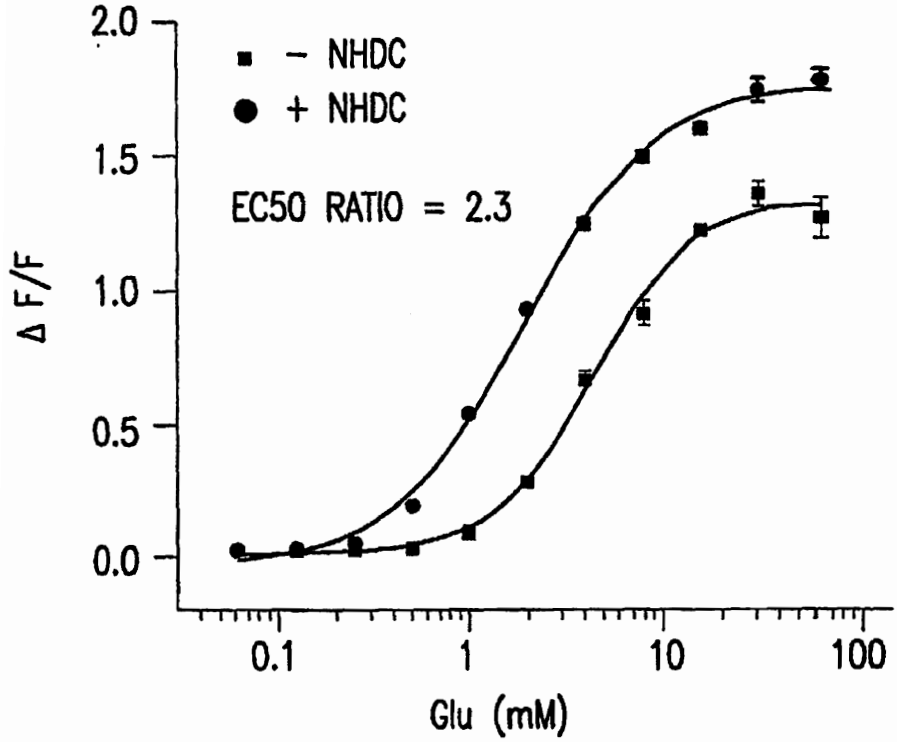


FIG.18A

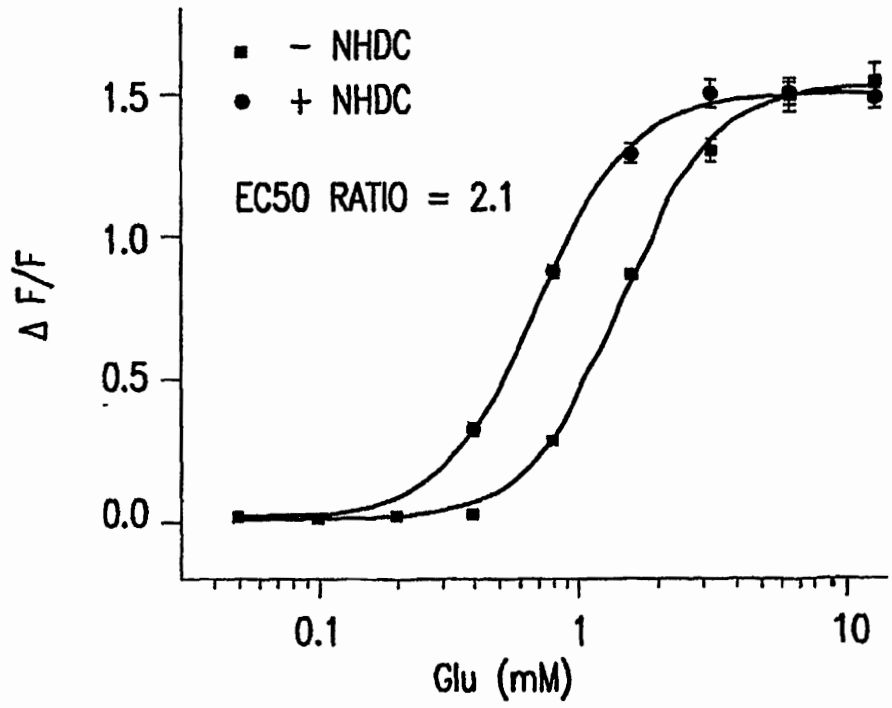


FIG.18B

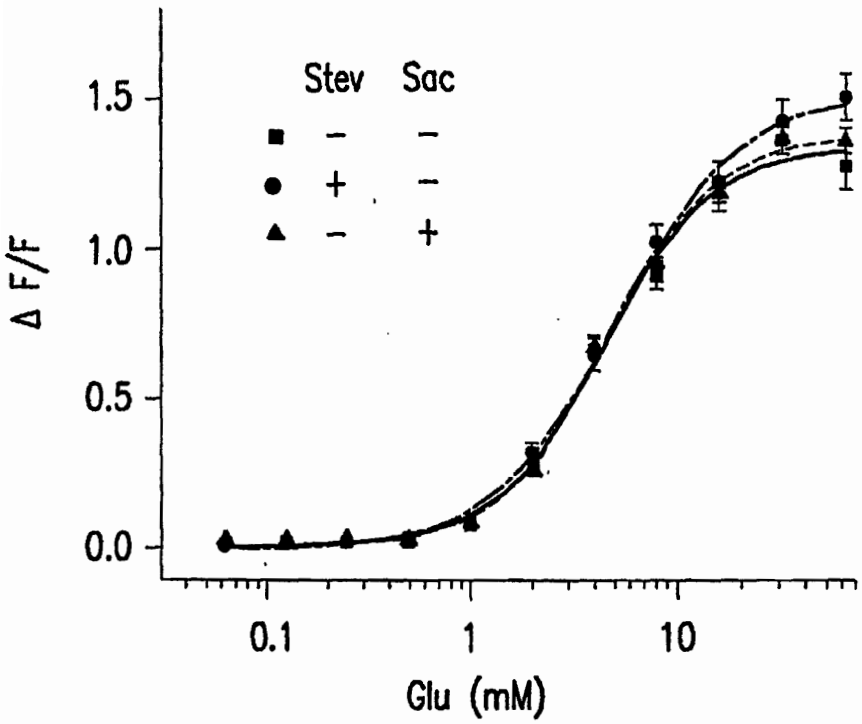


FIG.19A

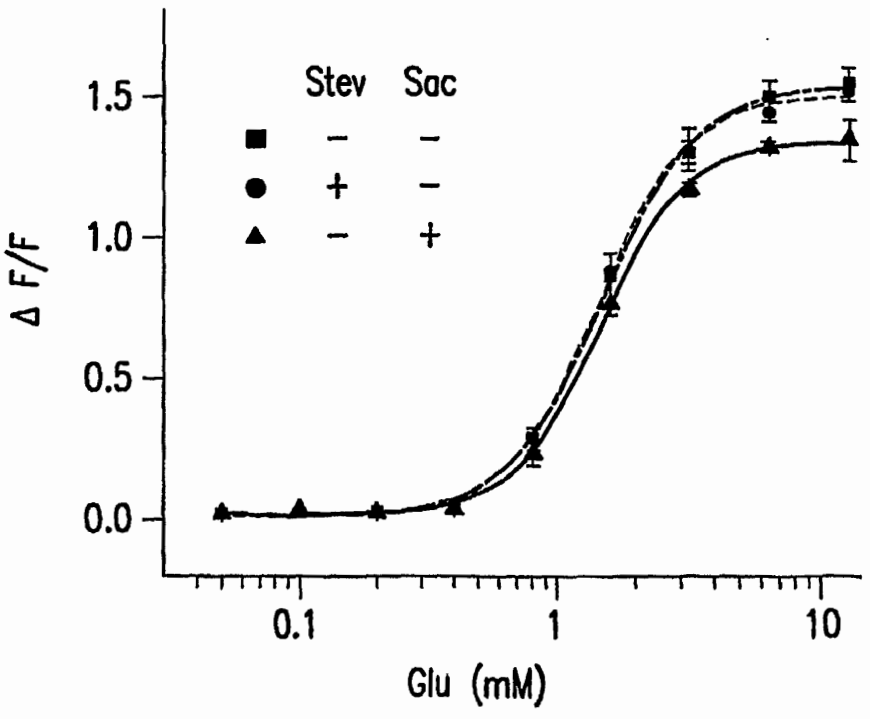


FIG.19B

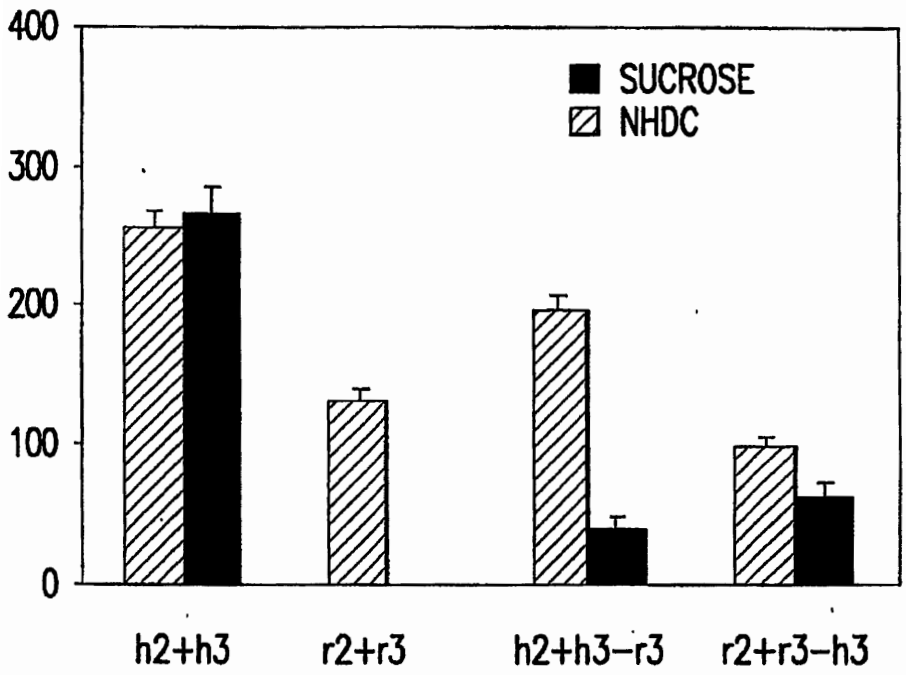


FIG.20

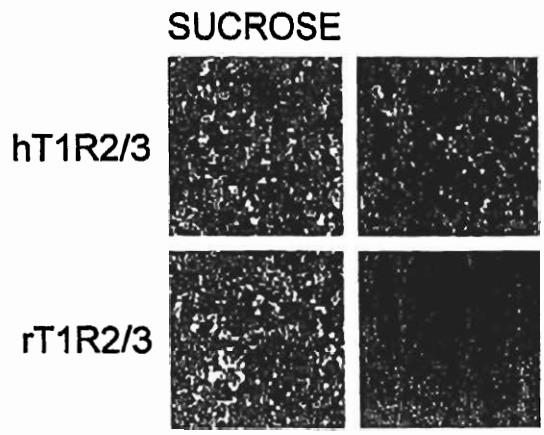


FIG.21A

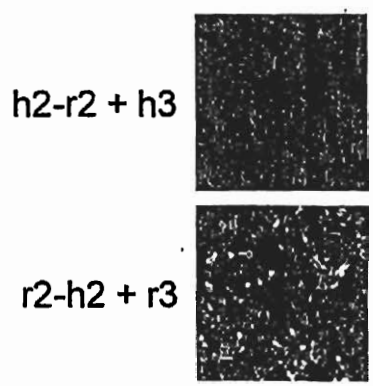


FIG.21B

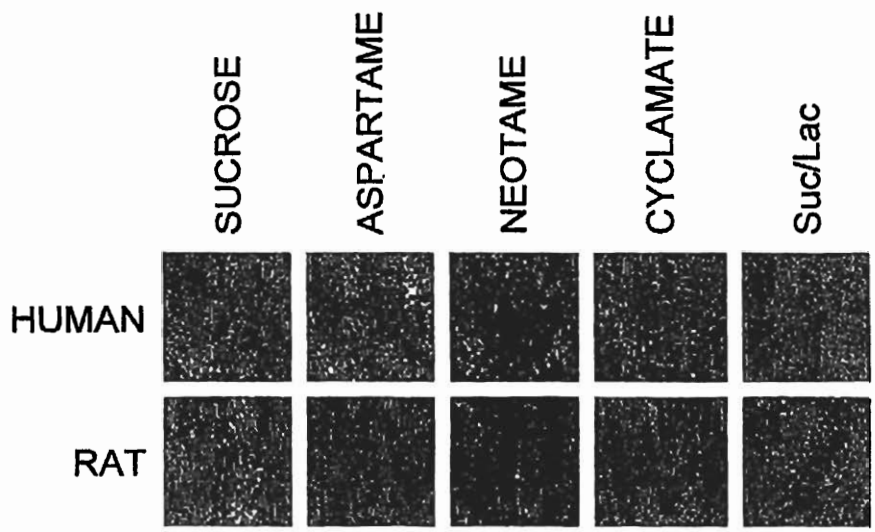


FIG.22A

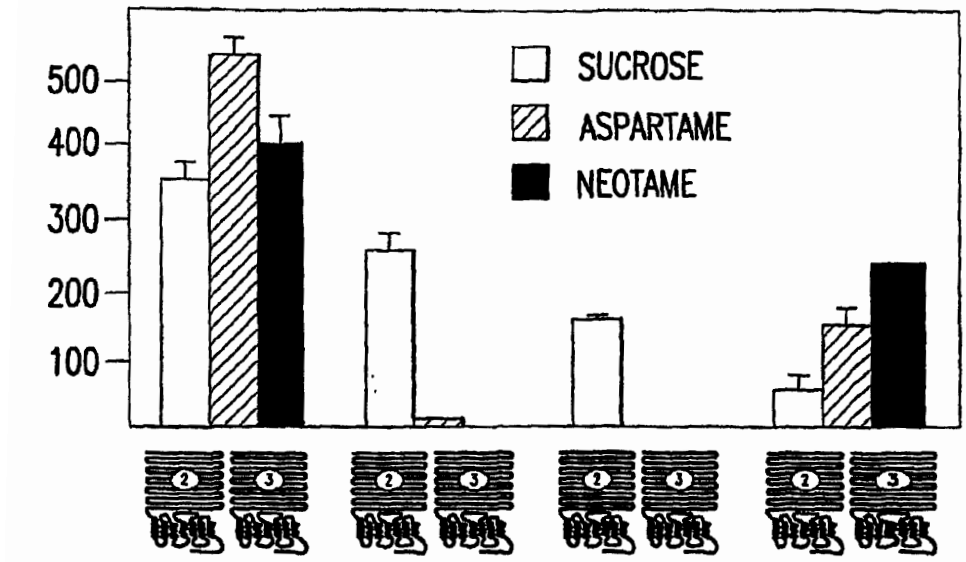


FIG.22B

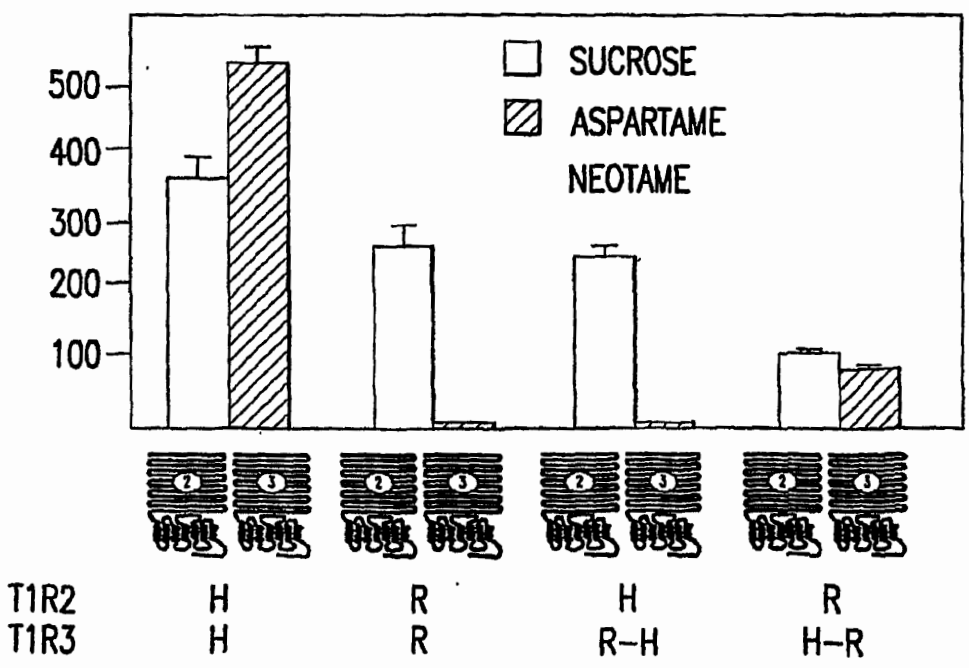


FIG.22C

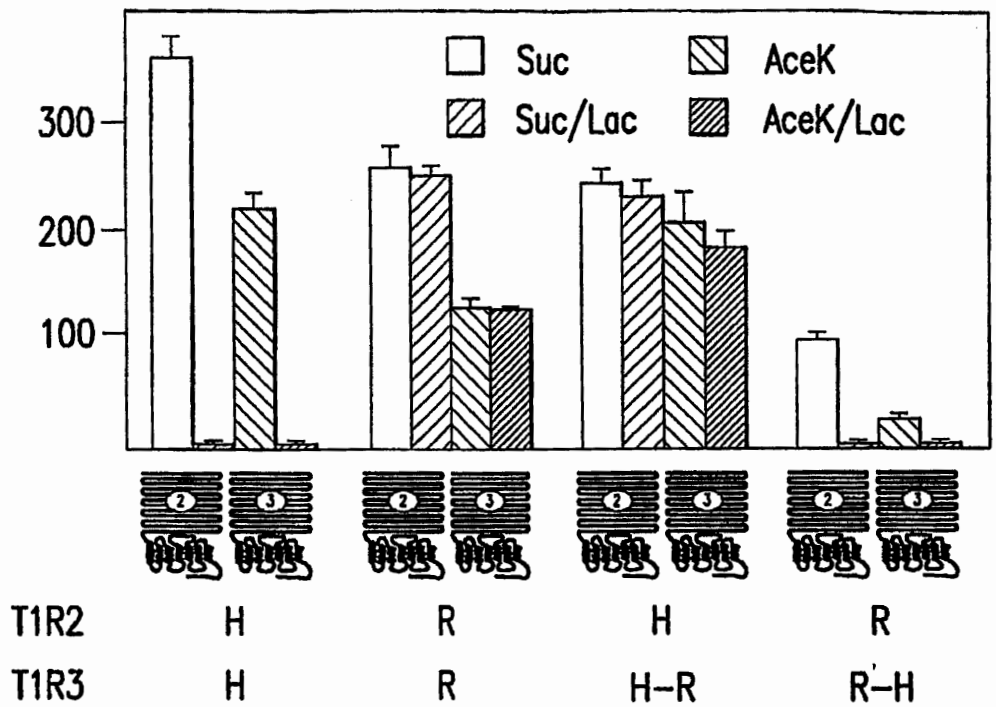


FIG.22D

```
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

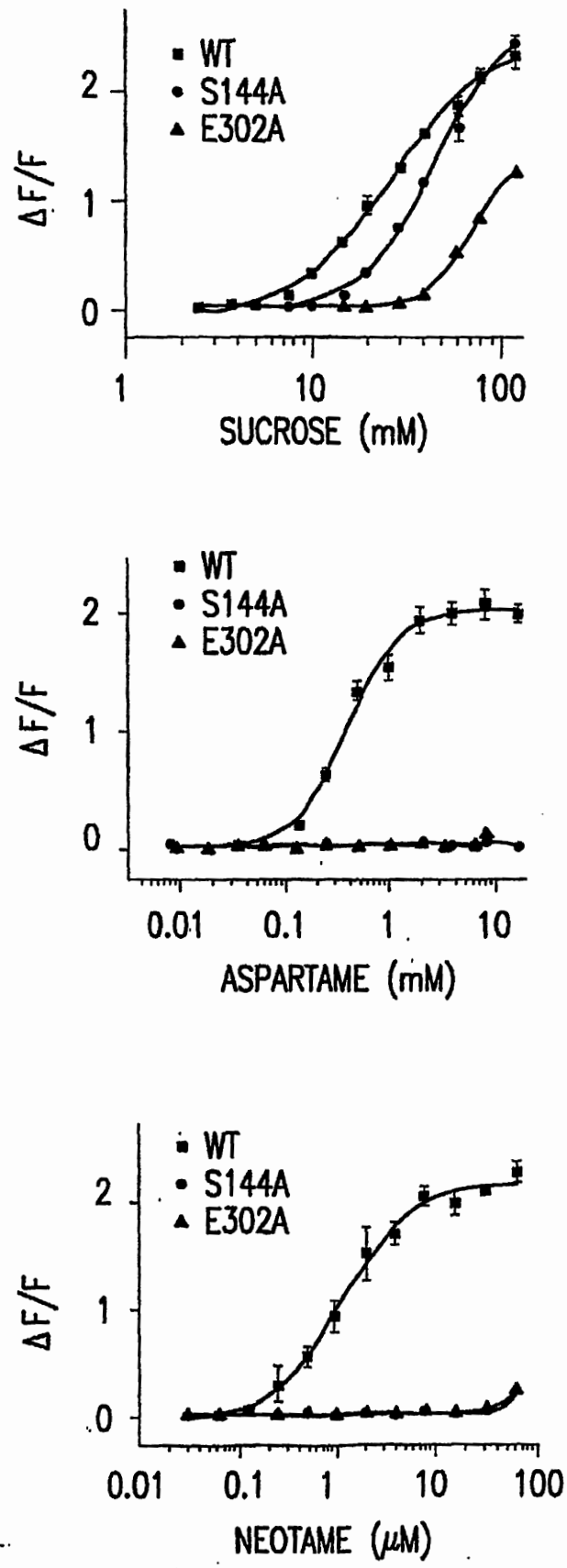
rT1R2   334 VSIPGFSQFRVRRDKPGYPVPNTTNLRTTCNQDCDACLNTTKSFNNILILSGER------
mT1R2   334 VSIPGFSQFRVRHDKPEYPMPNETSLRTTCNQDCDACMNITESFNNVLMLSGER------
hT1R2   330 VPIPGFSEFREWGPQAGPPPLSRTSQSYTCNQECDNCLNATLSFNTILRLSGER------
rmGluR1 349 SFDDYFLKLRLDTNTRNPWFPEFWQHRFQCRLPGHLLENPNFKKVCTGNESLEENYVQDS

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

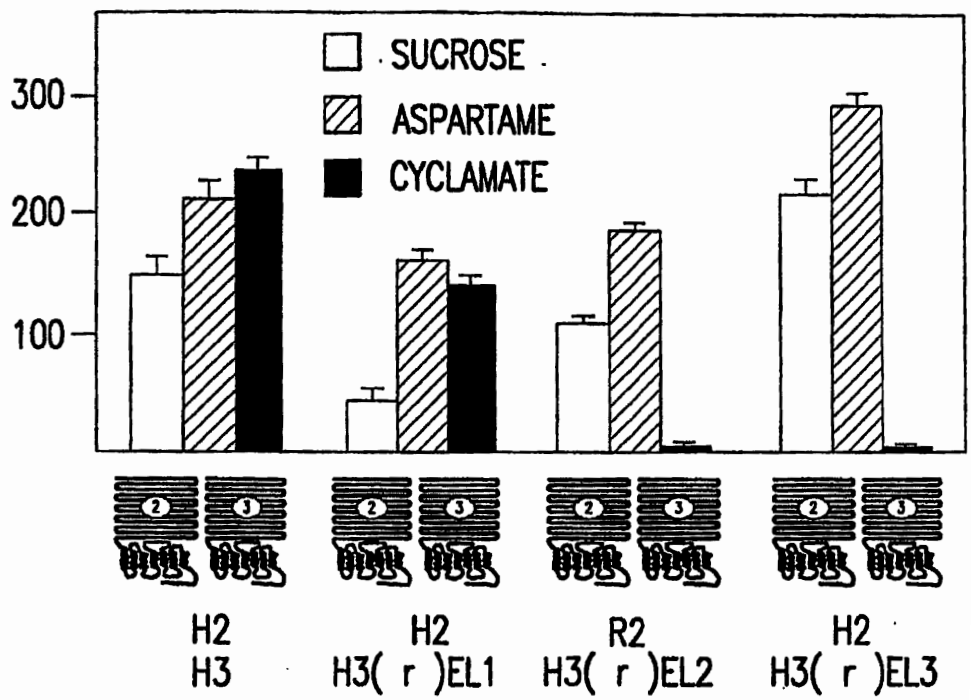

SUCROSE
ASPARTAME
CYCLAMATE
300
200
100
H2
H3
H2
H3(r)EL1
R2
H3(r)EL2
H2
H3(r)EL3

FIG.23D

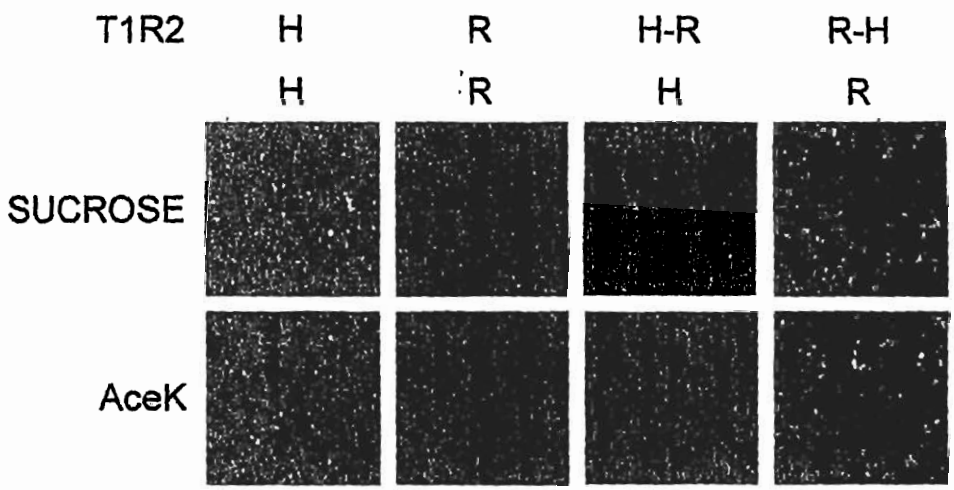


FIG.24A

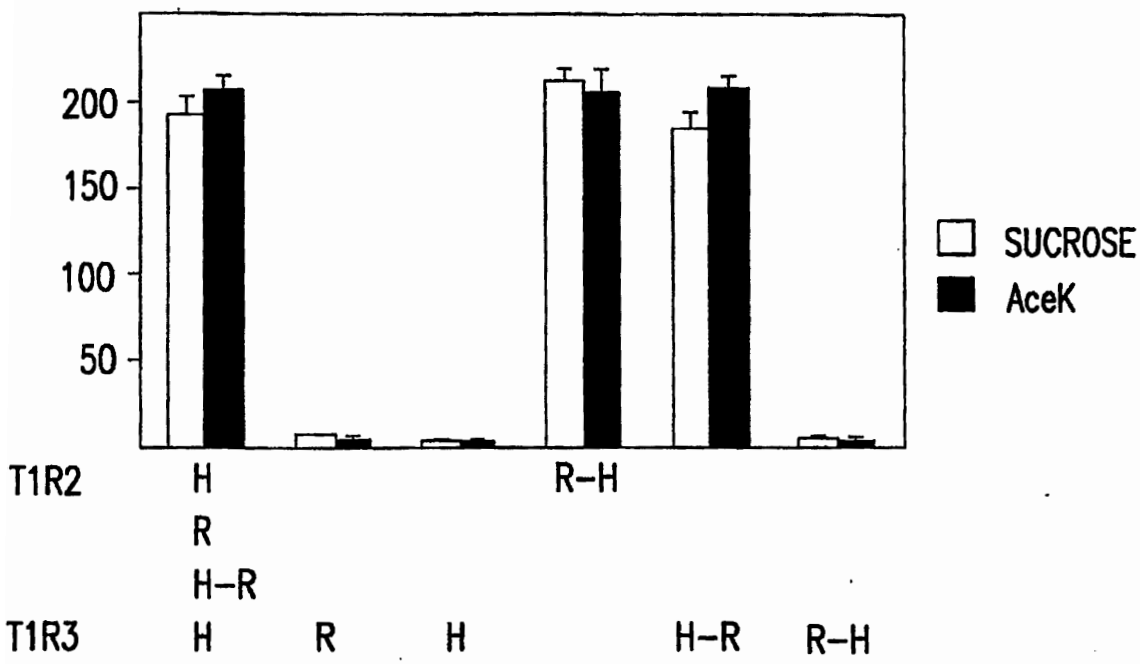


FIG.24B

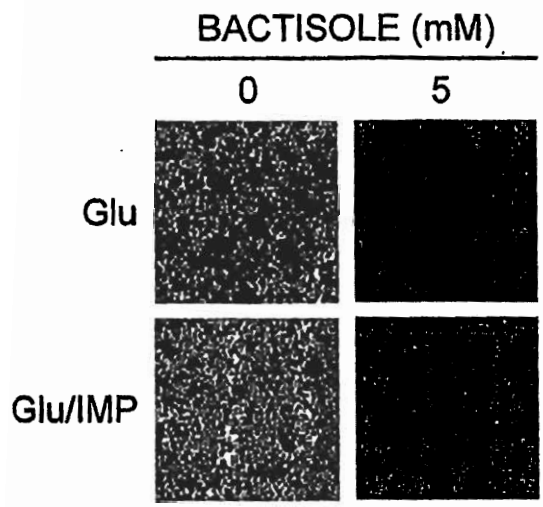


FIG.25A

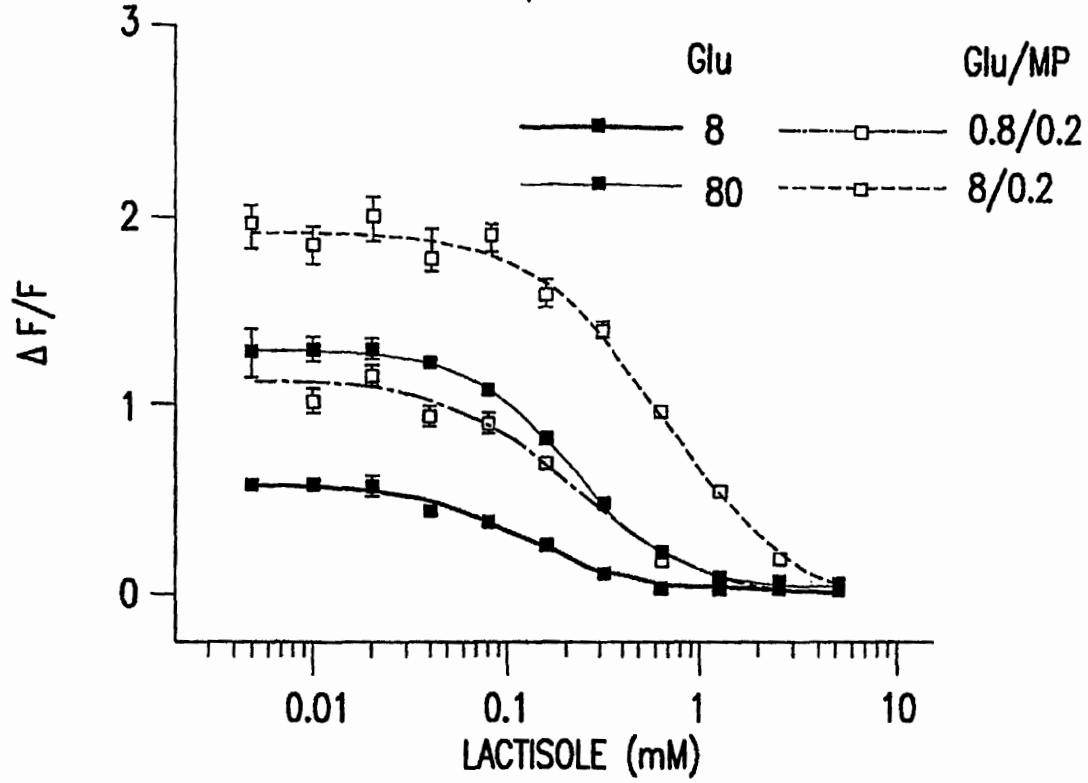
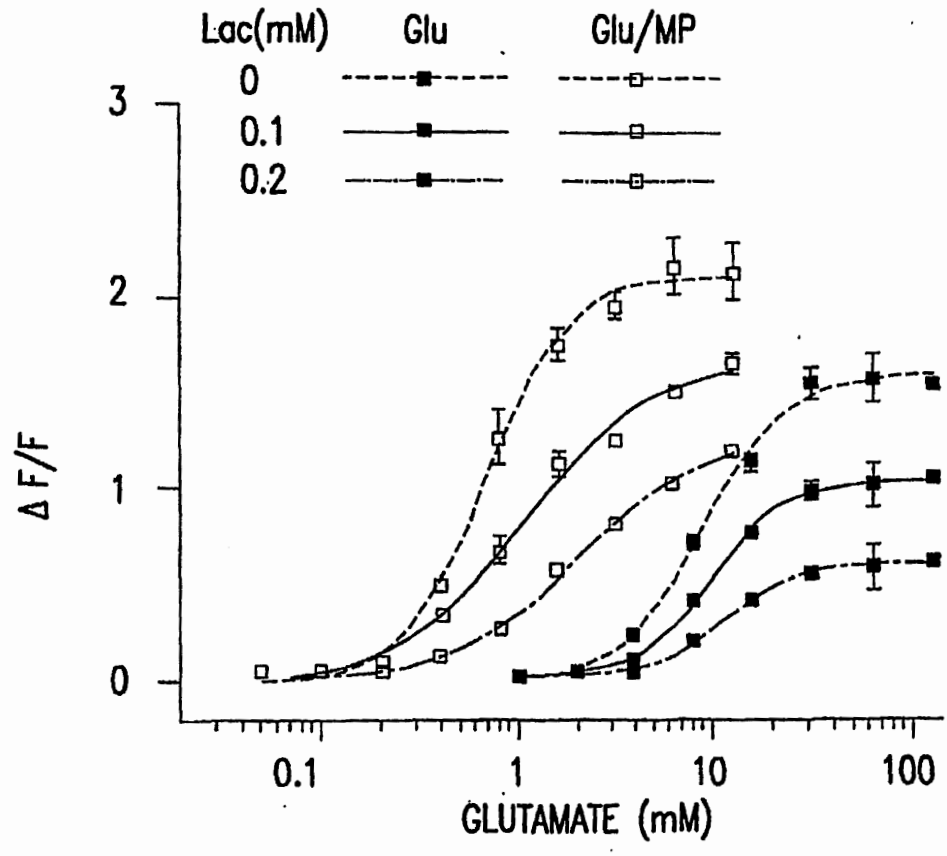

Glu
Glu/MP
8
80
0.8/0.2
8/0.2
ΔF/F
3
2
1
0
0.01
0.1
1
10
LACTISOLE (mM)

FIG.25B


Lac(mM)
Glu
Glu/MP
0
0.1
0.2
ΔF/F
3
2
1
0
0.1
1
10
100
GLUTAMATE (mM)

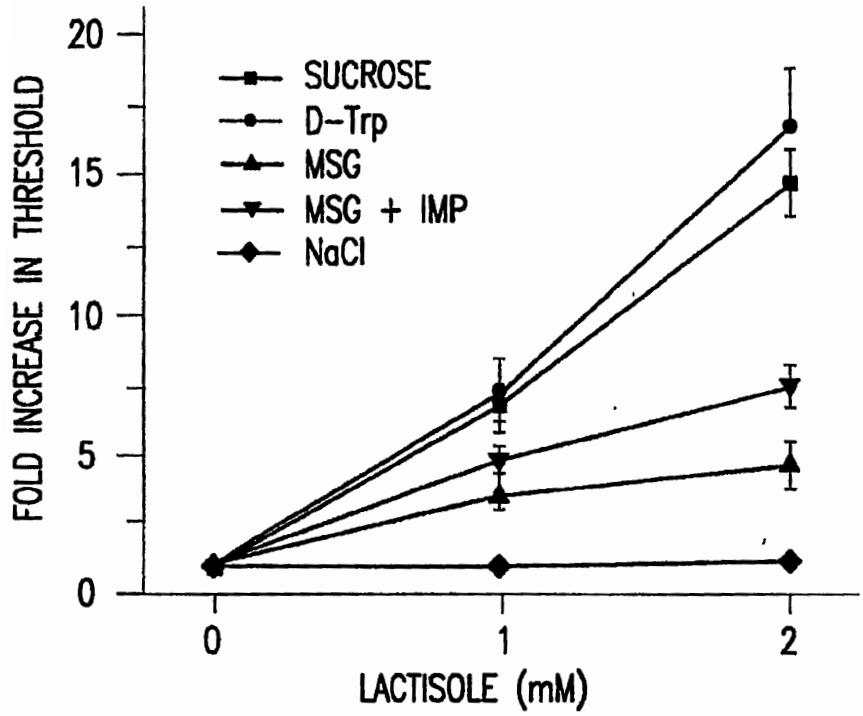


FIG.25D

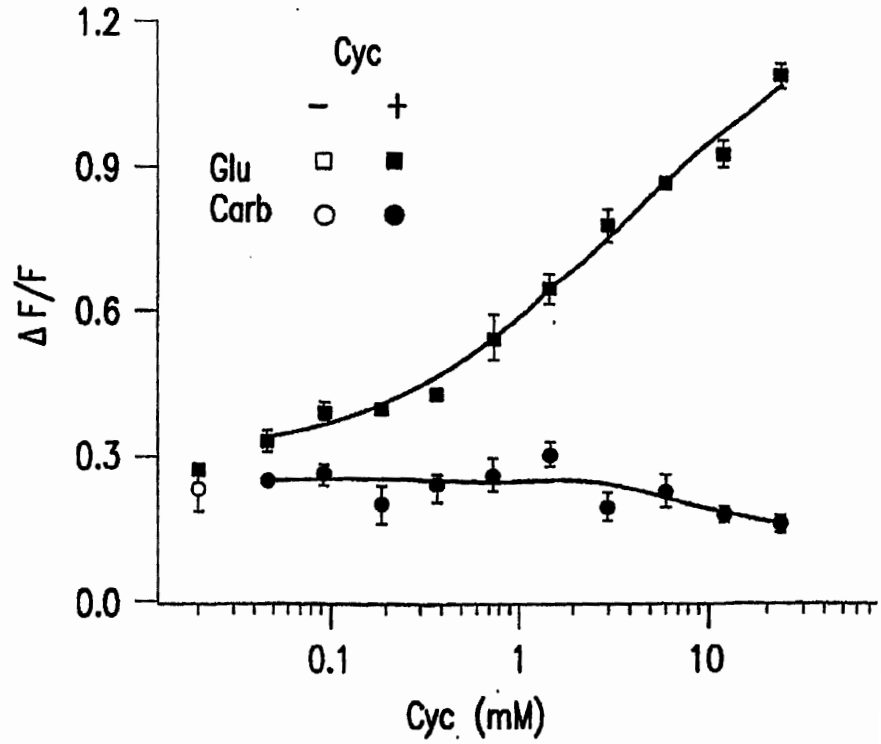


FIG.25E

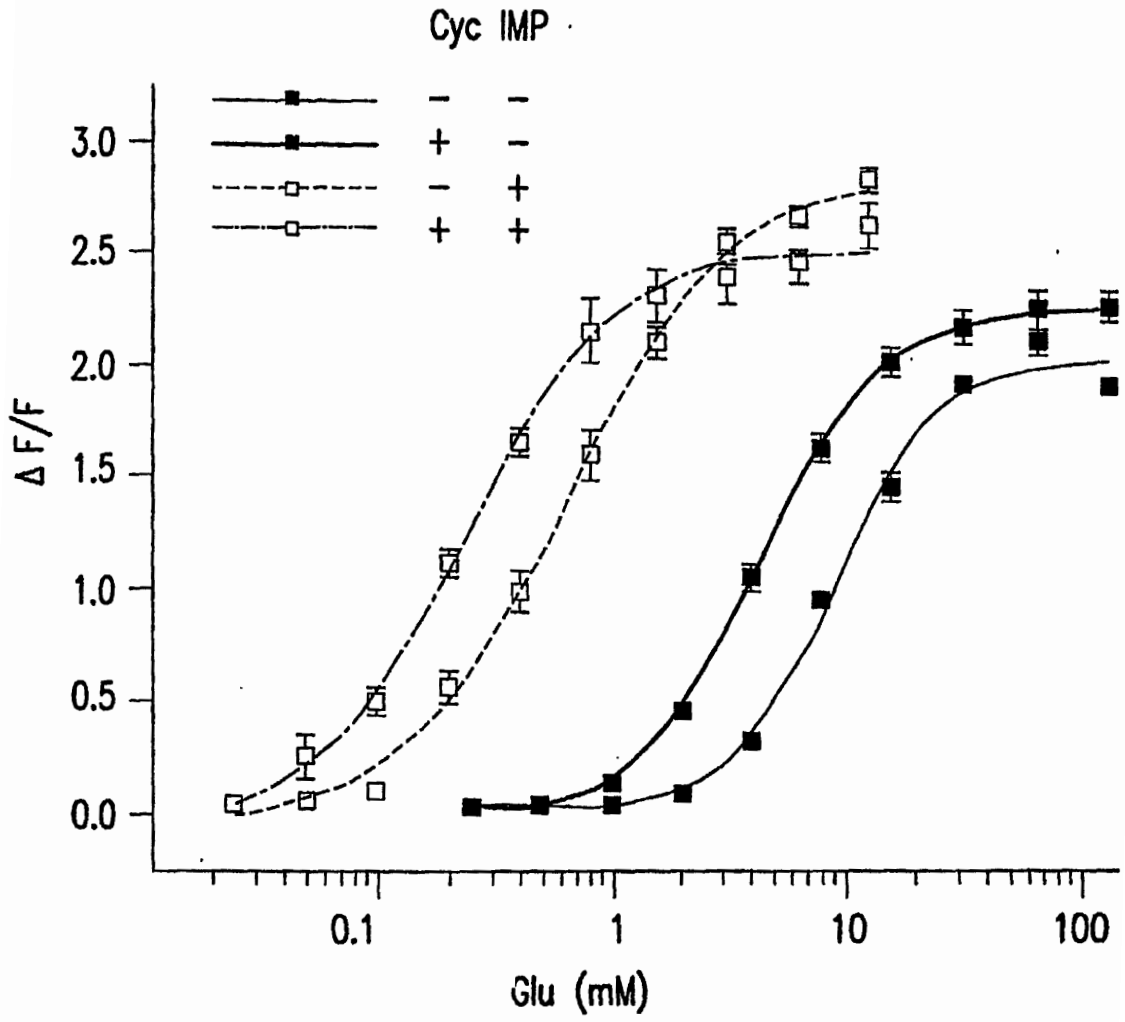


FIG.25F

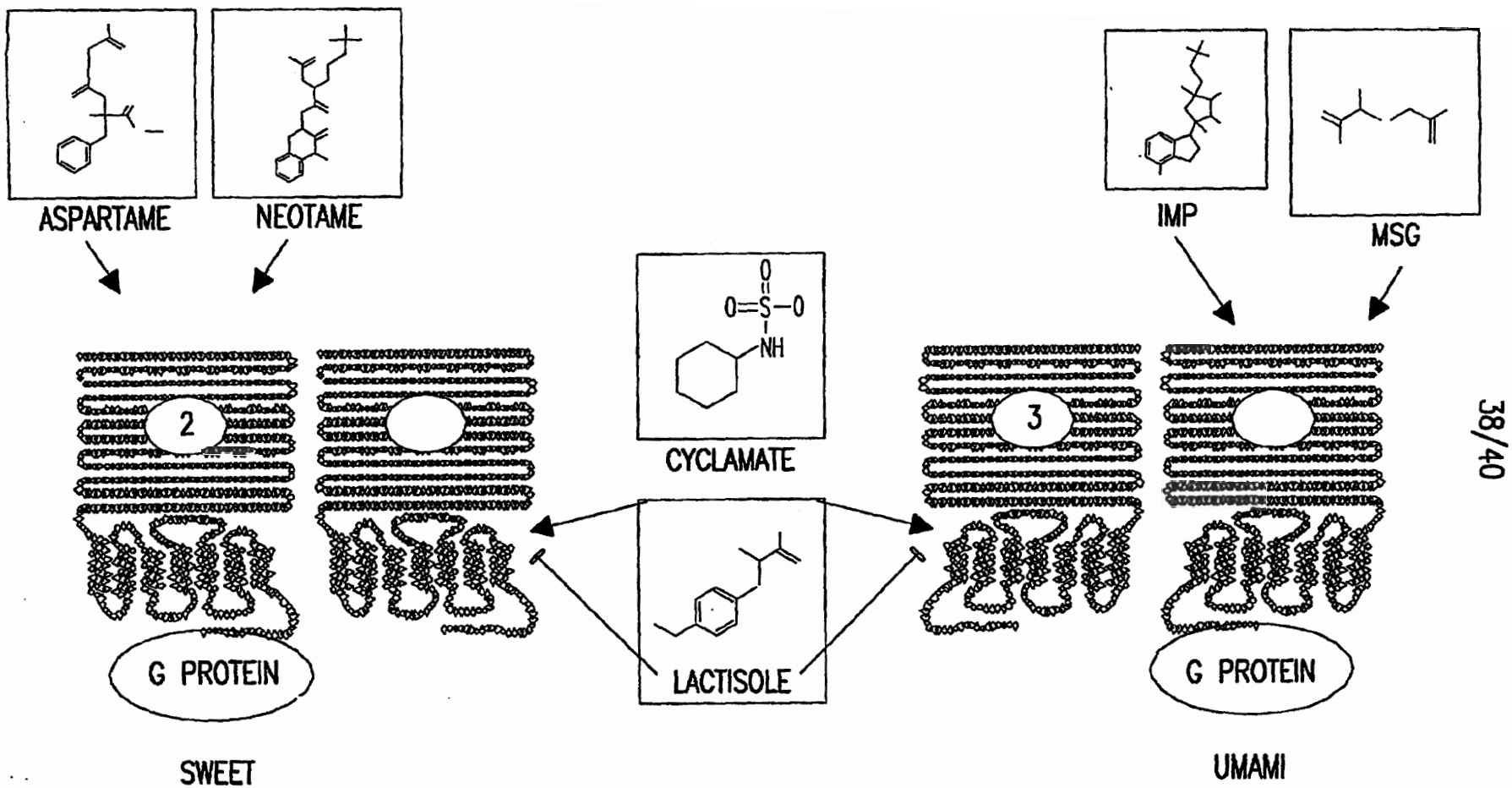

ASPARTAME
NEOTAME
IMP
MSG
CYCLAMATE
LACTISOLE
2
3
G PROTEIN
G PROTEIN
SWEET
UMAMI

FIG.26

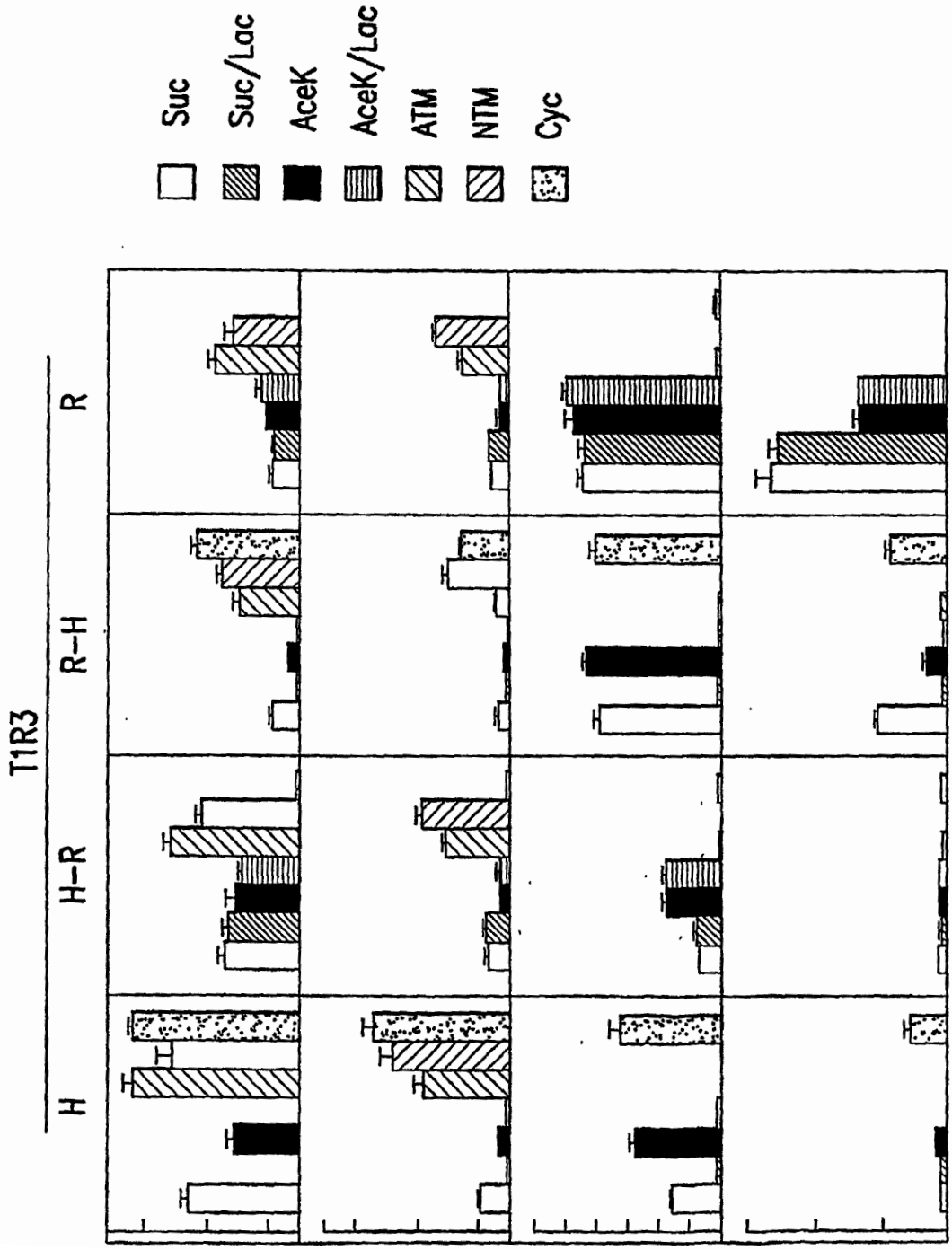


FIG.27A

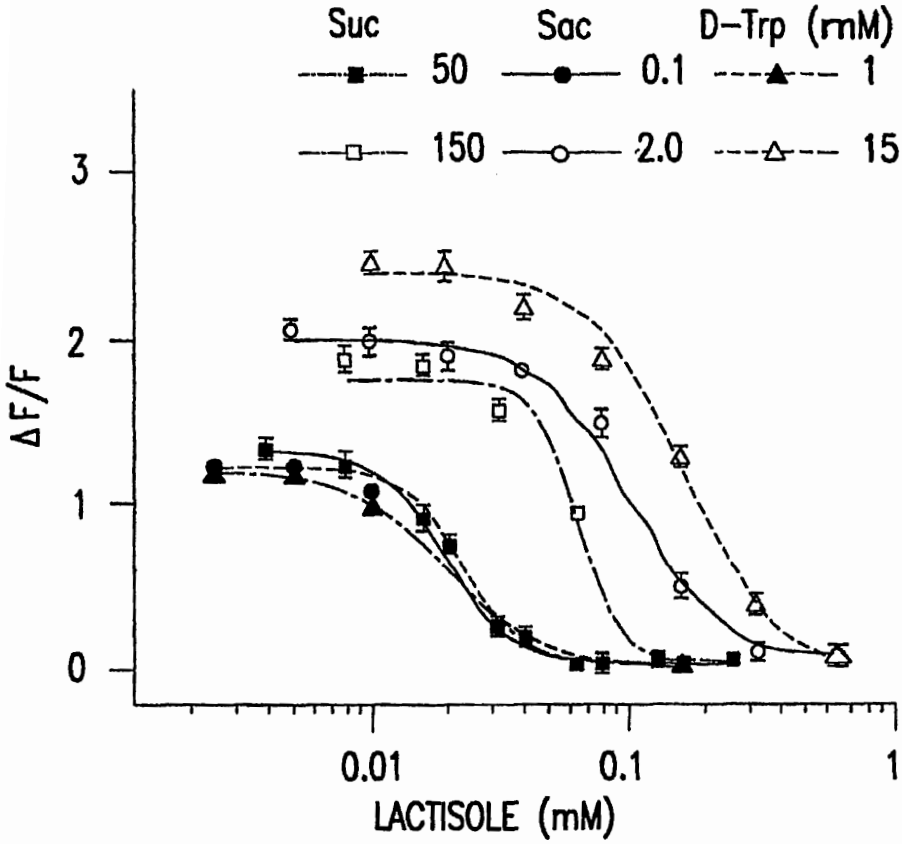
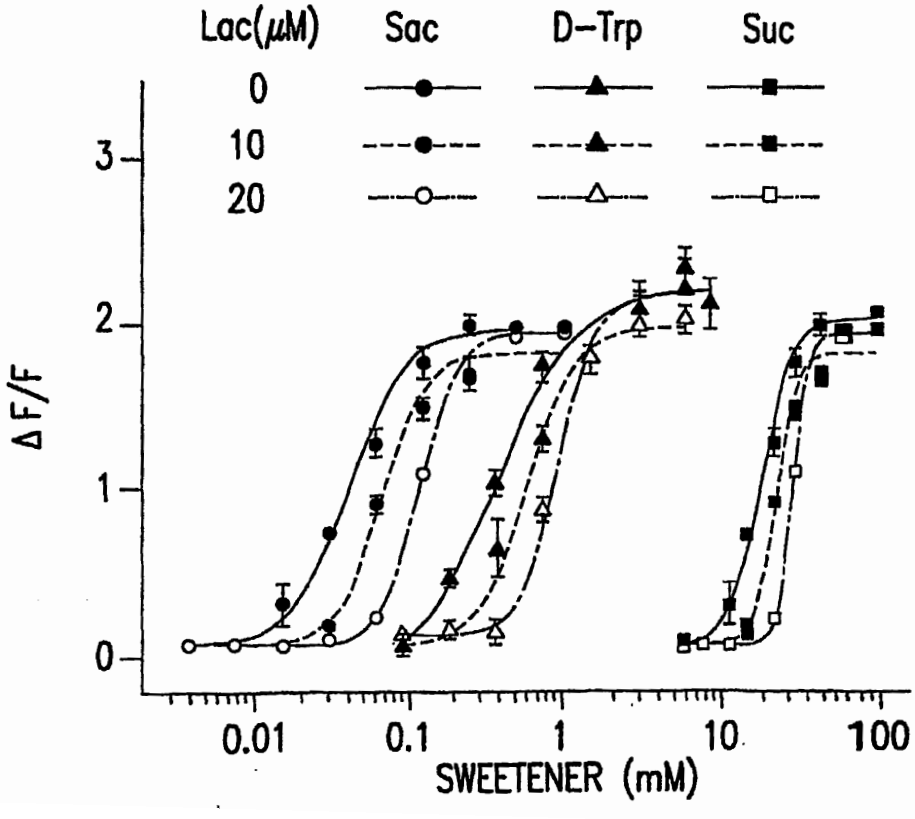

Suc
Sac
D-Trp (mM)
50
0.1
1
150
2.0
15
ΔF/F
3
2
1
0
0.01
0.1
1
LACTISOLE (mM)

FIG.27B


Lac(μM)
Sac
D-Trp
Suc
0
10
20
ΔF/F
3
2
1
0
0.01
0.1
1
10
100
SWEETENER (mM)